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Volume II, Book 1

ECOLOGICAL AND PHYSIOLOGICAL BASES OF SPACE BIOLOGY AND MEDICINE

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Volume II, Book One

ECOLOGICAL AND PHYSIOLOGICAL FOUNDATIONS OF SPACE BIOLOGY AND MEDICINE

CONTENTS

VOLUME II, BOOK ONE

(Chapters 10 through 19 of Volume II may be found in Volume II, Book Two.)

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.

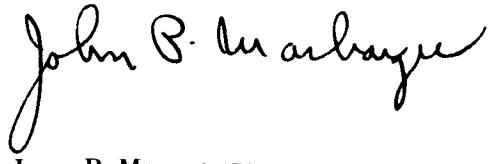
In a rapidly advancing field of study and development, the solution of one problem frequently introduces new and even more chal-

lenging 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 1

INFLUENCE OF AN ARTIFICIAL GASEOUS ATMOSPHERE OF SPACECRAFT AND STATIONS ON THE ORGANISM

Chapter 1

BAROMETRIC PRESSURE AND GAS COMPOSITION[1]

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Normal human vital activity and work capacity under spaceflight conditions are insured by the use of regeneration type pressurized cabins, where an artificial gas atmosphere (AGA) is generated before or during flight, then maintained for the duration of the flight. An AGA environment is vital for humans, animals, and plants during space flight, since AGA protects living organisms against the hostile effects of space, especially against the extremely dangerous effects of low barometric pressure. The artificial atmosphere also serves as a source of oxygen required for respiration.

The use of AGA in spacecraft cabins poses questions that specialists (biologists, physiologists, physicians, and engineers) must answer: What should the AGA be? What physiologic, hygienic, and technical requirements must it satisfy in particular? It is a matter of optimum choice of basic AGA parameters, such as total barometric pressure, its chemical composition: the choice of diluent gases, permissible range of variations in partial pressure of oxygen (P_{O_2}) and of carbon dioxide (P_{CO_2}), temperature, and other parameters.

The solutions of these problems, consequently, of the entire problem of the correct composition of the AGA are possible only if the complex interaction among many physiological and technical factors is taken into account. To summarize, production of a correct AGA is essentially a certain compromise between biomedical and technical approaches to this problem. The former determines the efforts to develop hygienic conditions close to comfortable, which requires consideration of design difficulties, i.e., the need to limit weight and size of the craft, danger of explosion and fire, and probability of various emergency situations arising. Emergencies require that in designing the AGA, it is necessary to examine it and consider possible cabin decompression. Another important design factor is to be sure that (depending on flight mission), astronauts can leave the spacecraft and go into space, or onto the surface of a celestial body around which there is practically no atmosphere (e.g., the Moon), or into extremely rarefied atmosphere (Mars), or very high-density atmosphere (Venus). For such conditions, design of the AGA obviously must take into account structural characteristics (especially pressure level) in space suits, pressurized compartments of transport vehicles, and astronaut's living quarters.

[1] Translation of, Barometricheskoye davleniye, gazovyy sostav, Vol. II, Part 2, Chapter 1, of *Osnovy kosmicheskoy biologii i meditsiny (Foundations of Space Biology and Medicine)*, Academy of Sciences USSR, Moscow, 1973.

Sincere gratitude is expressed with pleasure to Dr. E. M. Roth for his excellent survey of US authors' work: *The Effect on the Organism of an Artificial Gas Environment in Spacecraft and Space Stations*, which was used extensively in preparing this chapter. In effect, Dr. Roth is an ex officio author of this chapter. Considerable indebtedness is also expressed to my colleagues, A. G. Dianov and V. P. Nikolayev, who prepared a survey of papers by Soviet investigators dealing with AGA.

This chapter deals with the biomedical problems in designing an AGA for spacecraft cabins. The main emphasis is on the organism's reactions when barometric pressure falls, and changes in the AGA's chemical composition: decrease and increase in P_{O_2} and P_{CO_2}, total exclusion of nitrogen and inert gases from the AGA, or—use of several inert gases as "diluents" in the AGA instead of nitrogen.

Examination has not been made of such important AGA parameters as temperature, humidity, permissible concentrations of harmful impurities, and the aerosol's composition and electrical charge. These data are presented in other chapters.

BAROMETRIC PRESSURE

Spaceflight experience indicates that the level of barometric pressure in manned spacecraft cabins can vary as a function of their design characteristics within wide limits: from 1–1.2 atm in the Soviet Vostok, Voskhod, and Soyuz spacecraft to 258 mm Hg in US spacecraft Mercury, Gemini, and Apollo.

To estimate barometric pressure, one of the vital parameters characterizing the AGA during normal spacecraft operation and under emergency conditions, it is necessary to bear in mind that this parameter is closely linked to others, especially P_{O_2}. This can be seen in Figure 1, where three zones of P_{O_2} values determine the different levels of O_2 supply to the organism. Zone 1 corresponds to various degrees of hypoxia; Zone 2 is indifferent, where provision of the organism with O_2 remains at a normal or near-normal level; and Zone 3 is the zone of elevated P_{O_2}, which is intolerable due to toxic effects of oxygen, which develop the more rapidly, the higher the P_{O_2}.

The physiologic effects of reduced and elevated partial pressure of oxygen in the AGA will receive special attention in subsequent parts of this chapter. Normal oxygen supply to the organism is possible when the barometric pressure drops only to 190–200 mm Hg. (This is shown in Fig. 1 and Table 7.) Therefore, pressure P of the AGA in the cabin must not fall below these values.

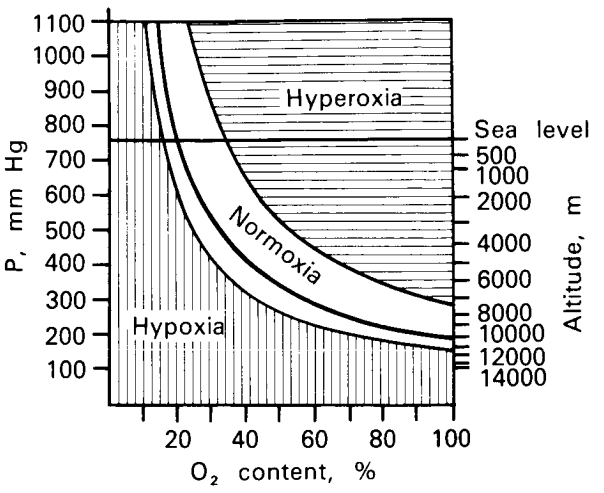

FIGURE 1.—P_{O_2} of the AGA as a function of barometric pressure. Three zones of oxygen supply: hypoxia, normoxia, and hyperoxia.

The oxygen supply is not the sole limiting factor, since when the barometric pressure falls considerably, even when the chemical composition of the AGA ensures normal oxygen supply to the organism, it is necessary to take into account the possibility of onset of dysbarism.

Various phenomena of dysbarism are manifested as functions of physical parameters which characterize the differential in barometric pressure: the absolute value of pressure differential ΔP, determined by the difference between the initial pressure (P_i) and final pressure (P_f)—($\Delta P = P_i - P_f$); the differential factor, which is determined by the ratio between the initial pressure and the final pressure (P_i/P_f), and the time of decompression (t), as well as the decompression rate ($\Delta P/t$).

There are three causes for onset of various dysbarism phenomena:

1. Elevated pressure in body cavities containing gas caused by difficulty in balancing pressures in body cavities with pressure on its surface (various effects of explosive decompression, altitude meteorism, aerootitis, and aerosinusitis).
2. Formation in tissues of gas bubbles formerly in a dissolved state—altitude decompression sickness (ADS).

3. Development in tissues of vaporization phenomena (ebulism, "boiling" of tissues, and altitude tissue emphysema).

There is varying probability of onset of these dysbarism phenomena during space flight. There is little probability of astronauts being exposed to explosive decompression resulting from a sizable defect forming in the cabin wall. However, it will increase as flight time increased. The probability of altitude decompression sickness is much greater.

EXPLOSIVE DECOMPRESSION (ED)

Explosive decompression, which develops from instantaneous depressurization of the cabin, is characterized by rapid and considerable pressure drop in the cabin. There has been no generally accepted definition of the concept of ED so far. Numerous authors [9, 69, 200] have attempted to give quantitative physical criteria for delimiting ED from ordinary dehermetization, which have not been accepted. Accordingly, and considering that onset of overpressure in the lungs is the most significant ED effect, we propose to define as ED all cases of rapid pressure drop in a hermetically sealed cabin during which a substantial overpressure in the lungs can arise of more than 20–30 mm Hg.

There is little probability of onset of ED during flight (it is usually associated with danger from a meteor). However, taking into account that during ED the crew may be subjected to trauma from fragments of the cabin wall, the mechanical action of the stream of gas flowing out from the cabin, and subsequent exposure to extremely low pressure, ED plays a small role in such a tragic situation. Regardless of this, ED must not be ignored when developing and evaluating the AGA, since its harmful effect depends largely on the AGA pressure level, and to a far lesser extent on its gas composition. Cabin volume (V), area of the opening—size of the defect (A), and pressure differential (ΔP) determine time (t_c) and *force* of the ED. Time (t_c) during which the ED occurs in the cabin can be represented at $t_c = V/(A \cdot c)$, where c is the speed of sound (Fig. 2).

The reaction of the organism during ED is a function of its three main parameters:

1. absolute value of the pressure differential ΔP, equal to the difference between the initial pressure P_i and the final pressure P_f in the cabin ($\Delta P = P_i - P_f$);
2. pressure differential—ratio of initial pressure to final pressure: P_i/P_f; and
3. time of decompression—t.

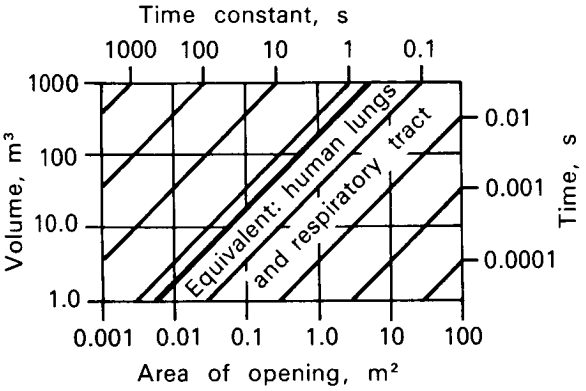

FIGURE 2.—Time characteristics of decompression. (After [126])

During space flight, as a rule, ED will occur under extremely low pressure of the external environment. Thus, evaluation of the harmful effect of ED will place particular emphasis on the P_i of the cabin, also the time of decompression which is a function of cabin volume V and the size of defect A.

A definite role in the reaction of the organism during ED is also played by gas volume in the lungs (V_l), that is, the phase of respiration where the ED action and resistance to airflow along the respiratory tracts coincide. Increases in air volume and in its resistance to flow through the respiratory tracts are factors which aggravate the action of ED.

During explosive decompression, there are rapid increases in the gas volume enclosed in the organs and parts of the body which have cavities filled with gas (lungs, gastrointestinal tract, middle ear, and accessory sinuses of the nose). Since the equilibration of pressure in these cavities, which are connected with the gaseous medium surrounding the organism by passageways of relatively small lumen, is delayed, pressure in them will rise for a certain period.

This leads to distention of tissues which may cause injury—rupture. Animal experiments have indicated that lung damage (development of hemorrhages as a result of distention and rupture of alveoli and vessels) is the most dangerous manifestation of ED [17, 21, 28, 92, 104, 107, 162, 175, 193]. When lungs are subjected to significant trauma, shock and gas embolism of the vessels have been noted, which can lead to death of the experimental animals [104, 107, 128, 162, 192, 193, 196].

To evaluate the harmful effect of ED, it is important to know the overpressure in the lungs (ΔP_l) which can lead to rupture of the alveoli. Since this factor is not known for the lungs of a healthy human, it was decided to use data from animal experiments, but these data are scanty and quite contradictory. Most authors [116, 174, 193, 200], based on the work of Adams and Polak [1], and Benzinger [27], state that at $\Delta P_l = 80$ mm Hg, when there is no protective stress on the stomach and chest muscles (limiting the distention of the lungs), lung injury is quite possible. Several authors give a lower value of 50 mm Hg [67, 170].

Determining the overpressure in the lungs ΔP_l in cases of ED is apparently of exceptional value in evaluating its possible damaging effect on the body. Accordingly, efforts were made to calculate ΔP_l as a function of conditions characterizing ED. In evaluating these studies, it must be kept in mind that when calculating ΔP_l, all authors assumed that the lungs expand uniformly.

To find ΔP_l is relatively simple when ED is acting on an individual with a closed rima glottidis. During passive expansion of the thoracic cavity walls, it can be determined, according to Luft [125], from the following relation:

$$\Delta P_l = \left[\frac{V_i}{V_{max}}(P_i - 47)\right] + 47 - P_f \qquad (1)$$

where V_i is the volume of lungs before ED
V_{max} is the maximum volume of undamaged lungs
P_i is cabin pressure before ED
P_f is final pressure in the environment.

Since the volume of the lungs V_i affects the value of ΔP_l during ED, it was decided to determine ΔP_l for three different V_i: under conditions of total inspiration, when $V_i/V_{max} = 1.0$; at the end of a normal expiration, when $V_i/V_{max} = 0.55$ and with complete expiration, when $V_i/V_{max} = 0.25$ [42]. This expression derived from the Boyle-Mariotte law includes a correction for P_{H_2O} at body temperature.

By using the above equality, it is possible to calculate the overpressure in the lungs during ED for various values of initial pressure (P_i) in the cabin and different volumes of the lungs.

The data in Table 1 show that the level of ΔP_l for astronauts with the rima glottidis closed will exceed the value which is critical for the lungs (80 mm Hg) at all possible levels of initial cabin pressure. Under conditions of ED, when gas escapes from the lungs, the levels of overpressure in the lungs will be less than shown in Table 1. Then the probability of harm to the lungs should be minor while maintaining the cabin pressure at a level of the order of 268–191 mm Hg.

The dynamics of ΔP_l during ED are illustrated in Figure 3 by graphs obtained experimentally by Luft [125]. Violette, in a fundamental monograph [200] dealing with the effect of ED on the living organism, had presented another expression for the calculation of ΔP_l; in contrast with Luft, he attempted to take into account the escape of gas from the lungs. He proposed an equation for the determination of ΔP_l:

$$\Delta P_l = P_c - P_f \cdot ch\, K_c \frac{S}{V}\sqrt{\frac{P_f}{\rho_f}}\,(t_0 - t) \qquad (2)$$

where P_c is cabin pressure
P_f is final pressure of environment
K_c is experimental equivalent of coefficient of flow compression
S/V is the coefficient of gas escape from the cabin
ρ_f is the final gas density
t is elapsing time.
t_o is time of decompression

This expression, derived in the mathematical treatment of experimental results, does not take into account changes in the lungs during decompression and considers air escape from the lungs as occurring from a rigid vessel with constant cross-sectional opening.

TABLE 1.—*Dependence of* ΔP_l *during ED on Pressure of AGA in Cabin (with closed rima glottidis)*

$\frac{V_i}{V_{max}}$	ΔP_l when $P_i=760$ mm Hg	ΔP_l when $P_i=362$ mm Hg	ΔP_l when $P_i=268$ mm Hg	ΔP_l when $P_i=191$ mm Hg
1.0	760 mm Hg	362 mm Hg	268 mm Hg	191 mm Hg
0.55	439 mm Hg	220 mm Hg	169 mm Hg	121 mm Hg
0.25	225 mm Hg	126 mm Hg	102 mm Hg	83 mm Hg

Thus, the expressions presented in the works of Violette, Luft, and others for calculating ΔP_l reflect one-sided processes occurring in the lungs during ED. This situation comes about from these expressions either not taking note of lung expansion during decompression (Violette), or not taking into account air escape from the lungs (Luft).

In a study by Burger [41], an effort was made to take into account—when calculating ΔP_l—both factors (lung expansion and simultaneous escape of air from the lungs). Based on a series of model experiments and investigations using animals, Burger was able to calculate ΔP_l under certain conditions. The theoretical basis of this work was the general theory of ED developed by Haber and Clement.

Burger elaborated on Haber and Clement's theoretical concepts and proposed a fairly simple expression for calculating maximum overpressure in the lungs during ED:

$$\Delta P_l=\left\{(P_i-47)\frac{V_i}{V_{\max}}+47-P_f\right\}\left[1-\frac{t_{cc}}{l_c}\right] \quad (3)$$

The structure of this expression denotes that its first term is the expression used by Luft to calculate ΔP_l where ED is with closed rima glottidis without gas escape from the lungs. The second term $(1-t_{cc}/l_c)$ is the original expression obtained by Burger which determines gas escape from the lungs during ED. The ratio t_{cc}/l_c is a dimensionless factor that takes into account the difference in rates of decompression of the cabin t_{cc} and of the lungs l_c.

The expression proposed by Burger for calculating the maximum value of ΔP_l was derived with the author's assumption that ΔP_l, maximum value, arises at the instant when the cabin pressure is equalized with the ambient pressure. The latter assumption is not always valid, since for small values of P_f, the maximum overpressure in the lungs can arise before the cabin pressure is equalized with the ambient pressure. Further, the formula proposed by Burger has a limited range of application since when $t_{cc}=l_c$, it approaches zero, while actually under these conditions, ΔP_l can reach substantial values, which was indicated by Burger. Comparison of experimental data with calculated data obtained by the authors using the formula presented yielded fairly good agreement.

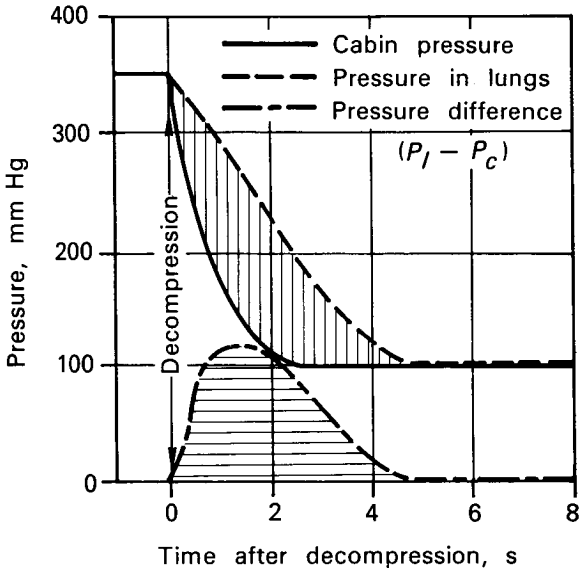

FIGURE 3.—Dynamics of overpressure in lungs during ED. (After [125])

Animal Experiments

The results of experimental investigations on animals permit evaluation, although approximated, of the hazard of ED as a function of its physical parameters.

In experiments with rats, Kolder [108] established that death of 10% of the animals when exposed to ED with ΔP_l of 662 mm Hg and a multiple P_i/P_f of the order of 10, was noted only when the ratio V/A reached 3.3 m^3/m^2. When $V/A = 1.2$ m^3/m^2, 50% of the animals died; when $V/A = 0.12$ m^3/m^2, 100% died. Protecting the lungs from distention by bandaging the trunk significantly protected the animals from the damaging effects of ED [193]. According to data [193, 200], hemorrhages in the lungs were noted only when their volume with regard to the volume in normal inspiration increased by 2.3 to 2.5 times; when the volume of the lungs was increased three times or more, a great number of pulmonary lesions were observed. Studies [128, 162], showed the possibility of reducing damaging action of ED by administering pharmacologic preparations to the animals: atropine and anesthetics. These data indicate the role of reflexive mechanisms in the genesis of grave pathologic states during ED.

Thus, considerable distention of the lungs—which also is probably nonuniform because of the features of regional ventilation—leading to their trauma, determines mainly the damaging action of ED on the organism. The damaging effect of ED when embolism arises can also depend on the gas composition of the AGA. Thus, O_2 embolism (for an AGA composition that includes mainly O_2) must occur, due to the high biological activity of O_2, more readily than embolism with He and N_2 bubbles. According to Gramenitskiy [81], He embolism—because of the more rapid desaturation of this gas—occurs more readily than N_2 embolism.

The composition of the AGA during ED must also affect the curve of the pressure differential in the cabin and the rate of gases escaping from the lungs and, therefore, the overpressure in the lungs ΔP_l. However, this effect evidently is not significant, especially if the pressure in the cabin is held at a level of the order of 0.5 atm or below. Thus, according to Waterspoon, Wibers, and Stand [170], no difference was noted in the damaging action of ED on rats with an AGA where the N_2 in air was replaced with He.

A generalization of results of experiments with animals subjected to ED action at different levels and durations enabled Violette [200] to postulate on dangerous and safe zones of ED action. He established, with a certain degree of approximation, the dangerous and safe zones of actions of ED as a function of the differential factor ($F_p = P_i/P_f$) and the coefficient of leakage $F = A/V$; that is, the ratio between the area of the opening through which gas escapes from the cabin to the volume of the cabin [200] (Fig. 4).

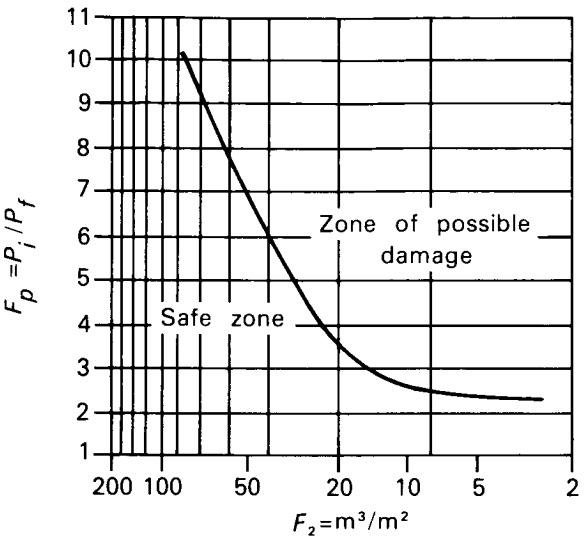

FIGURE 4.—Characteristics of dangerous action of ED. (After [200])

The opinion of Fryer [66] invites agreement—that the curve in Figure 4 divides two zones: the first, which must be considered absolutely safe, and the second, which has been insufficiently studied and a part of which unquestionably poses definite danger. In evaluating the curve in Figure 4, it can be concluded that whenever the ratio is $P_i/P_f < 2.3$, that is, when the volume of the lungs increases by less than 2.3 times, ED will not cause damage to the lungs. The same situation arises at some rate of decompression when the coefficient of leakage A/V does not exceed 1/100 m^2/m^3. The pressure in the lungs will be capable in part of striking a balance with the ambient pressure and will not exceed the critical level. Accordingly, it is extremely important to establish the "law" of gas escape from human lungs during ED.

Stresses During ED

In a significant study by Luft and Bancroft [126], the authors used an esophageal probe with a rheostatic sensor to record the intrapleural pressure in subjects during ED. They showed that the intrapleural pressure in man increases with an increase in both the differential factor P_i/P_f and in the absolute decompression value ΔP. It was established that the time characteristics of the lungs and respiratory tracts in subjects who had been subjected to ED at the end of expiration are equivalent to decompression of the cabin with an A/V ratio equal to 1/200 m^2/m^3. These data are in full agreement with the results of the Hitchcock studies; he found no injury in persons subjected to high-value ED for 1 s. In the studies of Kuznetsov, Zharov et al, no harm was found for ED times of 0.5 s and ΔP values of 300 to 400 mm Hg [92, 116, 214].

Studies with human subjects thus far have shown only isolated cases of lung damage [27, 42], which occurred only when the subjects' rima glottidis was closed at the time of ED.

ED always exerts a definite influence on the general state and work capacity of man, even when there is no damage to the lungs or other tissues. At the moment of ED, the subject feels a blow in the chest region and forceful expulsion of air from the lungs—there is, so to speak, a powerful and deep expiration. It disturbs the normal structure of respiration, quite substantially, when the ED coincides with the inspiration [42, 116]. Those subjects especially who are subjected to instantaneous exposure to ED for the first time cease carrying out their routine work and do not respond to conditioned signals. This period of "confusion" usually lasts 3–5 s, it is much shorter in individuals who have been subjected repeatedly to ED.

ED leads emotional stress, with increased heart rate and corresponding motor reactions. Subjects do not notice temperature drops, but the appearance of a "fog" in the cabin caused by water vapor condensation may cause them to believe (erroneously) that fire has broken out. Accordingly, it has been suggested that spacecrews be familiarized (by showing movies) with the situation that occurs under ED conditions. In anticipated long-term interplanetary flights, when the flight path will pass through regions with a high density of meteoric matter, the readiness of the crew may be questionable for flight in a cabin that has been depressurized because of an ED. This necessitates working out a mode for crewmembers to remain in their space suits. Conditions must also be provided to enable astronauts to begin effective exploitation of individual means of protection before manifestation of severe hypoxic disturbances of the central nervous system (CNS), that is, only 5–8 s after the ED.

INTESTINAL GAS EXPANSION AND OTHER MANIFESTATIONS OF DYSBARISM

ED may have a harmful effect on the gastrointestinal tract, which also contains gas. Studies with humans have shown that during an ED lasting 0.5–1.0 s with ascents to altitudes of 9000–10 000 m or more, just as in slower ascents to these altitudes (30–60 s) similar complaints from subjects are sometimes noted concerning unpleasant or painful sensations in the stomach region. The onset of these sensations is linked to the development of expansion of trapped gases and (indicated by x-rays) is essentially a function of the quantity of intestinal gas as well as its location and conditions of escape from the intestine. Hence, to prevent trapped gas expansion which, as a result of visceral reflex influences, can lead to disruption of cardiovascular system activity (extrasystole, bradycardia, and collapse), astronauts must be supplied with a diet that excludes foodstuffs that form gas in the gastrointestinal tract.

Grave pathologic states resulting from expansion of trapped gas are relatively infrequent. According to data generalized by Berry (cited in [25]), of 4259 cases when abdominal pain developed during ascents to high altitudes, extremely severe (fourth degree) functional disorders were observed in only 12 people. Development of these severe phenomena requires a differential diagnosis, since they can be caused not only by expansion of trapped gas, but also by the altitude decompression sickness. In either

event, assistance to the victim requires, first of all, transferring him as rapidly as possible to a gaseous medium with normal barometric pressure.

ALTITUDE DECOMPRESSION SICKNESS (ADS)

During space flights or while preparing for them, the transition of astronauts to an AGA with low barometric pressure can be the cause of their developing ADS.

ADS results, as a rule, from emergency situations (depressurizing the cabin and the use of space suits at low pressure). In some instances, it can arise from poorly planned conditions for the transitions of astronauts from one spacecraft into another. Such a situation could occur during transition of cosmonauts from an "air" AGA with gas pressure of 760 mm Hg in the cabin of the Soyuz craft to the hypobaric (pressure of 258 mm Hg) oxygen medium of the Apollo spacecraft cabin.

To prevent ADS in the joint Soviet-American space flight, it is planned to lower the barometric pressure in the cabin of the Soyuz craft to 550 mm Hg with a simultaneous rise in the O_2 content in the AGA.

ADS, like caisson disease, develops from gas bubbles in body tissues [83, 91]. The etiologic similarity of these two disorders also accounts for the considerable clinical similarity. Several authors use the term "decompression disturbances" instead of ADS, since they feel that ADS symptoms most often manifested—pain in the joints and muscles—are not caused by development of the sickness, which they link only to onset of relatively stable morphologic changes [80].

Formation and Growth of Bubbles

When the pressure of the gas medium surrounding the organism drops, blood and tissues become supersaturated with gases. Any supersaturated system is metastable, which determines the possibility of gas bubbles forming in it. According to Harvey [86] and others [62, 70, 153], gas bubbles originate from gas nuclei which are constantly being formed in the organism in the course of its vital activity. Gas nuclei arise in the blood at points where blood vessels branch, where there is pronounced turbulence of the blood [70, 86], or in muscle tissue during muscular contraction as a result of local decrease in hydrostatic pressure [51, 70]. During sudden movements in overexpanded portions of muscle tissue or fluid, the hydrostatic pressure becomes negative. The level of the negative pressure peak can periodically reach 100 atm or more [51, 70, 86]. During these brief intervals, the overexpanded portions of the tissue or fluid become supersaturated with gases. A cavity forms in it, into which vapors of the fluid initially try to penetrate due to "local" boiling, after which gas molecules diffuse. After the original pressure is restored the cavity contracts, but the trace of the space is retained in the fluid. The formation of gas nuclei and bubbles that have already formed are retained for long periods on lyophobic surfaces.

From these data, it can be concluded that the existence of gas nuclei is an essential factor in the formation of free gas bubbles in the tissues of the organism under conditions of reduced barometric pressure. It has, in fact, been demonstrated experimentally that conditions which exist for the formation of gas nuclei in the organism are extremely limited. For example, in ground squirrels that are hibernating, after they have been taken to high altitudes, regardless of considerable supersaturation of tissues with the gases dissolved therein, no gas bubbles are formed [70]. Gas bubbles are not formed in living tissues when gas nuclei have been dissolved prior to ascending to high altitudes, for example, as the result of action of extremely high pressure. This has been demonstrated by experiments on shrimps [62].

In experiments with biologic fluids and tissues, Harvey, the US biophysicist, determined that plasma, whole blood, and intact tissues which contain no gas nuclei remain free from gas bubbles even with great pressure differentials (from 1000 to 1 atm) [86]. This is explained by the fact that the formation of a gas bubble, which is free to grow for quite a time, is possible only when its initial size exceeds critical dimensions, that is,

$$R > \frac{2b}{P_b - H} \quad (4)$$

where R is the radius of the bubble (cm),

P_b is the pressure inside a gas bubble, which is the sum of the partial pressure of the gases and water vapor contained in the bubble (dyn/cm^2),

H is the hydrostatic pressure of the fluid, which in a majority of cases is practically equal to the external pressure in (dyn/cm^2),

b is the coefficient of surface tension at the interface between the bubble and the surrounding medium (dyn/cm).

Likewise, a gas bubble with a tendency toward further growth can form only if P_b at the focus of formation is extremely high, which can occur with sudden local supersaturation of the fluid with gases and vapors (freezing, superheating, and electrolysis), considerable extension of the fluid over a small area, that is, a decrease in the value H to negative values (cavitation and local stress). Formation of a gas nucleus with supercritical dimensions can be facilitated also if its surface is formed at points of contact between lyophobic surfaces and the fluid. Then the radius of curvature of the bubble can be large, while it will have a comparatively small volume. For a certain shape of a lyophobic surface, it is easy to imagine the situation (for example, in the formation of a gas nucleus in a conical depression, or in a crack between two lyophobic surfaces) when the capillary forces will not prevent, but will promote, the formation of a gas bubble [70, 152].

Hence, for gas bubbles to form in the organism, it is not sufficient for the tissues to be supersaturated with gases. Certain additional factors are required capable of disrupting the metastable state of the supersaturated solution. In the course of vital activity, especially during active muscular exertion, these additional conditions apparently arise constantly in the human organism. However, they are manifested to different degrees in different individuals and even in the same individual, as a function of many circumstances. This is largely responsible for homogeneity lacking in individual resistance to ADS and its considerable variation in the same individual.

The formation of gas bubbles in the human body is not always accompanied by onset of altitude decompression sickness. In the human and animal organism, following ascent to altitudes, x-ray and ultrasonic methods have frequently made it possible to detect gas bubbles without any manifestation of altitude decompression sickness. With special "traps" inserted into various parts of the circulatory bed of animals, Gramenitskiy [81] succeeded in detecting gas bubbles at altitudes of the order of 4000 m, when ADS does not yet arise. Unfortunately, the factors which determine transition from the latent forms of decompression disorders to the manifestation of altitude decompression sickness still remain insufficiently studied. An investigation of gas bubbles interacting with tissue structures of the organism should promote better understanding of the pathophysiologic mechanisms governing the manifestation of various symptoms of decompression sickness. This will aid in explaining questions about the immediate reason for development of various forms of ADS.

Characteristics of Evolution of Gas Bubbles in the Organism

Gas bubbles which are formed in the organism following decompression exert pressure on the surrounding tissues, which leads to their displacement and deformation, possibly causing painful sensations. When a bubble is in the blood or tissues of the organism, the interaction of bubbles with the tissue surrounding them may be described by:

$$P_b = H + 2b/R + DR \quad (5)$$

where H is the hydrostatic pressure of the tissue (blood), which is the sum of the external pressure (E) and the tissue turgor pressure (T) or the blood pressure (dynes/cm^2)

DR is the deformation pressure, which is produced by the bubble and is a function of its size as well as the volume and elastic properties of the tissue (dynes/cm^2).

Gas bubbles which are formed in the living

organism may be divided conditionally into two specific types:

1. Autochthonous bubbles, the evolution of which is governed solely by the exchange gases with the surrounding tissues through diffusion.
2. Bubbles capable of growth not only due to diffusion but also as the result of merging with each other. Apparently, most of the extravascular, intratissue slightly mobile bubbles should be included in the first group. They probably are important in development of the most frequently encountered osteoarticular form of ADS – the bends. Intravascular mobile bubbles usually must be listed among the second type; their onset determines development of the most serious forms of ADS. The only exception is intravascular bubbles that are "clogged" in the capillaries which must be listed among type–1 bubbles [152].

Evolution of the autochthonous bubbles (type 1) is essentially a function of the exchange rate of gases between the bubbles and their surrounding medium. Evolution of size of type–2 bubbles is governed by the same factors, that is, the value of ΔP in the medium surrounding the bubbles. However, estimation of the maximum sizes and the true growth rate or resorption of the "wandering" bubbles is practically impossible, since the merging of these bubbles or their breakup into individual parts take place in a purely random manner. Movement of bubbles changes distribution of the inert gas reserves in the organism. In those tissues where bubbles have accumulated, the total level of inert gas content rises above the average value; therefore, its washing out from the bubbles is delayed.

Bubbles which have settled in tissues that are slightly perfused by blood should be resorbed particularly slowly. Hence, migration of bubbles, in conjunction with redistribution of inert gas reserves in various parts of the organism, promotes formation of bubbles that are very slowly resorbed in certain tissues. This phenomenon apparently is sometimes associated with inefficient treatment of ADS following recompression to the original pressure and the effectiveness, in such cases, of hyperbaric therapy, as well as the more frequent onset of ADS during repeated ascents.

In conclusion, it should be repeated that the structural characteristics of the living organism and its physiological and biochemical processes are important factors that govern the rate of increase in size of the bubbles and their dimensions and, consequently, manifestation of ADS.

Clinical Aspects of ADS

Data indicate [67, 116] that as long ago as 1906, Schroetter described pains in his joints in a pressure chamber at an altitude of 9000 m, but did not link this phenomenon to the effect of decompression. In 1908, Holden and Boycott, and later Henderson, in 1917, postulated the probability of caisson disease (aeroembolism) affecting persons following ascents in a pressure chamber to high altitudes.

In 1929, Jongbloed [99], in a self-experiment, described the development of ADS in a pressure chamber at altitudes of 10 000–12 000 m, manifested as pains in the region of the talocrural and genual joints. This observation was supported later in 1931 by Barcroft et al, in 1932 by Strel'tsov, and later in many studies [5, 15, 93, 189] with various forms of ADS described. For quite a time, gas bubbles were not detected in tissues during development of ADS, but as the x-ray method became more widespread, and later the ultrasonic method, many investigators observed gas bubbles [9, 67, 174]. Gas bubbles after decompression were also observed in persons who did not suffer from ADS [8, 97].

The impression created among aviation physicians and physiologists at present is that the clinical course of ADS and its severity are governed to a significant extent by the amount and size of gas bubbles in the organism, location, and rate of their growth and resorption [42, 67, 154].

The location of gas bubbles in the vascular bed and in tissues varies considerably, which governs the diversity of clinical symptoms of ADS. Many years' experience of ascents with healthy persons in pressure chambers at altitudes of 6000–12 000 m, as well as onset of ADS on flights at various altitudes (5500–11 000 m), indicate that

the osteoarticular (bends) form of decompression sickness is substantially more frequent (in more than 90% of the cases) than its other forms [93, 94]. More rarely, decompression sickness is manifested as skin damage, the symptoms of which include pruritus, sometimes a urticaria-type rash, edema, and change of color in the affected skin area [5, 67]. The cutaneous form, noted in approximately 10% of the cases, precedes the development of serious forms of ADS that lead to collapse [42].

Serious forms of ADS are rarely found, fortunately. The reason is that during ascent in a pressure chamber, as a rule, prolonged desaturation of the organism to remove N_2 has been carried out in advance; should the first signs of ADS appear, usually pains in the joints, the subjects are brought down from the altitude to prevent development of serious forms of ADS. In flights where prophylactic treatment measures are more difficult to carry out, serious forms of ADS develop more often than during tests in a pressure chamber.

Serious forms of this disease manifest attacks of asthma which frequently precede coughing and chest pain, disorders in cardiovascular system activity including vasomotor collapse, and serious disturbances of the CNS. Such symptoms may lead to loss of consciousness, clonic spasms, hemiparesis, and other symptoms of local damage to various brain centers.

Mirolyubov and Apollonov [5], in 1938, in attempting to classify the various forms of ADS, isolated three forms of the disease in varying stages of seriousness. The first form, mild, included pain of varying intensity in muscles and joints, which disappeared without a trace during ascent to altitudes of 7000–8000 m. The second, more serious form, was characterized by pains in the region of the joints which intensified rapidly and spread to the surrounding tissues. In such cases, 2–3 h following the descent from altitude, palpation of the joint revealed painfulness and retention of a slight edema of the soft tissues surrounding the damaged joint. The third, serious form of ADS, includes severe pains in the joints, chest pains, and other symptoms of ADS accompanied by sharp deterioration of the general state.

This classification of ADS can be refined at present with greater detail. Thus, the osteoarticular form of ADS, which is most often encountered according to Gray [82] and others, may be divided into three stages: mild, moderate, and serious. The mild stage is characterized by low-intensity pains which arise primarily during movement and frequently disappear spontaneously during a stay at altitude, also when the tissues around the affected joint are pressed; the second stage is characterized by pains which are completely tolerable, intensify gradually and always disappear without a trace during descent. The third stage is distinguished by intense pains, sometimes intolerable, that lead to sharp deterioration of the general state.

The mild forms of ADS can include pruritus and paresthesias as the only manifestations; these symptoms sometimes precede serious forms of ADS.

The pulmonary form of ADS is very dangerous because it is frequently accompanied by a precollaptoid or collaptoid state. Researchers have proposed that a cough and attacks of asthma are caused by multiple formations of gas bubbles in vessels of the lesser circulation and possibly in lung tissues. In gradual development of asthma, according to Fryer et al [67], pains start in the chest in an attempt to draw a deep breath, followed by a dry cough in a short time, and the asthma attack begins. In serious cases, coughing attacks and asthma are culminated by loss of consciousness or collapse. After descent from altitude, some asthma attacks last for several hours. In examinations of such cases, lung x-rays and ECGs showed no deviations from the norm. Examination by a physician revealed only hyperemia of the larynx and pharynx mucous membranes.

Injury to the cardiovascular system is symptomatic of neurocirculatory ADS, one of the most dangerous forms. Serious manifestations culminate in loss of consciousness as a result of vasomotor collapse. Multiple gas embolism of the vessels in the greater and lesser circulation apparently account for collapse, as well as frequent and considerable loss of blood plasma from the circulatory system.

In a milder form of neurocirculatory ADS,

hypotonia develops as well as disturbances to cardiac activity rhythm. Some cases are accompanied by pronounced hyperventilation with its usual symptoms: dizziness, pounding, and sometimes tetanic spasms [42, 170].

The neurologic form of ADS is characterized by headache, general dysphoria, clonic spasms, and multiple symptoms of local damage to the brain: hemiparesis, monoparesis, scotoma, various aphasias, and hyperthermia [26, 31, 42, 67, 164, 170].

Manifestations of ADS are varied and often indicate mixed forms of ADS. For example, symptoms of simultaneous injury to skin and asthma attacks, or slight pains in the joints are followed by vasomotor collapse [42, 67, 157, 158].

The Course of ADS

A correct understanding of the course of ADS is important. If victims remain at altitude after the first mild symptoms of ADS appear (descent being impossible or undesirable), there is danger of serious forms of ADS developing. It should be noted that ADS can proceed with clear periods; that is, following descent from altitude, ADS symptoms disappear rapidly and the subjects feel well. However, there is sharp deterioration after a short time and, in serious cases, coma develops with loss of consciousness. Such late syncopes were noted when ADS culminated in the victim's death as a result of acute edema of the brain. These disorders are caused by multiple embolism from gas bubbles in the small vessels of the brain. These damages may be due largely to fat and bone-marrow emboli [42, 88], a question which has not been adequately studied.

Etiologic and pathogenetic studies of ADS, indicating that it results from gas bubbles in tissues and the vascular bed, may be considered proven. However, fat embolism as the leading factor is questionable; apparently, only rarely is fat embolism important in the pathogenesis of ADS, aggravating its course considerably. An indirect proof that fat embolism does not play an essential role, as a rule, in serious forms of ADS, was established by numerous authors: serious forms of ADS can be treated with considerable efficacy by staying at an elevated pressure.

Treatment of ADS

Descent from altitude (recompression) is highly effective in treating ADS. Pains in the joints and muscles at altitudes of 12 000–10 000 m disappear without a trace when the pressure is raised to 250–300 mm Hg during recompression. An important condition in effective ADS treatment by recompression to normal barometric pressure is the time between the first symptoms of ADS and the moment of descent from altitude. The earlier the descent is made, the more rapidly the ADS symptoms disappear. In rare cases, after total disappearance of ADS symptoms, they can reappear after a short time (usually 1–3 h). The course of ADS is then usually serious, making medical observation necessary, for several hours after the ADS symptoms have disappeared.

In all serious forms of ADS, it is advisable, while conducting symptomatic treatment, to place the victims in recompression chambers under increased pressure [42, 67]. The oxygen pressure in the chamber usually is raised to 3 atm, and the time the victim spends in the chamber is limited by the period it takes for toxic effects of oxygen to appear. In the symptomatic treatment of victims with serious forms of ADS, especially with deep brain activity disturbances such as loss of consciousness or comatose state, caution must be exercised to prevent brain edema. Injections of purified urea and similar compounds are recommended to stabilize osomotic pressure in the brain cells [42, 94].

Factors that Influence Probability of ADS

Essential factors that predicate the probability of ADS include: physical parameters characterizing magnitude, frequency, and rate of pressure differential; time spent by the individual at altitude; temperature and chemical composition of the AGA; and certain indices of the individual such as his physiologic state, age, and constitution.

The formation of gas bubbles in the organism following decompression is a function of the degree of supersaturation of the tissues by gases dissolved in them, thus, it would be expected that investigators would try [80, 171, 189] to determine

the significance of this factor for onset of ADS. Biophysically, simple supersaturation of the tissues by some gas is, although necessary, not sufficient for the formation of free gas bubbles in organic tissues. For this reason, the question cannot be answered on the degree of tissue supersaturation at which free bubbles of gas could cause ADS. Theoretically, free gas bubbles in tissues are possible when the barometric pressure drops to a value slightly exceeding the undersaturation degree of venous blood and tissues; for example, when pressure falls from 760 to 700 mm Hg, but, fortunately for man, ADS occurs at much higher pressure differentials [64, 67, 93, 152].

ADS regularly begins only after ascents from the ground to altitudes of 7000 m or more, according to experimental studies. Onset of ADS following elevations to lower altitudes is extremely rare, therefore need no special attention from the practical standpoint [67, 93, 171].

The probability of ADS increases with increase in ascent altitude and pressure differential factor following ascent to an altitude of 8000 m (256 mm Hg, differential coefficient of about 3.0). Experiments show that ADS is observed not only in persons performing physical work (15–25%) but also in those in a state of rest (in 3–5% of the cases) [67, 172] (Fig. 5).

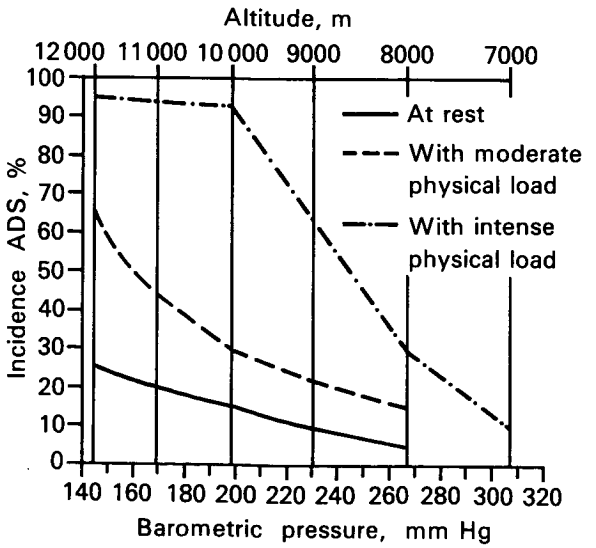

FIGURE 5.—Development of ADS at altitudes of 12 000–7000 m at rest and during various physical loads. (Based on [32, 67, 94, 171, 172, 173])

Following ascent to altitudes of 11 000–12 000 m, the frequency of ADS rises, to 25–48.5%, according to data of various authors, under conditions of relative rest, and to 62–93% when performing physical work [67, 81, 93, 94, 170, 172]. From various studies, the probability of ADS at altitudes of 8000–10 000 and 12 000 m differ, sometimes substantially, which is due to different rates of ascent, inhomogeneity of test subjects according to age, weight, and different activities at altitude.

ADS occurs as a function of the decompression rate. The higher the rate, the greater the probability of ADS during the subsequent stay at altitude. Thus, according to Hitchcock et al, in a normal, slow ascent (at 20–30 m/s) to an altitude of 11 600 m and subsequent stay at this altitude for 90 min, 62% of subjects carrying out standard physical exercises of moderate difficulty had ADS, while after rapid ascents (approximately 1 s), ADS was more frequent (in 88%), all other conditions being equal.

Time Spent at Altitude

A study of the distribution of ADS in time at altitudes of 8000–12 000 m indicates that during the first 3–5 min after ascent, ADS is extremely rare. For gas bubbles to form in tissues requires a certain time. The maximum number of ADS cases was in the interval from 20 to 40 min stay at altitude. After 1 h stay at altitude, the number of ADS cases dropped significantly; after 2 h, ADS was rare [67, 154, 172].

Hence, distribution of ADS cases in time following decompression is similar, to a certain degree, to the Poisson curve of normal distribution with maximum height at 20 to 40 min (Fig. 6).

Temperature of the AGA is a definite factor in the onset of ADS. Strel'tsov and others [24, 80, 189] noted that decreasing the temperature to values which create a sensation of cold promotes development of ADS. This is apparently due to the low temperature leading to spasm of vessels in skin and other parts of the body and thereby, after decompression, retarding desaturation of tissues in these regions with regard to nitrogen or another biologically indifferent gas [80, 171]. However, other data indicate that an

increase in environment temperature promotes acceleration of desaturation of the organism with regard to nitrogen, thereby decreasing probability of ADS [25].

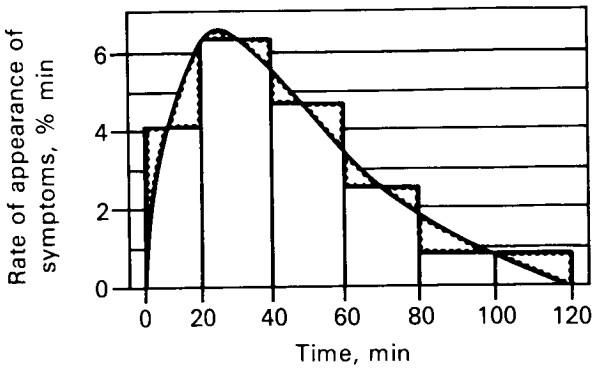

FIGURE 6.—Rate of appearance of ADS symptoms during 2 h at an altitude of 10 500 m. (After Nims [154])

Chemical Composition of the AGA

The role of chemical composition of AGA in forming free gas bubbles in tissues during decompression and, consequently, in the development of ADS has been insufficiently studied. It has been pointed out that increasing the P_{CO_2} in the AGA promotes the development of decompression sickness [24, 70, 80, 96, 209]. Decompression sickness occurred in animals that had been in a gas medium with P_{CO_2} = 22–45 mm Hg; following decompression to 200–145 mm Hg, ADS was significantly more frequent. Their blood gas traps showed a greater number of gas bubbles than in the animals of the control group which had been brought to the same altitude, but which previously had been kept in normal air [81].

Prolonged stay of humans at altitudes of the order of 3000–4000 m for several days [45], regardless of hypoxia developing (which should facilitate manifestation of ADS) to a significant degree, prevents their developing ADS during ascents to an altitude of 11 500 m. This is explained simply by partial desaturation of nitrogen from the organism during ascents to altitudes.

In the formation of AGA, roles played in the development of ADS following decompression by the various biologically indifferent gases comprising it are significant. Theoretical considerations of the basic physical and biophysical properties of inert gases and nitrogen (see Tables 2 and 3) permit a comparative estimate of the properties where one is used as a diluent gas in the AGA.

The group of inert gases includes: helium, neon, argon, krypton, xenon, and radon. Radon, because of its radioactivity, must be excluded from gases that can be used in the AGA.

Two parameters are of basic significance for the formation of free gas bubbles in the organism following decompression: solubility of the gas in various tissues (fat, muscle, and blood), and the coefficient of diffusion of the gas through cell membranes.

The Bunsen coefficient of gas solubility increases as the molecular weight increases, but the ability to diffuse (diffusion constant) decreases (Table 3). Hence, it might be concluded that gases with relatively high molecular weight (xenon, krypton, and probably argon) are scarcely advantageous as components of the AGA. Their use, aside from increasing the weight of the AGA, requires a greater expenditure of energy for cabin ventilation, leading to greater probability of ADS following decompression. Desaturation of the organism to remove these gases, due to their low diffusivity, requires a great deal of time which in certain situations (for example, when the crew is transferred to AGA conditions with low pressure), can be extremely disadvantageous. Consequently, the choice of biologically indifferent gases for the AGA at present can be limited to nitrogen, helium, and neon.[2]

There are no sufficiently convincing experimental data so far to give preference to one of the gases listed. Studies with human beings are needed in which, following total gas equilibrium of the organism with regard to AGA containing He or Ne, decompression would be carried out to 200–160 mm Hg, after which the rate of ADS would be determined. The probability of ADS—its osteoarticular form (bends)—after a pressure drop in the cabin, according to Beard et al [19], is somewhat higher when He rather than N_2 is included in the AGA.

[2]The possibility of using hydrogen (H_2) was not considered because of great danger of explosion in an oxygen-hydrogen gas medium.

TABLE 2.—*Physical Properties of Inert Gases*

Property	Gas					
	He	Ne	A	Kr	Xe	N
Atomic no.	2	10	18	36	54	7
Molecular wt.	4.00	20.18	39.94	83.80	131.30	28.00
Color	Colorless					
Density, g/l, at 0°C and 1 atm	0.1784	0.9004	1.784	3.708	5.851	1.251
Heat capacity (C_p) at 25° C and 1 atm, cal/°C-g mol	4.97	4.97	4.97	4.97	4.97	6.96
Specific heat ratio at 0 to 20° C, C_p/C_g	1.63	1.64	1.67	1.69	1.67	1.404
Sound velocity at 0°C and 1 atm, m/s	970	435	319	213	168	337
Acoustic impedance at 0°C and 1 atm, dyn-s/cm³	17.3	38.5	56.9	— —	— —	42.1
Thermal conductivity at 0°C and 1 atm, cal/° C-cm-s	34.0×10^{-3}	11.04×10^{-5}	3.92×10^{-5}	2.09×10^{-5}	1.21×10^{-5}	5.66×10^{-5}
Viscosity at 20° C and 1 atm, μP	194.1	311.1	221.7	249.6	226.4	175.0
Critical properties:						
Density, g/cm³	0.069	0.484	0.531	0.908	1.105	0.3110
Pressure, atm	2.26	26.9	48.0	54.3	58.0	33.54
Temperature, °C	− 267.9	− 228.7	− 122.44	− 63.8	16.59	− 146.9

TABLE 3.—*Solubility and Diffusion Constants of Inert Gases*

Property	Gas					
	He	Ne	A	Kr	Xe	N
Bunsen solubility coefficient in water at 38°C	0.0086	0.0097	0.026	0.045	0.085	0.013
Bunsen solubility coefficient in olive oil at 38°C	0.015	0.019	0.14	0.43	1.7	0.061
Bunsen solubility coefficient in human fat at 37°C		0.020	— —	0.41	1.6	0.062
Oil-water solubility ratio	1.7	2.1	5.3	9.6	20.0	5.1
Relative diffusion through gelatin at 23°C	1.0	(0.42)	0.30	0.21	0.13	0.35
Diffusion constants through liquids at 37° C $cm^2/s \times 10^{-6}$:						
Olive oil	(18.6)	(8.34)	(5.92)	(4.10)	(3.27)	7.04
Lard	(9.28)	(4.15)	(2.94)	(2.03)	(1.62)	3.50
Serum	(57.6)	(25.7)	(18.2)	(12.6)	(10.1)	21.7
Agar gel	(71.3)	(32.0)	(22.7)	(15.8)	(12.6)	27.0
Water	(79.2)	(34.8)	(25.2)	(17.5)	(13.9)	30.1
	63.2					

Animals administered equal volume amounts of He and N_2 showed that vascular embolism produced by He proceeded more easily than embolism following administration of nitrogen [81]. This is evidently due to the higher diffusivity of He, since its desaturation from gas bubbles is more rapid, and they disappear sooner than N_2 bubbles.

In rat experiments, replacing air nitrogen with helium or neon leads to (following decompression) approximately the same rate of ADS; however, these data can scarcely be extrapolated to man because of the exceptionally high metabolic rate in rats [84].

Theoretically, it has been indicated by several authors [19, 25, 170, 208] that Ne (use of this gas in AGA has been studied little) should have certain advantages over He and N_2. The use of Ne in a helium atmosphere (HEA) must lead to the lowest probability of altitude pains during muscular loads, also severe forms of ADS accompanied by dyspnea and neurocirculatory collapse [25, 170]. It must be added that the difference between He, Ne, and N_2 when used in an AGA will be smaller, the lower the barometric pressure in spacecraft cabins. At a pressure half the atmosphere value (380 mm Hg) and corresponding content in the AGA of 50% diluent-gas and 50% O_2, the probability of ADS will be so negligible that any difference between Ne, He, and N_2 need not be considered for their inclusion in an AGA.

Body Weight

Increased predisposition of overweight persons to ADS has been indicated. Cutaneous and serious forms of ADS are observed more often in those overweight.

Frequent ADS accompanied by dyspnea and collapse is usually related to the high solubility of nitrogen in fat tissues and the low level of their blood supply. These circumstances determine a high probability of free gas bubbles forming in gas in fat tissues. In fat tissue lesions caused by gas bubbles, fat particles can enter the vascular lumen, and with gas bubbles clog vessels. Data in Figure 7 indicate the higher rate of ADS in overweight persons [25].

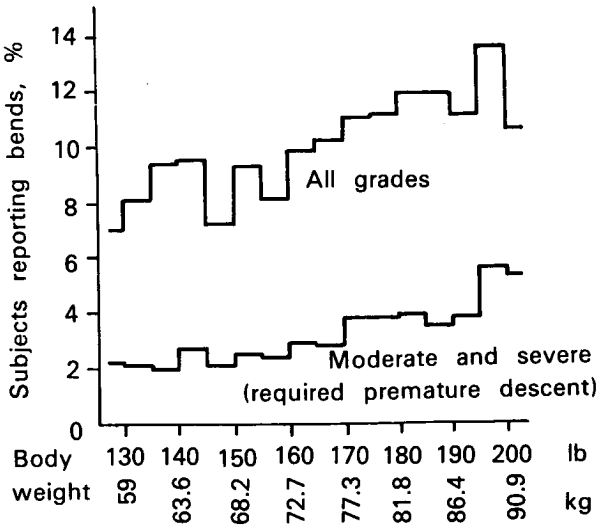

FIGURE 7.—Manifestation of ADS as a function of body weight. (Cited in [25])

Age

The incidence of ADS increases with age of subjects [42, 67]. In ascents of 2633 servicemen aged 17 to 36 (breathing pure oxygen), to 8500 m followed by 2-h exposure at this altitude, the smallest number (0.78%) of ADS cases in a rest condition was noted for persons aged 17 to 20. Among persons aged 21–23 years, the number experiencing ADS rose to 1.67%; among persons 24–26 years of age—4.98%; among those 27–29 years of age, 7.43%; and in the group aged 30–35 years, 5.99% [66].

One of the factors possibly affecting the distribution of ADS cases in relation to age is the change in weight (the increase of weight with age), as well as circulatory characteristics determining the higher rate of nitrogen desaturation from the organism among adolescents and young men.

Physical Exercise

Muscle exercises promote development of ADS. A direct relationship was established between onset of ADS and intensity of muscle activity [56, 67, 98], made clear from the data in Figure 8, which show the results of subjects who performed different numbers of deep knee bends at high altitude [64]. Localization of attack

of joints and muscles during ADS also depends on the kind of muscle activity. Pains are first felt in the same joints and muscles that participate directly in the exercises [93, 171]. For example, when the subjects' legs were flexed at the knee, the altitude pains usually developed in the knee area; similarly when the subjects' arms were raised periodically, the pains tended to appear most often in the shoulder joints.

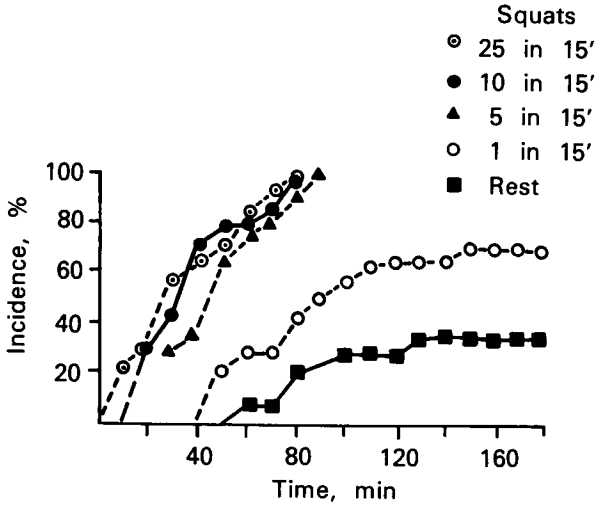

FIGURE 8.—Dependence of ADS incidence on physical load intensity [170].

Intense muscle activity, it has been held, leads to a decrease in the altitude threshold of ADS by 1000–1500 m. This is caused by local foci of low negative hydrostatic pressure in motor activity arising in the working joints, muscles, and ligaments, which promotes formation of gas nuclei and bubbles [51, 70, 86, 152]. During muscle activity the formation of CO_2 increases, which is a major factor in the formation of gas bubbles after decompression, and also promotes ADS during muscle activity [24, 96].

In addition to muscle work and other influences promoting the formation of increased gas nuclei in the organism, onset of gas ADS can be provoked and facilitated. Repeated ascents (after several hours) to altitude, as well as underwater immersion even to relatively shallow depth, preceding an ascent to altitude, promote the development of ADS [42, 80].

Prevention of ADS

Hermetically sealed cabins with a pressure of 1–1.2 atm in Soviet spacecraft and an HEA with a total pressure of 258 mm Hg in US spacecraft cabins increase the urgency of protecting crewmembers against ADS. Astronauts can develop ADS after transition from normal atmospheric pressure to reduced pressure in the cabin or space suit.

Hermetic cabins and space suits with sufficiently high pressure, of the order of 350–400 mm Hg, are effective means of preventing ADS in flights. This approach to solving the problem encounters serious technical difficulties: when the pressure in space suits is raised to the values indicated, the work capacity of cosmonauts wearing space suits falls off sharply due to restrictions on movement. With the use of high pressure in cabins and space suits, the probability of ADS cannot be entirely avoided, since in emergency situations pressure can drop to values where ADS becomes probable. Accordingly, different methods of preventing ADS based on desaturation of nitrogen from the organism, or any other inert gas that is part of the AGA, take on major importance.

The organism can be desaturated either by slow reduction in pressure—by ascent to altitude, or by breathing pure oxygen under normal or reduced barometric pressure. At even relatively rapid ascents to altitude at a rate of 10–20 m/s, there is partial washing out of nitrogen, which determines some decrease in the incidence of ADS.

Aviation medicine experience permits the assumption that desaturation of nitrogen from the organism by breathing oxygen is the most convenient and effective method of preventing ADS [6, 7, 23, 83, 98].

The curve of nitrogen removal from the organism reflects its dissimilar rate of removal from different tissues [83, 98, 207, 211]. The rate of desaturation for different tissues depends on their coefficient of nitrogen solubility and on the level of their blood supply. Individual differences in chemical composition of the body and in the level of blood supply of different tissues determine corresponding individual characteristics of the

desaturation curve of nitrogen from the organism or in any other gas while oxygen is being breathed.

The rate of nitrogen removal is the highest during the first minutes of breathing oxygen, due mainly to the removal of nitrogen from respiratory tract, lungs, and blood. Further, the rate of nitrogen removal slows markedly in 10 to 20 min and its desaturation is predominantly from muscle tissue and internal organs. In the first hour of breathing oxygen, the organism loses approximately 50% of the nitrogen dissolved in its tissues (Figs. 9 and 10).

Desaturation proceeds slowly in the second to third hour of breathing oxygen; about 48 h are required for practically complete washing out of nitrogen [211]. Such slow removal of nitrogen from the organism is because some tissues, such as tendons, joint sacs, and fat tissue, have very low levels of blood supply; the solubility of nitrogen in fat is more than five times higher than in other tissues, where its content is low.

In aviation and astronautics, methods of nitrogen desaturation from the organism should be developed so that a fairly high preventive effect would be achieved in minimum time. Various means of increasing the desaturation rate have been proposed: arbitrary hyperventilation, physical exercise, and intake of caffeine [7, 23, 57]. Ardashnikova [7] noted an increase in the rate of nitrogen removal by arbitrary hyperventilation with oxygen, which was followed by an investigation with 3–5% CO_2 oxygen added. The same effect was anticipated as a result of the nonarbitrary hyperventilation caused by the stimulating action of CO_2 on the respiratory center. The experiments showed that adding CO_2 to O_2, in spite of increased pulmonary ventilation, does not lead to an increase in the rate of nitrogen desaturation for the organism, but slows it by 10–15%. The reason for the slowdown, evidently, is redistribution of the blood flow resulting from vasoconstrictive action of CO_2 on the vessels in many regions of the body. Physical exercise during oxygen breathing time appreciably accelerates desaturation of nitrogen and helium from the organism, which is clear in Figures 9 and 10.

Pure oxygen breathed under normal barometric pressure leads to constriction of vessels

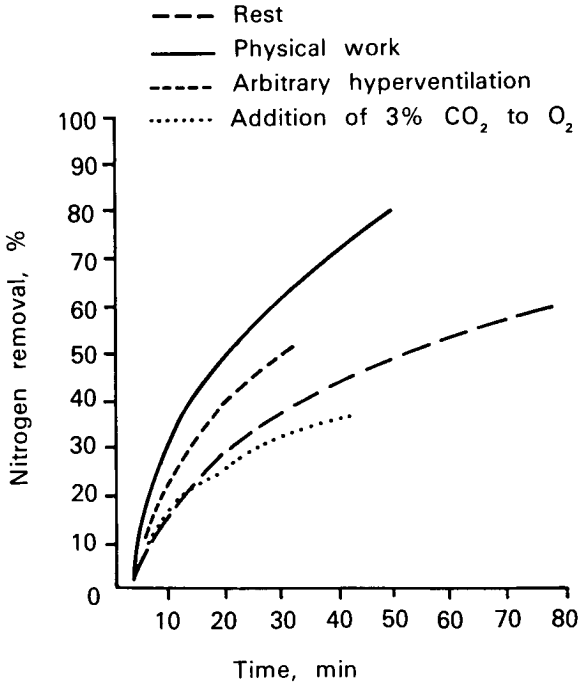

FIGURE 9.—Rate of nitrogen removal from humans while breathing oxygen under different conditions. (Based on [6, 7, 23])

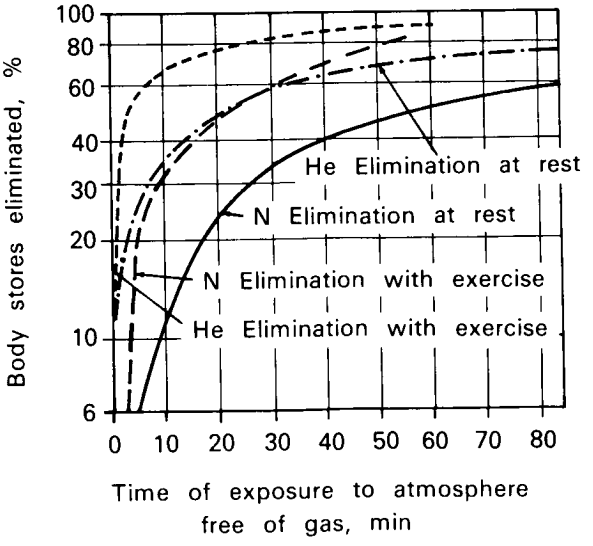

FIGURE 10.—Rate of nitrogen and helium removal when O_2 is breathed at rest and when physical exercises are performed. (Based on [25])

and reduced blood supply in many tissues. This effect was noted as having an unfavorable effect on desaturation; for its elimination, desaturation by breathing pure oxygen at different altitudes was investigated.

Nitrogen removal. The total amount of nitrogen removed in 1 h of breathing oxygen at normal pressure and at an altitude of 8000 m is approximately the same [6]. However, at an altitude of 8000 m during the first 10–15 min, more nitrogen is removed than at normal barometric pressure. In 20 min oxygen breathing, nitrogen removal is slowed at an 8000-m altitude to a greater extent than during desaturation under normal barometric pressure. This is of definite interest in understanding causes determining the reduced protective effect of desaturation when oxygen breathing is under reduced barometric pressure.

According to the data of Marbarger et al [137], the protective effect from 2 h of oxygen breathing before ascent to an 11 600-m altitude decreases with increase in altitude (beginning at 3600 m), when there is desaturation [137]. Thus, when oxygen was breathed under normal conditions after an ascent to 11 600 m, ADS developed in 6.1% of the cases; when desaturation was in the pressure chamber at 3600-m altitude, ADS was noted in 15% of the cases. ADS arose in 21% of the cases when desaturation was at 6700-m altitude; but when ascent was made to an altitude of 11 500 m without preliminary desaturation, ADS was noted in 48.5%. An explanation of the results of this investigation is that during saturation at altitudes of 3600–6700 m, nitrogen, washed from the tissues slowly losing nitrogen, proves to be impeded by the formation of bubbles in the tissues in which N_2 accumulates, even at these altitudes.

When individuals are in the mountains at an altitude of 3000–4000 m for several days, the result is that all tissues uniformly lose approximately 35% of their nitrogen content. This has a more pronounced preventive effect against ADS for subsequent ascents to altitudes of 10 000–11 500 m than preliminary 1-h oxygen breathing under normal barometric pressure, where the organism is freed of 50% of the nitrogen. These data indicate that the preventive effects of desaturation are determined not only by the amount of nitrogen or other biologically indifferent gas removed from the organism, but also by tissues from which the gas is removed. Thus, it is vital that there is desaturation from tissues that are slowly freed of the indifferent gas.

To determine the effectiveness of preventing ADS, after different periods of breathing oxygen at normal pressures, is also important. Since protection against ADS after nitrogen desaturation from the organism depends on many factors, the extent of the anticipated preventive effect can be expressed by three values: minimum, mean, and maximum.

Roth calculated from data of Jones [98], the protective effect for ADS prevention in relation to the time of oxygen breathing for cases subsequently being under reduced (down to 179 mm Hg) pressure when performing moderate physical work.

When the age and weight of the subjects, and the associated curve of nitrogen desaturation from the organism are not known, calculating the preventive effect must be based on "minimum" protection. The extent of the protective effect can be calculated by the percentage of probable reduction in the number of ADS cases. This is compared with the proposed percent of ADS cases in ascents to an altitude of 10 500 m (179 mm Hg) without preliminary oxygen breathing at a rate of no more than 1000 m/min (Table 4).

Determination of probable loss of the protective effect is important when desaturation is disrupted; when the oxygen breathing is interrupted, and the individual again breathes air for some time. Such situations can arise in different periods of flights or flight preparation. Table 5 shows calculated losses of the protective effect under different conditions when nitrogen desaturation from the organism was disrupted. The data provide for only an approximate estimate of the protective effect against ADS after different periods of oxygen breathing before ascents to altitudes of 10 000–11 000 m.

Experimental data indicate that breathing pure oxygen, in addition to reducing the probability of ADS, lowers the incidence of severe forms of ADS and shifts in time the manifestation of different ADS symptoms. For example, breathing oxygen for 1 h before ascent to an altitude of

12 000 m, when light work is performed in this altitude for 1 h, reduces the incidence of ADS nearly twice and leads to ADS being noted 10–20 min later than after ascents without desaturation [94]. Determining the time of breathing sufficient oxygen for the greatest possible protective effects is vital in preventing ADS.

TABLE 4.—*Preventive Effect of ADS in Ascents to Altitude after Preliminary Breathing of Oxygen for Different Periods*

Time of breathing O_2, h	Minimum protection %	Probable protection %
0.5	16	26
1.0	29	45
1.5	41	59
2.0	50	70
2.5	58	77
3.0	61	83
3.5	70	87
4.0	75	91
4.5	79	
5.0	82	
5.5	85	
6.0	86	
6.5	89	
7.0	91	

Oxygen and altitude. Breathing oxygen for 2 h at 4500 m (430 mm Hg) is sufficient to prevent ADS at 7000 m for 5 h while performing work of moderate intensity (300–400 kcal/min) [32, 73]. Without desaturation, ascents to, and work in, this altitude cause ADS in more than 10% of the cases. Breathing oxygen for 5 h at 4500 m is sufficient to prevent ADS at an altitude of 10 000 m for 5 h with work of moderate intensity. This can be achieved by a preliminary 10-h stay at an altitude of 4500 m in an AGA of 45% O_2 and 55% N_2. Subjects remaining for 4–6 h at altitudes of 4000–5000 m in a gas atmosphere with 45% O_2 and 55% N_2 were not provided adequate protection against ADS; in a subsequent ascent to 11 000 m when intense work was performed, ADS symptoms were noted in nine of 30 persons [73]. Preliminary oxygen breathing for 4 h can prevent ADS symptoms at 8000 m. To achieve "maximum" protection against ADS at altitudes of 10 000–12 000 m, preliminary oxygen breathing for 8–10 h is evidently required [73, 170]. The conditions under which there is nitrogen desaturation from the organism must be considered; it must be remembered that when oxygen is breathed under normal pressure, the danger of fire is considerable, since the probability of inflammation is nearly five times greater than in normal air [33, 73].

It has been suggested that, to prevent ADS, individual selection should be made for the crew in order to eliminate those highly sensitive to ADS. Individual differences in resistance to ADS have been shown [67]. After 2 h at an altitude of 8500 m, ADS developed in 71 of 2273 persons (3.12%); in an ascent repeated to the same altitude, of 2202 persons in whom no ADS had been noted in the first descent, ADS appeared in 47 (2.13%). But when 60 of the 70 persons that had been affected earlier by ADS made an ascent, it developed in 13 (21.7%) [67].

TABLE 5.—*Assumed Losses of Protective Effect After Disruption of Desaturation*

	Oxygen	Air	Oxygen	Air	Oxygen	Air	Oxygen	Air
Time, h	1	½ 1	2	½ 1	3	½ 1	4	½ 5
Mean protection	29	26 20	20	40 33	64	54 46	75	62 53
Probable protection	45	33 25	70	52 39	83	62 46	91	67 50

	Oxygen	Air	Oxygen	Air	Oxygen	Air
Time, h	5	½ 1	6	½ 1	7	½ 1
Mean protection	82	68 60	86	74 62	91	74 62
Probable protection	95	70 52	97	72 54	97	73 54

Jones, in 1942, noted positive correlation ($K = 0.56$) between the rate at which radioactive krypton was excreted by the tissues and individual sensitivity to ADS; however, this method can scarcely be used advisedly for selection. Selection for ADS prevention can scarcely be significant, it is assumed, since it is impossible to cancel out entirely the probability of ADS in persons who successfully pass this selection [5, 67, 190].

In conclusion, in selecting the gas composition of cabin AGA, it is vital to obtain information about the rate of desaturation from the organism not only of nitrogen, but also of inert gases that can be part of the AGA.

Experimental data on this problem are limited and apply mainly only to He. The rate of desaturation of He from the organism after sufficiently long stays in a helium-oxygen medium considerably exceeds the desaturation rate of nitrogen. This is evident from data in Figure 10.

Data have not been obtained on neon desaturation from the organism after establishment of gas equilibrium in an oxygen-neon atmosphere; for argon (A), it can be concluded that it is similar to N_2 [80, 170].

Vaporization Phenomena in the Organism

At barometric pressure below 47 mm Hg, the pressure of the gas medium surrounding a person becomes less than the vapor pressure of water at 37° C. Vaporization phenomena develop in organic tissues which determine the distinctive trend of decompression disorders.

The development of vaporization in different body tissues and cavities depends on barometric pressures—ascent altitude, hydrostatic pressure, temperature, elastic properties of tissue, and presence of gas nuclei.

This question has been dealt with in many studies [9, 116, 119, 201]. Vaporization phenomena were first observed by Boyle [36] in 1670, in animal organisms under extremely low barometric pressure. They were then described by Hoppe-Zayler in 1857, whose evaluations were not precise enough, since acute hypoxia at high altitudes eliminated the physiologic effects associated with vaporization in tissues.

Experiments where vaporization phenomena were observed in animals were described by Armstrong (US) and Strel'tsov and Parfenova (USSR), in 1938 [9, 159]. In Strel'tsov's experiments, newly born rats were highly resistant to acute hypoxia. This made it possible to detect, in a pressure chamber, in animals still alive at altitudes of 20 000 m and higher, a sudden, abrupt increase in metabolism, which the investigators considered tissue "boiling." Armstrong also noted in experimental rabbits, when pressure in the pressure chamber was lowered to 47 mm Hg, development of "boiling" of tissues, judging from depressions under the skin and gas bubbles in saliva and blood. Vaporization phenomena in different tissues in animals were later investigated in detail [12, 104, 113, 119, 201].

The roentgenogram method was used extensively by Kuznetsov [116] in animal ascents to high altitudes in a pressure chamber, which enabled him to observe successive vaporization phenomena in different tissues. After rapid pressure drop in the pressure chamber to 40 mm Hg and less, he noted some increase in the body volume of the animals (white rats and dogs) due to expansion of intestinal gases. In 12–15 s, areas of swelling under the skin appeared suddenly in white rats, that is, subcutaneous altitude emphysema developed, subsequently spreading over the entire body surface. It was confirmed that emphysema occurred due to "boiling" by its rapid, explosive development, and only occurred when barometric pressure was lowered to 47 mm Hg or less, also that it was possible to prevent emphysema by cooling the animal body.

The roentgenograms established that in 2–3 s after the pressure was lowered to 47–48 mm Hg, small foci of gas accumulated under the skin. In 7–10 s, the gas was detected in the abdominal region—between the diaphragm and the liver; in 10 to 20 s, gas was observed in the pleural cavity, right ventricle of the heart, and veins. Gas in the veins is due to the pleural cavity and right side of heart being body regions with low pressure. Gas was noted later in the left side of the heart and arteries, which is associated with relatively high blood pressure in these cardiovascular regions. The same phenomenon—vaporization in pleural cavity, heart,

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and vessels of dogs after pressure in the pressure chamber had been lowered to 25–30 mm Hg—was observed by Burch, Kemph, et al [40], not only roentgenologically, but also visually through small "windows" mounted in thoracic cavities.

Experiments on dogs and monkeys [22, 106, 112] indicate that when animals stay in the pressure chamber no longer than 2 min, subsequent rapid recompression—descent from altitudes—leads, as a rule, to the preservation of life. The death of animals in more rapid exposures at high altitude when vaporization arises, is evidently associated mainly with acute hypoxia. This conclusion can be based on the lifespan of animals at altitudes of 15 000–17 000 m when "boiling" of tissues does not yet develop, being approximately the same as at altitudes of 20 000–40 000 m, where it does occur [112, 116].

Thus, acute pathologic state in animals exposed to extremely low pressures is caused chiefly by hypoxia, and decompression phenomena (vaporization and formation of intravascular bubbles) are only factors that aggravate the effect of hypoxia and complicate its course. It must be noted that when first aid is given to individuals severely affected at high altitudes, administration of drugs into the blood and arterial compression of blood can prove ineffective due to gas bubbles in the vasomuscular lumen and heart.

In studies of the mechanism of subcutaneous decompression emphysema, the chemical composition and pressure of the gases forming it have been determined [12, 104, 113]. Kemph, Beman and Hitchcock [104] measured the pressure in subcutaneous emphysema bubbles in animals, developing after pressure in the pressure chamber had been lowered to 25–30 mm Hg. The pressure was determined with a capacitive strain gauge, an ordinary mercury manometer, and an indirect fluoroscopic method, which records external pressure where bubbles disappear in the x-ray. These experiments established that differential pressure fluctuates from 25–40 mm Hg, and absolute pressure from 55–70 mm Hg. The composition of gases in subcutaneous emphysematose bubbles varies widely [12]. In gas samples collected from rat emphysematose bubbles at altitudes of 20 000–22 000 m in different experiments, N_2 content was in the range 25.4 to 78%; CO_2—1.2 to 68%; and O_2—6.3 to 20.8%. In vaporization phenomena, the primary role is attributed to water vapor and carbon dioxide gas, which act as a "second liquid." Accordingly, vaporization in tissues can begin at barometric pressure somewhat exceeding 47 mm Hg, that is, the pressure at which water vapor pressure at 37° C is equal to the ambient pressure.

According to the data of Kovalenko, chemical composition of emphysematose bubbles undergoes a change simultaneously with gradual rise in their pressure: the content of O_2 and N_2 becomes smaller, and CO_2 content rises. In the first 4–5 s after decompression, pressure in emphysematose bubbles is 15–20 mm Hg, subsequently rises to 30–60 mm Hg and remains constant, since at these pressures the skin is already peeling [113, 114].

Investigations on vaporization phenomena in the human organism are few, so that this problem has not been adequately studied.

Subcutaneous decompression emphysema. Decompression emphysema has developed locally in wrists and feet in the course of astronautics. Subcutaneous emphysema was noted in wrists of individuals in pressure chambers who wore altitude suits without gloves when ascending to an altitude of 20 000–40 000 m [97, 170].

In the data relative to subcutaneous emphysema, certain characteristics are striking:

absence of emphysema in the first 1–3 min after ascent to altitude even when pressure in the pressure chamber was reduced to 8 mm Hg;

appearance of emphysema in only one hand;

individual instances of absence of emphysema for relatively long stays (15 min and longer) at altitudes of 20 000–30 000 m.

These results can be explained by the tissue turgor acting as a determinant of the ability to withstand stretching and lesion which are important in the development of emphysema.

Absence of subcutaneous altitude emphysema during the first minutes and its individualized manifestation are associated with tissue turgor which differs in degree among individuals [97].

It may be added that gas nuclei, the sources of decompression bubbles, also probably contribute to individualized manifestations of emphysema, since vaporization of water vapor in the cavity of this kind of gas bubble can determine the initial period of emphysema development.

For altitude emphysema to be manifested, the total of the values of intratissue pressure (*Pt*-turgor) and barometric pressure (*Pb*) must be smaller than 47 mm Hg ($Pt+Pb<47$ mm Hg). It is immediately apparent that various indifferent gases (N_2, He, A, and Ne) that can be part of AGA will not appreciably affect the development of subcutaneous decompression emphysema, since H_2O and CO_2 are its main constituents. Different gases can have effect only on the latent period of emphysema, which is due to decompression gas emphysema apparently having two phases. During the first phase, gases diffuse and bubbles are formed; in the second, fluid in the cavities of these bubbles evaporates.

Emphysema does not cause deterioration in self-awareness and the total state of subjects during several minutes; this makes it possible to observe the dynamics of its development for some time. Emphysema occurs, as a rule, only in one hand—at first in the rear surface of the wrist in the skin between the first and second fingers, and gradually spreads to the entire wrist. The first unpleasant sensations—tightening of skin, prickling, and pain—are noted by subjects only 3–5 min after onset of emphysema. Pain sensations were sometimes absent even in pronounced emphysema when the wrist took on a spherical shape [97].

Roentgenograms of all subjects at altitudes of 12 000 m and higher showed a small amount of gas in the radiocarpal joint. Subcutaneous emphysema at altitudes of 20 000–30 000 m was manifested first by a small accumulation (in the form of a narrow strip) of gas beneath the skin. Later, the amount of gas beneath the skin increased steadily (Fig. 11). After rapid descent from altitude, signs of gas in the radiocarpal joint disappeared. However, in some roentgenograms there were still considerable "lightening" bands in soft tissues of the wrist, which had earlier been affected by emphysema. The ability for delicate differentiated motions was rapidly restored [97].

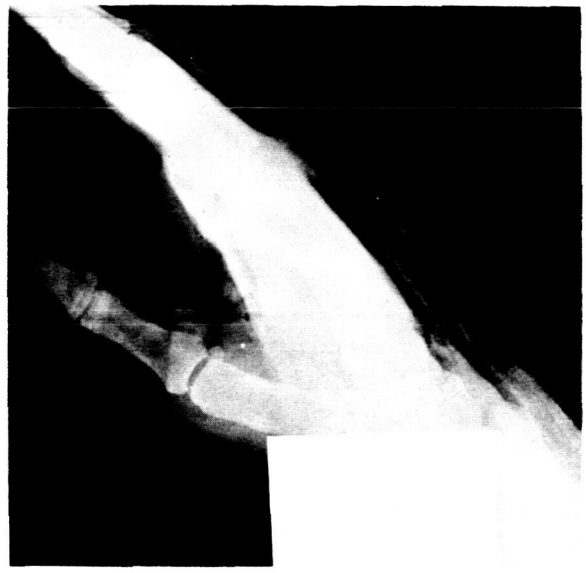

FIGURE 11.—Evidence of subcutaneous altitude emphysema at 20 000–30 000 m. The first manifestation was a small accumulation of gas in a narrow strip beneath the skin. (Based on [97])

HYPOXIA

The biological equivalence of AGA complying with the normal terrestrial atmosphere in terms of P_{O_2} is one of the main principles in AGA design. Maintaining a P_{O_2} in a cabin AGA that is close to the normal P_{O_2} of the atmospheric air is most important for determining flight safety. During flights, unfortunately, instances of cabin depressurization cannot be entirely eliminated, as well as improper operation of the regeneration unit, inevitably leading to decreases in P_{O_2} in the AGA and of high toxic states in crewmembers. Information on the effects of different degrees of hypoxia on the human physiologic state and work capacity is of great importance. Hypoxia has drawn the attention of space medicine specialists as means of selecting and conditioning astronauts. To prevent the unfavorable effects of weightlessness and hypodynamia on the organism, this conditioning should be carried out during actual space flight by periodically decreasing P_{O_2} in the AGA [76, 134].

Acute Effects of Hypoxia

Metabolic processes underlie life. In man and animal, these processes include oxidation of

proteins, fats, and carbohydrates by oxygen intake from atmospheric air. In contrast to the relatively high reserves of fats, carbohydrates, and proteins in the organism, its reserve of O_2 is extremely low. This dictates the necessity for virtually continuous intake of O_2 from the ambient medium.

P_{O_2} must not fall below a certain level for normal, vital activity of organic cells, which is 3–5 mm Hg for brain cells—the most sensitive to O_2 insufficiency [112]. When P_{O_2} in the intercellular fluid drops below this level (called the critical level), the rate of oxygen consumption by the cells is reduced, that is, to actual oxygen starvation.

Intake of O_2 into the tissues is determined mainly by diffusion; effectiveness of diffusion depends on its gradient in different sections of O_2 transport. Figure 12 shows the main step-cascades characterizing the normal diffusion gradients of P_{O_2} in different stages of O_2 transport.

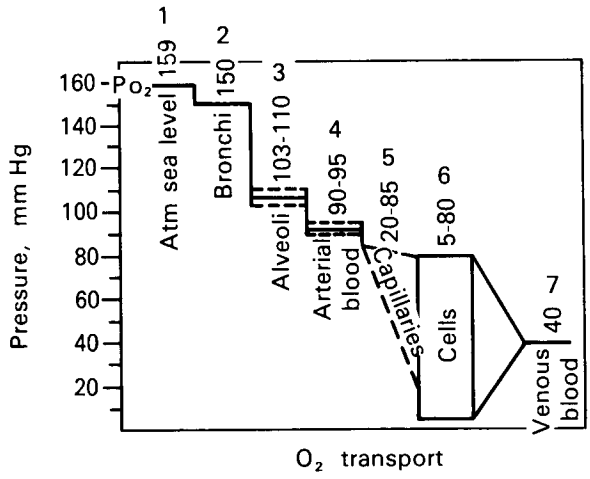

FIGURE 12.—Normal P_{O_2} values in different sections of O_2 transport in the organism.

When O_2 content in the AGA is reduced, just as when barometric pressure in the cabin is lowered, according to Dalton's law, P_{O_2} in the inspired air decreases which inevitably leads to decreased intake of O_2 in the tissues, that is, development of hypoxia. The cells farthest removed from the capillaries are the first to suffer, and diffusion of O_2 to the cells is the most reduced. With increase in hypoxia, the number of these cells undergoing actual oxygen starvation rises steadily, which is significant as a symptom of oxygen starvation.

In evaluating the clinical pattern of oxygen insufficiency, it must be remembered that underlying its pathogenesis—besides effects of hypoxia on cellular metabolic processes—adaptational shifts caused primarily by reflexive increase in pulmonary ventilation also play an essential role. Intensifying pulmonary ventilation promotes, in moderate hypoxia, preservation of P_{O_2}, but at the same time leads to hypocapnia and alkalosis, that is, to new homeostasis disturbances. In acute forms of oxygen insufficiency when severe pathologic states arise rapidly, during 1 to 2 min (after ascents to altitudes of 10 000 m and higher), significant hyperventilation cannot develop, and in the pathogenesis of these states only the oxygen deficit is decisive. In less acute forms of hypoxia, to which the organism can adapt in time (e.g., while remaining in mountains), in the pathogenesis of the functional disorders, including mountain sickness, adaptational shifts contribute to hypoxia, which leads to hypocapnia, disturbance of acid-alkaline equilibrium regulation, acute polycythemia, and so on.

The partial pressure of O_2 in alveolar air (P_{AO_2}) and the partial pressure of O_2, which is close to this value in arterial blood during (P_{aO_2}) indicate the severity of the hypoxic state. Accordingly, it is important to determine these indicators in ascents to various altitudes or when O_2 content changes in the AGA. An approximate calculation of P_{aO_2} relative to barometric pressure was first proposed in 1885 by Sechenov [181] while analyzing the causes of death of two French aeronauts who had reached an altitude of 8600 m in the Zenith balloon. He also considered a drop in P_{aO_2} to 20 mm Hg incompatible with short-term preservation of life. Later, calculation of P_{aO_2} was refined relative to P_{O_2} in ambient gas medium; in particular, the respiratory coefficient was corrected [61]. This quantity is calculated by the formula:

$$P_{aO_2} = (B - P_{H_2O}) \cdot C - P_{aCO_2}\left(1 - C \cdot \frac{1-R}{R}\right) \quad (6)$$

where P_{AO_2} is partial pressure of O_2 in alveolar air, B is barometric pressure, and

P_{H_2O} is partial pressure of water vapor in lungs, which depends only on temperature, and at body temperature of 37° C is 47 mm Hg,

P_{ACO_2} is partial pressure of CO_2 in alveolar air, C is concentration, percent content of O_2 in the AGA, and

R is respiratory coefficient.

The critical value of P_{aO_2} is also revised, based on experimental studies; it varies from 27 to 33 mm Hg [25, 112]. But the critical value of P_{O_2} in mixed venous blood is 19 mm Hg [112].

Significant and rapid decrease in P_{O_2} in the ambient gaseous medium is usually classified as acute hypoxia; as the result of which in healthy persons, but those not previously adapted to hypoxia, pathologic states of varying severity appear in a relatively short time. These effects are apparent after rapid ascents to altitudes of 4000–5000 m and higher or if the O_2 supply is suddenly cut off during altitude flights.

Data on acute hypoxic effects on animal organisms in rarefied atmosphere were first collected by Bert in 1878 [30]. When animals ascended to high altitudes in a pressure chamber they developed pathologic states, the severity of which depended on the decreasing P_{O_2} in inspired air and on the length of time the animals stayed in rarefied atmosphere. Cerebral activity disturbance was symptomatic of severe hypoxic states followed by irreversible disturbances in respiration and blood circulation.

The effects of hypoxia on CNS, shown by electrophysiologic investigations on intact cortices and neuronally isolated cortical flaps, are associated with the direct as well as the reflexive (via chemoreceptors) effects on neurons from O_2 insufficiency in the blood [34, 133]. In the initial period of oxygen starvation when hypoxemia is still relatively limited, stimulation of chemoreceptors with sinocarotid and aortal zones leads, simultaneously with stimulation of respiration, to raised functioning of the reticular formation of the brain stem and its subsequent activating influence on higher brain levels, including the cortex of the cerebral hemispheres [52, 133, 185].

Thus, the first phase of hypoxic influence on CNS is manifested in increased excitability of numerous brain structures. In the EEG, this phase of oxygen starvation is manifested in activation of the β-rhythm [10, 52, 133]. In this same phase of hypoxia, adaptive reactions are also manifested: intensified pulmonary ventilation, increases in heart rate and minute blood volume oriented toward increasing the O_2 transport to the tissues.

With significant degrees of hypoxia and O_2 tension in cerebral tissues dropping off, a second phase commences, characterized by deep disturbances of cerebral activity: complete inhibition of conditional reflexes, loss of active posture, clonus appearance, then tonic spasm [112, 113, 116]. At this time, the δ and θ-waves predominate in the EEG after which—with aggravation of hypoxia—a gradual suppression of bioelectric cerebral activity is noted [10, 112, 133, 156]. The δ-rhythm is accompanied by slowdown or total suppression of neuronal impulse. After restoration of normal oxygen supply, bioelectric activity of several neurons is no longer restored, evidently indicating their death.

Hypoxic reactions. Extensive experimental materials describe the development of acute oxygen starvation in man. Human responses during hypoxia in general are quite similar to those of animals. First, the extremely high sensitivity of CNS to hypoxia was revealed. Disturbances of CNS activity in man are manifested by: reduced intellectual capacity; disturbance in long-term memory; loss of concentration; disturbance of sensory organs, mainly sight; disturbance in coordination of sign movements (handwriting disorder); emotional changes—sluggishness, sleepiness, or in contrast, euphoria, sometimes resulting in loss of adequate response to the immediate environment [8, 57, 61, 132, 139, 163, 190, 191].

Symptoms of an acute, uncompensated hypoxic state can be classified into two symptom complexes [132]. In the first, the collaptoid state develops with bradycardia, drop in arterial pressure, and hyperhydrosis. Simultaneously, there are external changes of paleness or hyperemia, with sluggishness and disinclination to participate. Bioelectric brain activity changes slightly:

initial depression of α-rhythm in EEG followed by low amplitude of θ- and δ-waves, becoming visible against the β-rhythm.

These symptoms characterize relatively mild hypoxia, noted mainly after ascents to altitudes of 5000–6000 m, accompanied in many cases by growing discomfort. Sensations of oxygen, hotness in the head, vertigo, nausea, and appearance of a "gray film" are also noted. Switching to oxygen breathing at times for 5–10 min and longer does not lead to improvement, several functional disturbances are not recovered, and ECG indicators do not improve. Such manifestations suggest that hypocapnia sometimes makes different contributions to the genesis of this pathologic form.

The second symptom complex includes altitude fainting with symptoms of decreased intellectual capacity, loss of adequate evaluation of the immediate environment and physiologic condition, disturbance of motor coordination (handwriting disorder with clonic spasms which begin with hand muscles—writing spasms), and profound consciousness disorders including faints. These CNS disturbances are associated with increased pulmonary ventilation, sinus tachycardia, and some elevation of arterial blood pressure.

Changes in cerebral bioelectric activity are objective indicators of the development of this form of CNS hypoxic disorders [10, 50, 79, 133, 155]. The first visible handwriting disturbances and sluggishness coincide with EEG isolated and short groups of θ-waves of increased amplitude. Spasms and consciousness disturbances coincide in time with the predominant EEG of high-amplitude, slow oscillations of θ- and δ-waves [12, 79, 132].

When θ- and δ-rhythms predominate on the EEG, auditory and light signals or speech commands can temporarily suppress slow waves on the EEG, with partial recovery of work capacity and general improvement. Lack of EEG response to electrical stimuli and persistent θ- and δ-rhythms usually indicate profound consciousness disturbances [10 133].

Profound CNS disturbances develop without the victims' detection. For example, before ascent to a 7000-m altitude, subjects were instructed, in case of oxygen starvation signs, to use oxygen masks and breathe oxygen. Only two of 16 persons carried out the instructions, two other subjects noted that they were in need of oxygen, but did not use the readily available oxygen mask. The remaining 12 felt well during the entire test, despite CNS disorders—loss of consciousness and spasms.

When victims descend from altitude or breathe oxygen, there is rapid restoration of a normal physiologic state and the capacity for intellectual work (in 10–20 s). At this time, retrograde amnesia is noted—events immediately preceding loss of consciousness are not remembered, which can be puzzled out only from indirect data [9, 10, 133]. The insidious course of acute oxygen starvation led investigators to build automatic devices for signaling medical personnel that hypoxia of varying severity was developing [132, 163].

The two classifications of acute hypoxic symptoms formed the basis for an apparatus that automatically signals the development of acute hypoxia [132].

The onset of acute hypoxia in flight is a major danger, since at even relatively low altitudes (5200–6000 m), when oxygen supply is stopped, it can lead to death [9]. When acute hypoxia leads to prolonged or repeated loss of consciousness, the victims' return to normal does not always result in complete recovery. Cerebral edema resulting from hypoxia is evidently the main reason for such serious complications as encephalopathy and persistent disorders of memory and intellectual function [42].

O_2 *Protection.* Data are useful on the time required for retaining consciousness and the ability to work for periods at different altitudes without O_2 breathing, that is, when hypoxic states of different severity develop. This problem was studied pre-World War II mainly in the USSR and Germany. Soviet investigators determined generally the "altitude ceiling," that is, altitude at which disturbances of CNS activity appeared; consciousness disorders; and decreased work capacity during a continuous ascent in a pressure chamber [10, 184, 190]. German investigators introduced the concept of "reserve time," or the time during which a minimum level of work capacity adequate to take rescue measures

is still retained at the altitude after the O_2 supply has been cut off [109, 127, 156]. The term "time of useful consciousness" [8, 61] is referred to in US and British literature.

The reserve time – time of useful consciousness available at different altitudes is shown in Figure 13. Its value depends primarily on the altitude, also on individual resistance to hypoxia. With increase in altitude, individual fluctuations of the reserve time become narrower, which are virtually erased at altitudes above 9000 m [9, 186, 191]. At altitudes of 15 000 m and higher, the reserve time is practically absent (8–10 s). After rapid ascents (1–2 s) to these altitudes, whether air or pure oxygen is breathed, loss of consciousness without previous indications was noted in 15 s [9, 186].

When the time at these altitudes is limited to 8–10 s, followed by rapid descent, there is loss of consciousness in 5–7 s during the first descent – the blood with reduced O_2 content reaches the brain vessels in 5–7 s after start of the descent [127, 186]. The nearly complete absence of reserve time, similar to disappearance of the protective effect of O_2, is due to the fact that when the barometric pressure is reduced to 87 mm Hg (altitude of 15 200 m), P_{O_2} in the lungs equals zero, even if pure O_2 is breathed. The partial pressure of water vapor (P_{H_2O}) in alveolar air at body temperature (37° C) is 47 mm Hg, and P_{ACO_2} under normal conditions is close to 40 mm Hg. Thus, the overall pressure ($P_{ACO_2} + P_{AH_2O}$) is 87 mm Hg. Accordingly, the altitude of 15 200 m at which barometric pressure is

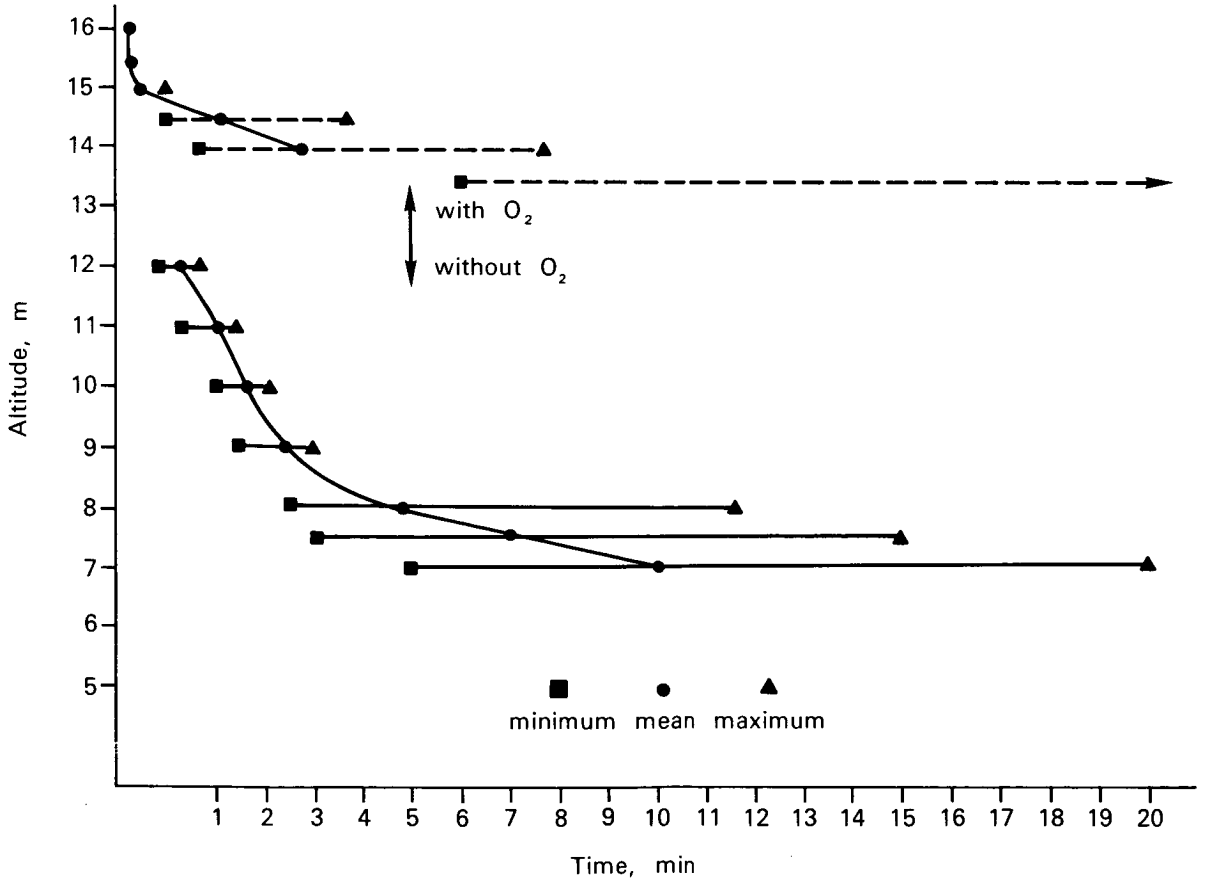

FIGURE 13. – Reserve time at altitudes of 7000–12 000 m (without using oxygen for breathing) and at altitudes from 13 000–16 000 m with O_2 breathing. (Graph plotted from [10, 186])

87 mm Hg, from the oxygen supplied to the organism, is regarded as "equivalent" to outer space.

As pressure is reduced [112, 113], the rate of deoxygenation in tissues must rise steadily, causing the reserve time to decrease also [113]. Animal experiments established that at altitudes exceeding 15 000 m, if the reserve time was shortened, it was negligible.

After cabin depressurization during space flight, an astronaut without protection of a space suit has an extremely short time (5–8 s) to evaluate the situation, reach a decision, and act on it. Severe pathologic states in acute hypoxia arise extremely rapidly—in 20–30 s. Further predictions can be based on animal experiments; animals succumbed in 1–2 min [112, 119].

In anthropoid apes, after 2–3 min in vacuum, subsequent recompression brought about recovery of a normal physiologic state [22, 106]. It is risky to extrapolate these data to predict a human's reactions under these conditions; the data only provide hope that in depressurization during flight, some time will remain for rescue.

Chronic Hypoxia

The establishment of minimum permissible P_{O_2} values in an AGA is essential to space medicine. The chronic effect of hypoxia was studied in detail in high mountain regions as well as in a pressure chamber; during moderate O_2 deficit in the inspired air, adaptive reactions developed. For this reason, after slow ascents, an individual who had previously remained at altitudes of 2000–3000 m for a number of days can remain at altitudes up to 4000–5000 m for quite a time while retaining relatively high work capability [9, 14, 15, 83]. These adaptive reactions can be conditionally divided into two groups.

One group of these reactions is directed toward increasing O_2 transport to tissues. Such reactions show hyperventilation, increased minute blood volume, and increased blood circulation in lungs and tissues, especially those sensitive to O_2 deficiency (brain and heart). There is also a rise in oxygen capacity of blood due to increased erythrocytes and hemoglobin, as well as resulting from adaptive shifts in oxygen-combining properties of hemoglobin due to increased content in erythrocytes of 2,3-diphosphoglyceric acid. Other causative factors are an increased number of functioning capillaries, as well as changes in membrane permeability leading to higher O_2 diffusion [61, 112, 132, 156, 172].

The second group of adaptive reactions is associated with restructuring of tissue metabolism including intensified glycolysis, which arises during hypoxia because the oxidative resynthesis of adenosine triphosphate (ATP) is disrupted and simultaneously ATP expenditure in tissues is increased. The functional activity of ATP rises sharply in heart, marrow, and motor musculature. This process in adaptation to hypoxia is probably limited, due to the low energy effectiveness of glycolysis. When one glucose molecule undergoes glycolytic degradation into two pyruvate molecules, only two ATP molecules are formed. In adaptation to hypoxia, the capacity of mitochondria to remove O_2 from oxygen-deprived intercellular medium intensifies, probably due to increased activity of cytochromes [14] or to their increased content [14, 141]. This type of adaptation is debatable.

The value has been shown of intensified synthesis of nucleic acids and proteins in heart and brain for adaptation to chronic hypoxia [141].

Erythropoesis increases and hemoglobin synthesis intensifies during chronic hypoxia as well as development of hypertrophy of the heart, especially of the right ventricle, indicating that protein synthesis is activated in tissues involved in the hyperfunction. The adaptational character of these reactions is obvious. When evaluating this concept of adaptation to long-acting hypoxia, it must be remembered that the synthesis of the nucleic acids and proteins intensifies in vitally important organs (in brain and heart) due to decreased importance of these processes in other tissues, including sex glands. This is evidently associated with reduced reproduction capacity and weight loss in persons at altitudes of 4000–5000 m and higher for long periods.

Study of the arrangement of villages in mountainous regions suggests that aborigines' adaptation to hypoxia is limited to altitudes of about 4500 m, which evidently is the natural limit of adaptation. Alpinists attempted to stay at an

altitude of 5800 m for many months in the Himalayas, which proved unsuccessful due to a break in adaptation. A chronic form of mountain sickness developed in spite of experienced participants in the expedition that included Hillary, who with Tensing, was the first to climb Mount Everest in 1953.

In the course of adaptation to moderate hypoxia or when it is interrupted, mountain sickness can develop. Its acute forms are manifested by: headache, dizziness, dyspnea, nausea, intestinal disorders, loss of fine coordination of movement, rapid fatigue when performing light physical work, sleepiness; and less often, euphoria, reduced intellectual capacity, and increased irritability. In chronic mountain sickness there is increasing poor health, progressive weight loss with pronounced negative nitrogen balance, sometimes acute erythrocythemia, hypertension of the lesser circulatory system, hypertrophy of heart, arterial hypotension, and sometimes reduced level of pulmonary ventilation.

In both forms of mountain sickness, symptoms of "disease adaptation" are manifested distinctly. In the acute form, there is the unfavorable effect of hypocapnia resulting from hyperventilation; in the chronic form, protein synthesis intensifies greatly in several structures, with simultaneous suppression of protein synthesis in most tissues.

Precaution against mountain sickness must be taken in designing an AGA. It is important to know when symptoms of mountain sickness can appear when there is slow reduction of P_{O_2} in the cabin.

A reduction in P_{O_2} to 120–110 mm Hg in an AGA while maintaining normal barometric pressure in the cabin is the assumed limit; exceeding this limit is not recommended. From investigations in mountains, it was noted that discomfort, especially when performing muscular work, and symptoms of mountain sickness in those in mountains for the first time, are manifested at altitudes of about 2000 m [42, 76, 142, 183].

The effect of various decompression rates simulating gas escaping from the cabin was studied; when pressure chamber pressure is reduced 0.1 m/s and less, symptoms of acute mountain sickness appear at altitudes of 4500–5000 m, that is, 8–13 h after the leakage begins. When O_2 content is reduced 1%/h in a cabin simulator with normal barometric pressure and normal air environment, followed by stabilization of P_{O_2} at 110 mm, subjects continue working satisfactorily for up to 48 h. When the P_{O_2} is stabilized in an AGA at 75–90 mm Hg, in 8–10 h most subjects experienced acute mountain sickness [140].

Individuals who have not previously been adapted to hypoxia can apparently work satisfactorily up to the second or third day only if they are in a gas medium equivalent in P_{O_2} to altitudes up to 3000–3500 m. Crewmembers in flight who perform physical work and simultaneously are in weightlessness, with its undesirable effects on the cardiovascular system and vestibular apparatus, must have an oxygen supply not lower than the level provided for an altitude of 2000 m, especially if the astronauts were not previously adapted to hypoxia.

Two of the devices for expanding human limits of adaptation to prolonged effects of hypoxia should be noted: preliminary conditioning for hypoxia in a pressure chamber or at high altitude [9, 39, 160, 190, 197, 198, 210]; and the addition of carbon dioxide gas instead of nitrogen when there is an O_2 deficit in the HEA.

The effect of adding CO_2 to the inspired gas mixture is favorable when there is acute hypoxia, which is manifested at altitudes up to 7000–8000 m [9, 112, 146, 186]. In a cabin simulator at normal barometric pressure, when the P_{O_2} in the AGA was reduced to 75–90 mm Hg, the addition of 2–3.5% CO_2 prevented acute symptoms of mountain disease, and maintained partial capacity for work up to the second day [134]. Such effects are produced by a rise in pulmonary ventilation resulting in increased oxygen saturation of arterial blood, and by partial elimination of hypocapnia. When there is irreversible reduction of P_{O_2} in a cabin AGA to approximately 1.5–2 times below the normal value, an increased CO_2 level in the AGA should be maintained—P_{CO_2} from 15 to 25 mm Hg [134].

Altitude resistance increases after conditioning in a pressure chamber, especially at high altitudes [39, 125, 160, 183, 197]. The extent of the effect is determined by the time length of con-

ditioning of subjects at certain altitudes versus stay at normal pressure. The question of how useful this conditioning can be is open for discussion.

Changes in individuals' physiologic states and work capacities for different P_{O_2} reductions in the AGA are shown in Figure 14. These data provide a general outline for evaluating the effects of hypoxia relative to the extent of manifestation.

HYPEROXIA–TOXIC EFFECT OF OXYGEN

The toxic effect of oxygen is vital to space medicine and biology since the spacecraft cabin AGA can contain a higher P_{O_2} than in atmospheric air.

Increased P_{O_2} values are used in an effort to utilize a technically most convenient one-gas medium as an AGA with sufficiently high pressure to prevent ADS, and with an O_2 reserve necessary when gas leakage from the cabin increases. This is exemplified by the AGA in Mercury, Gemini, and Apollo spacecraft where P_{O_2} was 258 mm Hg. In certain flight stages, P_{O_2} in the AGA can be much higher; for example, before transition of the crew into an AGA with lower barometric pressure for desaturation of N_2 or another inert gas. Besides planned increase of P_{O_2} in an AGA, heightened P_{O_2} in the AGA can result from improper operation of the regeneration unit.

Studies on the toxic effects of O_2 under normal

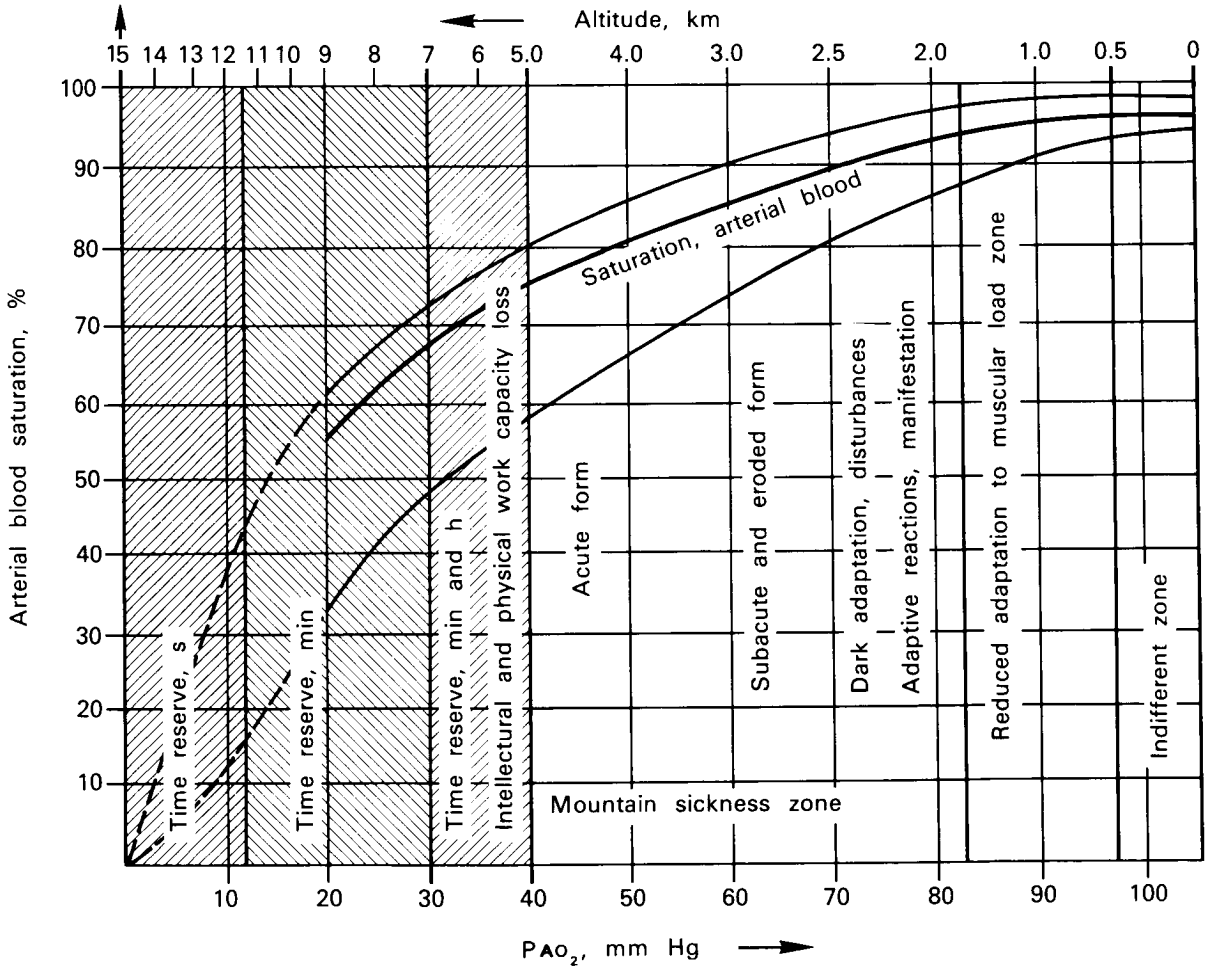

FIGURE 14.–Effects of different altitudes on a person previously unadapted to hypoxia. (After [25, 170])

or reduced barometric pressure are significant in space biology and medicine, since barometric pressure that exceeds normal atmospheric pressure will scarcely be maintained in spacecraft cabins.

An early observation in the study of O_2 toxic effects on living organisms was made by Priestley in 1775, ". . . that although dephlogisticated air can prove highly useful as a medicine, it nonetheless would not be as suitable for us in the ordinary healthy state of the body: like a candle burns faster in dephlogisticated air than in ordinary air, thus also we can live too fast and our vital forces will be too rapidly expanded in this purified air."

Experimental data on the effects of high O_2 concentrations on living organisms were presented by Bert in 1878 [30], who concluded that O_2 in high concentrations is a "general-protoplasmic" poison, exerting a toxic effect on plant and animal cells. This hypothesis was later confirmed [44, 63, 78, 87, 102, 122, 215]. In spite of many years' study of the toxic effect of O_2, information is still inadequate on biochemical changes determining symptoms of oxygen intoxication. Chance et al [44] noted changes in the oxidation-reduction state of reduced nuclear pyridine, and the energetic pathway of pyridine nucleotide reduction in mitochondria of rat liver and guinea pig heart. The oxidation of enzymes or coenzymes containing SH-groups are assumed to be important in the toxic effect mechanism of O_2 at the cellular level, which may be associated with earlier injury when cellular membranes undergo hyperoxia.

Experiments with enzymes containing SH-groups being inactivated in vitro (such as succinic dehydrogenase) are not always confirmed by experiments conducted in vivo. Most enzymes in the organism are evidently protected against the toxic effect of O_2 by their own substrate-coenzymes and other compounds that are permanently in cells [87, 122, 215]. It has remained unclear whether the mechanism of the O_2 toxic effect on a cell includes the influence of O_2 molecules as such, or whether it is associated with the effect of other free radicals produced during hyperoxia.

The mechanism of the O_2 toxic effect is attributed by many to free radicals, which evidently form H_2O_2 and organic peroxides, breaking intramolecular bonds of enzymes containing sulfhydryl groups [78, 87, 102, 215]. This hypothesis is based on increased formation of free radicals in the animal tissue and hyperoxia, and on the possibility of reducing the O_2 toxic effect, in particular, injury to erythrocyte membranes, by administering antioxidants (mexamine, tocopherol—vitamin E, and so on) to inhibit the action of free radicals [100, 101, 102, 215].

Symptoms of the O_2 toxic action, to be understood, require knowledge of the action mechanism of hyperoxia in various organic functional systems. Figure 15 of the Lambertsen scheme, modified according to studies [78, 102, 215], illustrates the mechanisms of O_2 toxic action on animals and humans.

Investigations with humans and animals established that O_2 toxic action depends on the P_{O_2}, length of time in the hyperoxic medium, and sensitivity of animal and man. The latent period of manifesting the O_2 toxic effect differs for various tissues and also depends on P_{O_2}.

Relative to P_{O_2} in the AGA, there are three zones with different manifestation of O_2 toxic action.

1. When O_2 is 1500–2000 mm Hg and higher, symptoms of poisoning are manifested, typical of attack on the CNS: nausea, dizziness, visual disturbances, and local and generalized clonic spasms. There are pathologic changes in blood circulation and respiration. Thus, Wood et al [205] discovered a sharp rise in arterial pressure in animals subjected to hyperbaric pressure, evidently of neurogenic origin; cardiac insufficiency with pressure rise in lesser circulation vessels, also probably the cause of primary disturbance of the pulmonary capillaries structure and subsequent acute pulmonary edema.
2. When P_{O_2} is 760–400 mm Hg, the O_2 toxic action is primarily an attack on respiratory organs: irritation of the upper respiratory tracts, including bronchitis, then pulmonary inflammation and edema.
3. For P_{O_2} of 400–280 mm Hg, prolonged stay in an AGA can evidently cause

changes in respiratory organs, blood, and lymph tissues.

Considering astronautic activity, it is important to determine the maximum permissible P_{O_2} at which the O_2 toxic effect is not yet manifested, for setting standards of O_2 content in AGA. When animals remain in virtually pure oxygen under normal barometric pressure, they die from pulmonary inflammation.

White rats, which are highly sensitive to the toxic action of O_2, were tested to establish the morphologic change sequence in lungs during different periods in the hyperoxic AGA. When P_{O_2} was 1 atm, the animals showed: atelectasis—in 1 h; disturbances of capillary structure and changes in their permeability—in 3 to 6 h; pulmonary edema, thickening of alveolar membranes, enlarged capillaries, and diapedetic hemorrhages—during the first day; pulmonary hyperemia and foci of inflammation—in 1.5 d; further inflammation, leading to "hepatization" of lungs—in 2–2.5 d [105, 111, 153].

Pulmonary inflammation resulting from hyperoxia is assumed to lead inevitably to hypoxia, culminating in death [13, 122, 153]. Genin et al dispute this view [72]; they detected high O_2 tension in cerebral tissues of animals during development of severe hyperoxic toxicosis along with pulmonary inflammation.

Pathologic changes in lungs of rats depend mainly on P_{O_2} in the AGA. An animal which was exposed to pure oxygen developed inflammation in lungs by the second or third day; when O_2 content in the AGA was reduced to 75% (P_{O_2}= 570 mm Hg), the lung inflammation was noted after 2–3 weeks, and in 50–60% O_2 content in the AGA, no lung damage was detected in spite of 30 days spent in this medium [13, 38, 43, 111, 215].

When P_{O_2} increases slightly in the AGA, the primary toxic effect is pulmonary atelectasis [130, 136]. This was concluded from experiments with rats exposed to an AGA consisting almost entirely of O_2 under reduced barometric pressure. The atelectases led to the death of several animals.

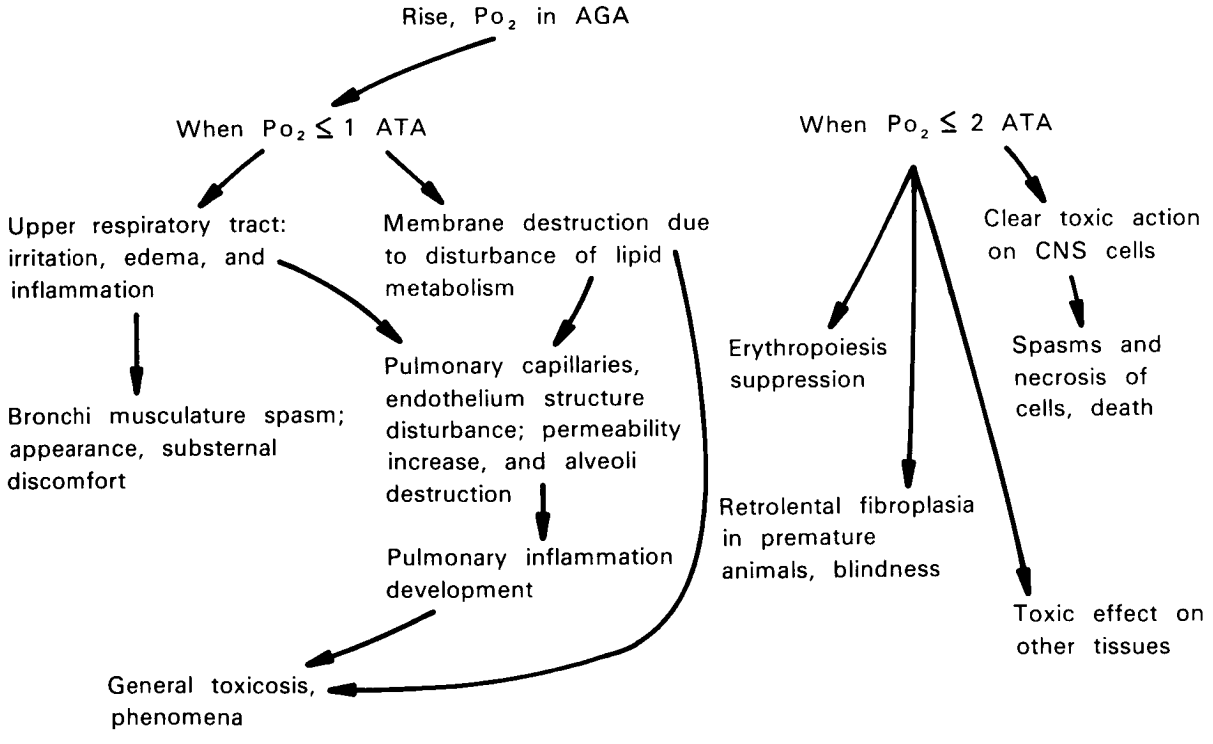

FIGURE 15.—Mechanism of oxygen toxic action on humans and animals. (After [122] modified)

Atelectases developed also in humans breathing pure oxygen [13, 59, 73], caused by mucus congestion in the smaller bronchi. This causes the O_2, from the alveoli associated with the congested bronchus, to diffuse rapidly into the blood. The rate of alveoli collapse depends on the chemical composition of the gases filling them; collapse is slowed when N_2 and other inert gases are present. DuBois et al [59] noted individual differences in predisposition to atelectases, which they attributed to dissimilar patency of air passages.

It is not established that pulmonary atelectases are associated primarily with the toxic effect of O_2; it probably develops from the absence of N_2 gas or another inert gas in alveoli. When elevated P_{O_2} values persist in the AGA, addition of a small amount of a biologically inert gas to the AGA prevents pulmonary atelectases [59, 61, 180, 215]. It was noted in animal experiments that toxic effects of O_2 can develop into "oxidative" and hemolytic anemia, which evidently results from the accelerated breakdown of erythrocytes and simultaneous suppression of hemopoiesis.

In morphologic investigations, changes in red cell growth were noted in animals and man in hyperoxic AGA, indicating suppression of erythropoiesis. Changes were also detected in erythrocyte structure—appearance of sickle-shaped evaginations—acontocytosis, providing grounds to conclude that damage to erythrocyte membranes, like suppression of erythropoiesis, is caused by O_2 toxic action. Administering an antioxidant—vitamin E—prevented damage to erythrocytes [100, 101]. These data apparently were confirmed somewhat in humans; when astronauts completed Gemini 4, 5, and 7 flights, a reduction of hemoglobin and erythrocyte content in peripheral blood was noted [29, 65]. In spite of these results, there are not yet adequate grounds to associate anemia only with the toxic effect of oxygen. Its onset can be caused by the effects of other flight factors as well.

It has also been stated that when there is a slight rise in P_{O_2} (300 mm Hg), the toxic action of O_2 leads to suppression of the immunity system, causing pathologic changes in lymph tissues [103, 161].

The maximum permissible O_2 concentrations, establishing the upper limit of P_{O_2} in AGA where man and animals may remain for long periods, has not been adequately studied. Before hyperoxic AGA was used in spacecraft cabins (P_{O_2}= 258 mm Hg), its effect on animal and human organisms was studied by US investigators [38, 90, 145, 202]. The studies (one lasting 8 months) permit the conclusion that remaining in an AGA with P_{O_2}=258 mm Hg does not cause profound pathologic disturbances, but probably has some unfavorable effects; periodic morphologic changes in internal organs of animals have been noted [101]. The same conclusion was reached in mice experiments conducted with Gramenitskiy. After 23 days in an AGA with P_{O_2} = 260–280 mm Hg and a total pressure of 720 mm Hg, experimental animals, not differing visibly from the controls, succumbed much faster than the controls when placed subsequently in a hyperbaric medium of 4 atm with 98% O_2 content. An autopsy revealed acute hyperemia and pulmonary edema.

Functional Changes

To evaluate the significance of changes in various functional systems during hyperoxia, and to set up means of increasing resistance, the mechanism of the O_2 toxic effect must be understood as well as if there is adaptation to this factor, and its manifestations. This problem is still in the initial stage of study.

Adaptational shifts were studied in animals remaining for a long time in an AGA with elevated P_{O_2}. Animals were placed in an AGA with elevated P_{O_2} followed by prolonged exposure to virtually pure O_2 at a pressure of 760 mm Hg. The results were not well-defined: increased lifespan was noted in the conditioned animals, while in others a reliable effect was absent, nor were acute manifestations of the O_2 toxic action noted in the conditioned animals [11, 83, 215].

The functional state of the adrenal glands is important in the mechanism of nonspecific adaptation to various unfavorable factors. On the question of adaptation to hyperoxia resulting from nonspecific adaptational reactions, investigations are significant on the effect of O_2 toxic action in animals with adrenals removed. The

results of these investigations are contradictory. When high O_2 pressures were used (3 atm and higher), increased resistance to hyperoxia was noted in adrenalectomized animals [18, 81]. But in another study [135], there was depressed resistance to hyperoxia in adrenalectomized rats exposed to an AGA with Po_2 of 690–720 mm Hg. Toxicity associated with lung damage was manifest in the operative animals earlier, and progressed to a more severe form than in intact animals.

In normobaric hyperoxia, in contrast to hyperbaric hyperoxia, the mechanism of nonspecific adaptation plays a definite role. Differences in the mechanism of O_2 toxic action at high oxygen pressures and with normal barometric pressure also evidently determine the different effects of adrenalectomy. From a generalization of the literature, animal and human organisms exhibit adaptive reactions to normobaric hyperoxia, but with low effectiveness.

Information on the toxic action of hyperoxia is important in AGA design. Considerations of this matter are difficult because precise criteria for O_2 toxic action are lacking; i.e., symptoms indicating that continuing in a hyperoxic medium will endanger health. The question is further complicated by differences in individual resistance to hyperoxia, and other flight factors that influence resistance to hyperoxia.

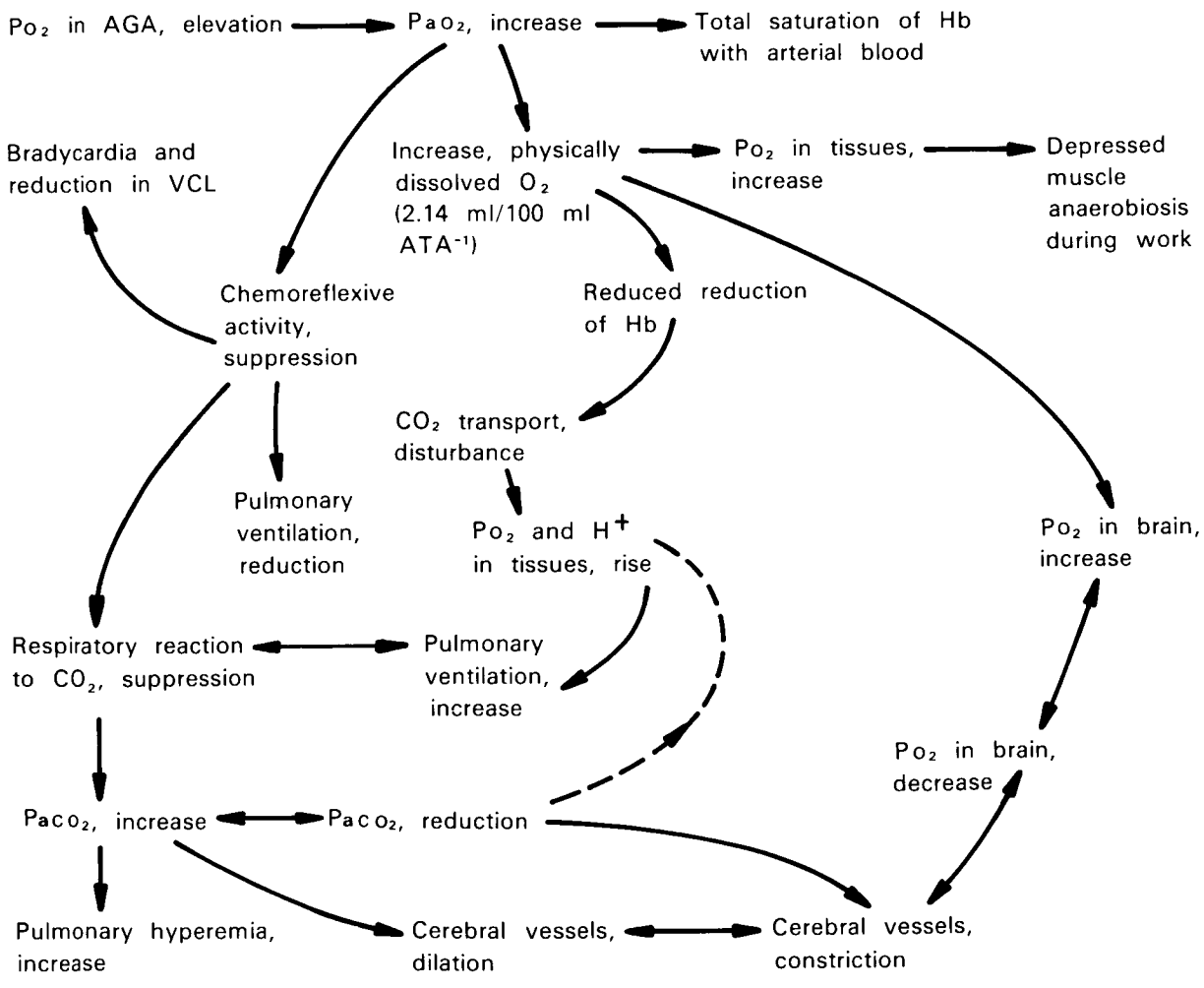

FIGURE 16.—Physiologic shifts on hyperoxia. (After [122])

The physiologic and pathophysiologic mechanisms of the hyperoxic effect on the human organism must be clarified to substantiate earlier criteria on manifestation of O_2 toxic action. Figure 16 shows diverse reactions to hyperoxia, some of which must be considered adaptive since they tend to reduce O_2 transport to tissues. This involves decreased pulmonary ventilation, heart rate, reduced minute blood volume, and narrowing of cerebral vessels. Such reactions start during the first minutes in a hyperoxic medium [47, 75, 215]. Some reactions (decreases in heart rate and minute blood volume) persist for almost the entire time spent in the AGA with elevated P_{O_2}, others gradually disappear. In the initial period of hyperoxia when subjects breathe pure oxygen under normal barometric pressure, pulmonary ventilation is reduced an average 10%, evidently due to inactivation of chemoreceptors in the sinocarotid zone [75, 122, 215]. This effect persists until there is a gradual rise in pulmonary ventilation. This increase is due to retention in tissues of CO_2 produced from reduced transport by blood, which is associated with less content of reduced hemoglobin in blood.

A decrease in vital capacity of the lungs (VCL) during hyperoxia is a significant symptom for early diagnosis of O_2 toxic action. A 20–30% reduction or more in VCL indicates pronounced toxic action of O_2. Such a significant drop usually develops immediately before chest pains or when subjects have chest pain during deep inspiration; that is, during pronounced development of oxygen intoxication.

Since pulmonary pathology is the most important factor limiting man's remaining in AGA with added P_{O_2}, gas exchange parameters and biophysiology of lungs, such as diffusion capacity and extensibility, should help in early diagnosis of O_2 toxic action.

Data are limited and contradictory on changes in the diffusion capacity of lungs (D_L) in hyperoxia. Some authors find no changes in this indicator when several hours are spent in an O_2 medium with pressure of 1 atm; there are also studies establishing decreased D_L while in this kind of AGA. A decrease in an individual's D_L was evident 3 h after he began breathing pure oxygen under normal barometric pressure. A clear reduction in D_m was detected, indicating that this was caused by changes in permeability of lung membrane [25].

Genin [70] also noted progressive reduction in D_L during 24 h O_2 breathing at 1 atm pressure, beginning the 8th hour. In several subjects, in 24 h, D_L reduction was 12%. No reliable correlation was established between this indicator and manifestation of O_2 toxic action. A reduction in extensibility of lungs was also noted, averaging 16%. Extensibility of lungs is an integral indicator, which depends on the elastic properties of the pulmonary parenchyma, condition of hyperemia in lungs, and surface tension of the liquid film underlying the alveoli. Evidently, reductions in extensibility of lungs and in the VCL during hyperoxia are associated with development of atelectases and, possibly, with increased hyperemia of lungs. Thus, changes in D_L and extensibility of lungs can have significance in evaluating O_2 toxic action, but it is difficult to use this indicator in practice.

Clinical Symptoms

Clinical manifestations of O_2 toxic action include coughing, dryness in mouth, and thoracic pain, which indicate pronounced oxygen intoxication. The symptoms, especially the chest pains, usually are signals to end the investigations. This is because chest pains, after starting, usually intensify and are accompanied by pains in intercostal muscles, dyspnea, and worsening of the subject's general condition [47, 75, 202]. Chest pains and substernal discomfort are associated with atelectases, and possibly with bronchial spasm. The bronchial mucosa is probably involved also.

Chest pains are often preceded by irritation of the upper respiratory tracts: dryness in the mouth, tickling in the nasopharynx, and coughing. In 6 to 12 h after the investigation and removal from the hyperoxic medium, these phenomena and chest pains disappear completely. However, irritation of the upper respiratory tracts should be heeded since this manifestation has preceded acute tracheobronchitis and pulmonary inflammation [20, 75].

When P_{O_2} in the AGA is elevated (up to 1 atm),

individual differences are noted in sensitivity to O_2 toxic action [59].

When oxygen was breathed (1 atm) for 24 h [75], O_2 toxic action was not noted in all subjects; the observations were made at different intervals. Figure 17 shows the incidence and time of upper respiratory tract irritation and chest pains [75].

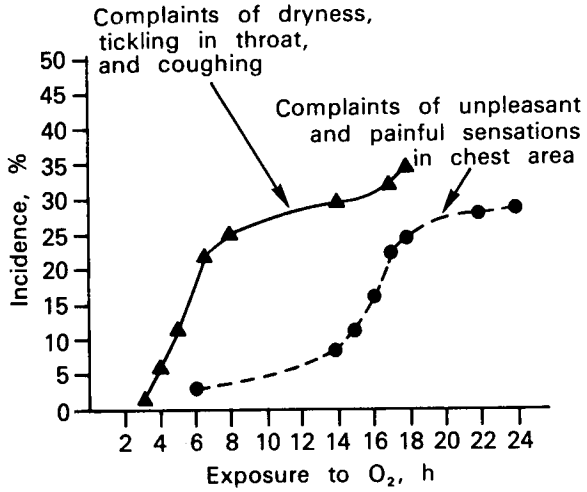

FIGURE 17.—Dynamics of various oxygen toxic action symptoms during 24 h of oxygen breathing. (After [75])

Individual differences in manifestation of O_2 toxic action are probably the reason for discrepancies in the literature on the limit to O_2 toxic manifestation. For example, Genin, Zharov, et al [72] did not detect symptoms of O_2 toxic action after 30 days in an AGA with P_{O_2} equal to 290–280 mm Hg, while Welch [202] found O_2 toxic action during less time in an AGA with lower P_{O_2} (200 mm Hg). Such individual differences in sensitivity to hyperoxia make it difficult to determine the maximum permissible O_2 content in cabin AGA for long flights.

P_{O_2} in AGA

The time when O_2 toxic action appears depends on P_{O_2} in the AGA and it decreases as O_2 increases. Figure 18 shows the time and nature of O_2 toxic action manifestation for different P_{O_2} values in the AGA. Remaining in an AGA with slightly elevated P_{O_2} (200 mm Hg) for 220 h can lead to toxic action of oxygen in some individuals [202]. Since some individuals have high sensitivity to O_2 toxic action, an AGA with P_{O_2} exceeding its value in atmospheric air can scarcely be considered for flights of many months [75, 215]. The causes of different individual sensitivities to hyperoxia have not been adequately studied; there are no reliable criteria for selecting highly sensitive persons, nor are there agents to increase resistance.

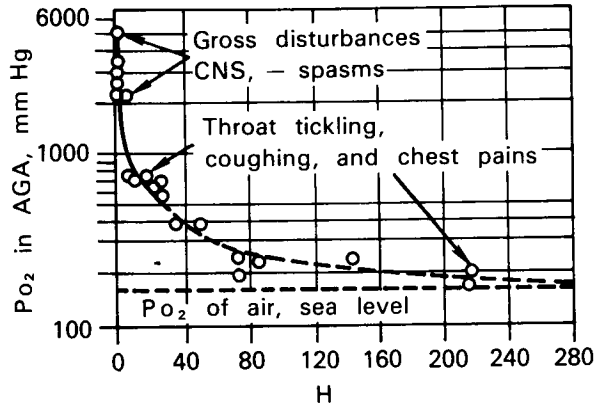

FIGURE 18.—Time of oxygen symptoms toxic action as a function of P_{O_2} in AGA [170].

Thus, the upper limit of P_{O_2} in AGA for flights of many months has not yet been determined. However, studies of O_2 toxic action suggest that the limit to the toxic action decreases steadily, and at present it can only be determined hypothetically in the range of P_{O_2} values in AGA, at which P_{AO_2} increases approximately 150 to 200 mm Hg.

Additional information must be obtained to establish precisely the upper limit of the P_{O_2} in an AGA. There are no data on the influence of physical labor on resistance to hyperoxia, the effects of increase and decrease in ambient temperature, and other flight factors.

When flights in high-radiation zones are necessary and whenever crewmembers may be exposed to ionizing radiation, an elevated P_{O_2} in the AGA probably would prove undesirable. This is based on animal experiments where increased sensitivity to ionizing radiation was established during a hyperbolic AGA [170, 215].

To explain this effect, there is a certain similarity between the mechanism of O_2 toxic action on tissues and the mechanism of ionizing radiation toxic action on tissues.

Thus far we have not discussed the question of whether the sensitivity of an organism to increased O_2 content in an AGA can be affected by such an important flight factor as weightlessness. There are reasons to assume that weightlessness, just like physical labor, or temperature influences, can lead to some elevation in an organism's sensitivity to hyperoxia. One of the adaptive reactions in hyperoxia is constriction of brain, heart, and lung muscles to reduce oxygen transport to tissues of these organs. In weightlessness, there is a blood flow redistribution, and an increase in hyperemia of areas above the heart, hence the above-noted adaptive vascular reactions probably cannot be fully manifested.

In prolonged flights, besides man, plants and various species of animals will be present that may prove highly sensitive to hyperoxia. Accordingly, information is needed on O_2 toxic effects on plant and animal species for use in flights.

HYPERCAPNIA–CO_2 TOXIC EFFECT

During space flights, emergency situations reducing the effectiveness of the AGA regeneration system cannot be entirely avoided. Carbon dioxide in the AGA can increase at different rates to different levels, hence study of its toxicity on the human organism is essential for space biology and medicine.

Man is the source of CO_2 in the gas medium of a hermetic cabin since CO_2 is one of the main end products of metabolism in animal and human organisms. At rest, man gives out about 400 l CO_2/d; during physical labor, CO_2 and its corresponding excretion from the organism is considerably higher. In addition, CO_2 is continuously formed during rotting and fermentation. Carbon dioxide gas is colorless, has a faint odor, and acidlike taste. When several percent of CO_2 accumulate in the AGA, it cannot be detected by man. Its properties (odor and taste) can be detected only at extremely high concentrations of the gas.

Breslav [37] showed that subjects exposed to a "free choice" of gas medium began to avoid an AGA only when P_{CO_2} in it exceeded 23 mm Hg. Here the CO_2 detection is not associated with odor and taste, but with the effect on the organism, especially a rise in pulmonary ventilation and reduction in physical work.

The terrestrial atmosphere contains a small amount of CO_2 (0.03%) from turnover of matter. A tenfold increase of CO_2 in inspired air (to 0.3% [sic]) does not yet have a marked effect on human vital activity and work capacity [83, 138, 179]. Man can exist in this gas medium for a very long time, maintaining normal health and a high work level. This is due to CO_2 formation in tissues during vital activity. The gas is subjected to significant fluctuations, exceeding by tenfold changes of this compound in inspired air. A substantial increase of P_{CO_2} in an AGA causes predictable changes in physiologic state; these changes are due mainly to functional shifts in the CNS, respiration, blood circulation, acid-alkaline equilibrium, and disturbances in mineral metabolism. The functional shifts during hypercapnia are determined by the level of P_{CO_2} in the inspired gas mixture and its action time on the organism.

Acute Hypercapnia

Bernard showed that severe pathologic states in animals, after being in hermetically closed, unventilated rooms for a long time, are associated with CO_2 increase in inspired air. The physiologic and pathologic action of CO_2 was studied in animal experiments [28].

A physiologic mechanism of the hypercapnia effect is evident in Figure 19.

When remaining in AGA where the P_{CO_2} reaches 60–70 mm Hg and higher, physiologic reactions and CNS reactions change appreciably. With CNS changes (besides the stimulating influence shown in Figure 19), hypercapnia has a sedative action and leads to a narcotic state which develops rapidly when P_{CO_2} reaches 100 mm Hg and higher.

Intensified pulmonary ventilation, when the CO_2 in an AGA rises to 10–15 mm Hg and above, is determined by at least two mechanisms:

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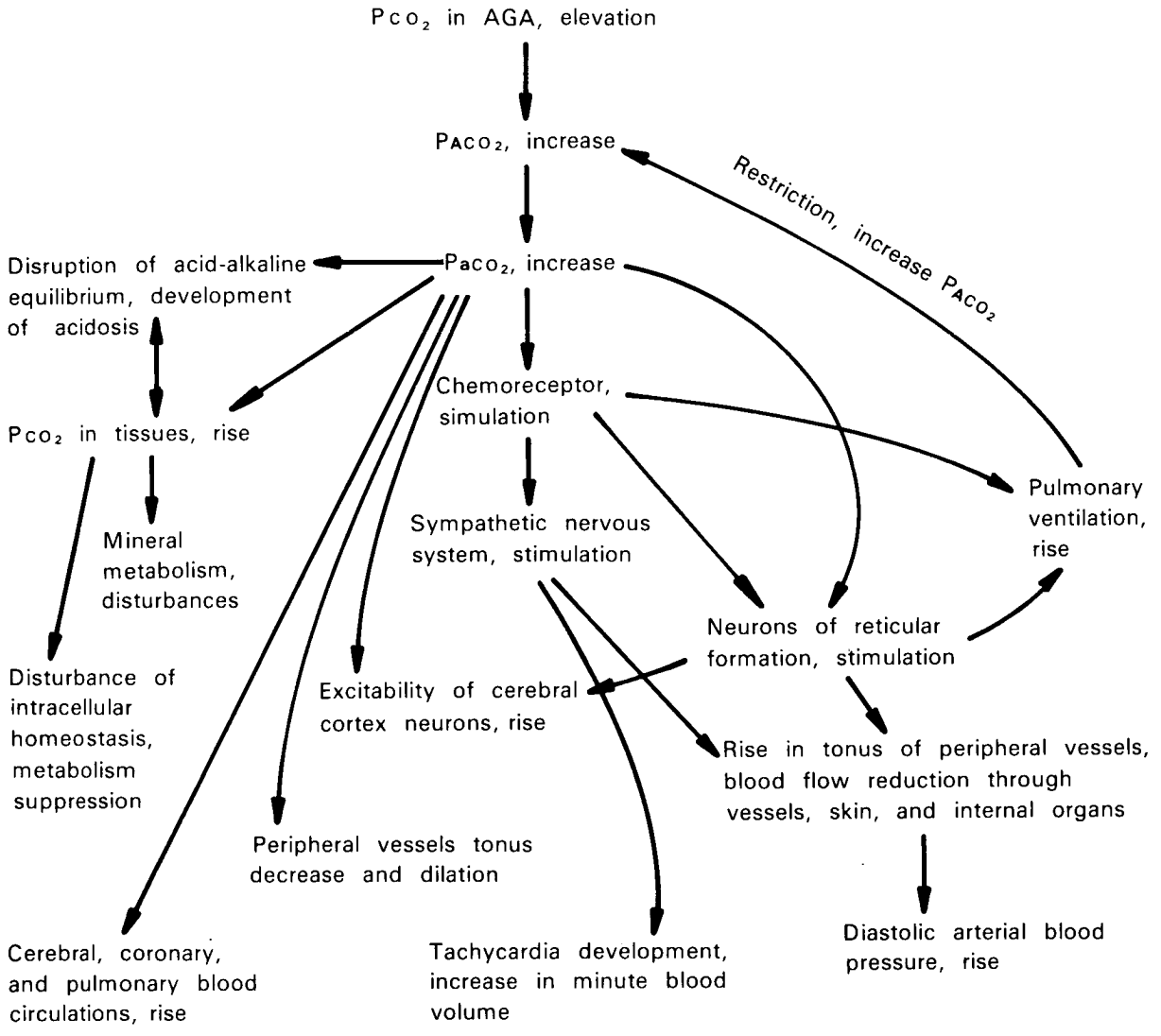

FIGURE 19.—Mechanisms of physiologic and pathophysiologic action of CO_2 on animals and humans.

reflexive stimulation of the respiratory center with vascular zone chemoreceptors (especially those of the sinocarotid zone), and stimulation of the respiratory center with central chemoreceptors. The main adaptive organism reaction maintaining the P_{aCO_2} at a normal level is increased pulmonary ventilation during hypercapnia. Effectiveness of this reaction diminishes as P_{CO_2} is increased in the AGA, since, in spite of the steadily intensifying pulmonary ventilation, P_{aCO_2} also rises steadily.

Increased P_{aCO_2} has an antagonistic effect on central and peripheral mechanisms regulating vascular tonus. The stimulating action of CO_2 on the vasomotor center and the sympathetic nervous system determines the vasoconstrictive action and leads to increased peripheral resistance, quickened heart rate, and increased minute blood volume. Simultaneously, CO_2 has a direct effect on vessel muscle walls, promoting their dilation. Interaction of these antagonistic influences then determines ultimately cardiovascular system reaction during hypercapnia. It can be concluded that upon a sudden drop in

the central vasoconstrictive action, hypercapnia can lead to collaptoidal reactions, which have been observed in animal experiments at a considerable CO_2 elevation in AGA [138].

When there is a great P_{CO_2} increase in tissues, which inevitably develops at a considerable P_{CO_2} elevation in AGA, a narcotic state accompanies a drop in metabolism. This reaction can be considered adaptive, because it sharply reduces CO_2 formation in tissues during the period when the transport systems, including the blood buffer systems, are no longer able to sustain Pa_{CO_2}—the most important constant of the internal environment at a near-normal level.

The threshold of the reactions of various functional systems differ in the development of acute hypercapnia. Thus, hyperventilation becomes evident when P_{CO_2} in the AGA is raised 10–15 mm Hg, and at 23 mm Hg, this reaction is pronounced—ventilation increases nearly twofold. Tachycardia and elevated arterial blood pressure are manifested when P_{CO_2} in the AGA reaches 35–40 mm Hg. Narcotic action was at still higher values of P_{CO_2}, 100–150 mm Hg, in the AGA while CO_2 stimulation on cerebral cortex neurons was noted when P_{CO_2} was 10–25 mm Hg. Effects of various P_{CO_2} levels in the AGA on the organism of a healthy individual can be examined.

When practically healthy persons were in AGA with excess P_{CO_2} levels, the investigations were highly significant in evaluating resistance of an individual's hypercapnia and in setting CO_2 standards. The nature and dynamics of reactions of CNS, respiration, and blood circulation were established, as well as changes in work capacity at different P_{CO_2} levels in the AGA.

No appreciable shifts in physiologic state were found, despite slight respiratory acidosis, when an individual was in AGA with P_{CO_2} to levels of 15 mm Hg for relatively short intervals. Persons retain normal intellectual work capacity and do not complain of deteriorating condition when in such an environment for several days. Some subjects showed reduced physical work capacity, especially when performing heavy work, when the P_{CO_2} was 15 mm Hg.

Increased P_{CO_2} in the AGA to 20–30 mm Hg caused respiratory acidosis and increased pulmonary ventilation. After a relatively short rise in the rate at which psychologic tests were performed, reduced intellectual work capacity was observed. The ability to perform heavy physical work was markedly diminished and there was disturbance in night sleep. Subjects complained of headaches, dizziness, dyspnea, and lack of air sensation on performing physical work [131, 180].

When P_{CO_2} in the AGA was raised to 35–40 mm Hg, pulmonary ventilation of subjects increased three times and higher. Functional shifts appeared in the circulatory system: the heart rate and arterial pressure increased. Subjects complained of headache, dizziness, vision disturbance, and loss of spatial orientation after brief periods in this AGA. Performing even light physical work involved considerable difficulties and led to acute dyspnea. Psychologic tests proved difficult, and intellectual work capacity diminished. When P_{CO_2} in the AGA was raised above 45–50 mm Hg, acute hypercapnic disorders arose rapidly—in 10 to 15 min [42, 46, 131].

Generalization of data is difficult on man's resistance to CO_2 toxic action and the maximum permissible time in an AGA with increased CO_2 content. An individual's resistance to hypercapnia depends largely on his physiologic state and the level of physical work. Investigations were mostly with subjects at rest and psychologic tests were performed only periodically.

Zones of Hypercapnia Toxic Action

Based on studies, four zones of hypercapnia toxic action in relation to P_{CO_2} level in the AGA (Fig. 20) have been suggested.

The P_{O_2} rate of increase in the inspired gas mixture is vital to physiologic reactions and resistance to hypercapnia. When placed in an AGA with a high P_{CO_2} level, just as when the individual is switched to breathing a gas mixture enriched in CO_2, Pa_{CO_2} rises rapidly accompanied by more acute hypercapnic disorders than when P_{CO_2} in the AGA is slowly elevated. Fortunately, the latter is more characteristic of a CO_2 toxic effect under spaceflight conditions, since the increasing volume of spacecraft cabins permits a relatively slow rise of P_{CO_2} in the AGA whenever the air regeneration system breaks down. More acute hypercapnia can occur

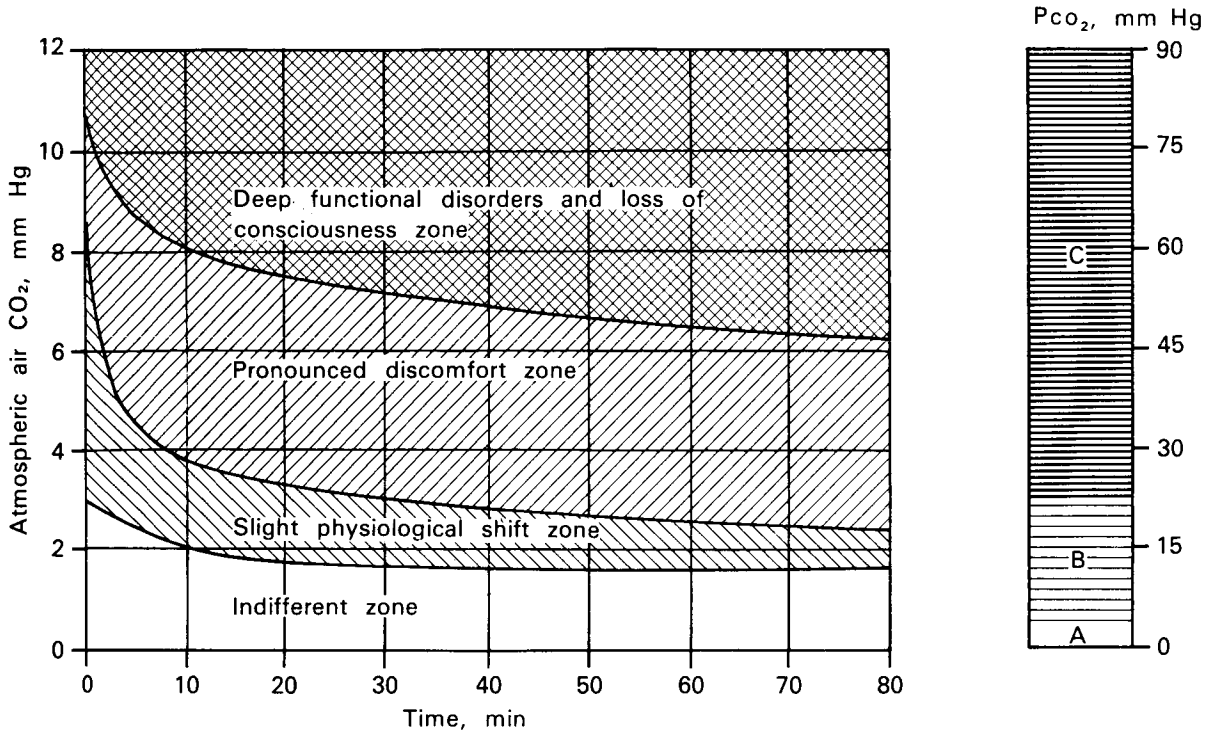

FIGURE 20.—Classification of CO_2 toxic action effects in relation to P_{CO_2} value in AGA. (Graph plotted from [25])

when the space suit regeneration system malfunctions. In acute hypercapnia, the difficulty of precisely delimiting the zones determining the qualitatively different manifestations of CO_2 toxic action, relative to P_{CO_2}, is associated with "primary adaptation" phase, the duration of which is the longer, the higher the CO_2 concentration [131]. After an individual's rapid entry in an AGA with a high CO_2 content, pronounced shifts develop in the organism, which are usually accompanied by complaints of headache, dizziness, spatial orientation loss, vision disturbance, nausea, lack of air, and chest pains. Hence, investigation is often discontinued 5 to 10 min after the subject has entered the hypercapnic AGA.

When P_{CO_2} in the AGA is raised to 76 mm Hg, this unstable state gradually passes and a seemingly partial adaptation to the altered gas medium develops [131]. Some normalization of intellectual work function is noted in subjects who complain less of headaches, dizziness, visual disturbances, and so forth. Duration of the unstable state is determined by the time during which P_{aCO_2} increases and continuous rise in pulmonary ventilation is noted. Soon after stabilization at the new level of P_{aCO_2} and pulmonary ventilation, a true adaptation begins, accompanied by improved well-being in the general state of subjects. Considerable deviations in evaluation by different investigators of possible time limit of man under high P_{CO_2} in the AGA is caused by the dynamics of acute hypercapnia.

Unfortunately, in evaluation of various P_{CO_2} level effects (Fig. 20), "primary adaptation," although recorded in time, still does not show that the physiologic state of an individual differs in different periods in an HEA with high CO_2. The results shown in Figure 20 were obtained while subjects were resting. Accordingly, these data, without appropriate correlation, cannot be used to predict physiologic changes of astronauts when CO_2 accumulates in the AGA, because it may be necessary in flight to work physically at different intensity levels.

It was established that an individual's resist-

ance to CO_2 toxic action decreases with increase in physical work. Accordingly, studies of CO_2 toxic action on practically healthy persons working physically at different intensity take on vital importance. There are few reports in the literature, so this problem needs further study. Nonetheless, based on available data [42, 80, 131, 138, 142, 180, 210] it is possible to approximate the length of time and varied physical work in an AGA relative to its P_{CO_2}.

When the P_{CO_2} is raised to 15 mm Hg, prolonged heavy physical work proves difficult, according to Table 6. When the P_{CO_2} is raised to 25 mm Hg, even moderate work is limited and heavy work is difficult; when the P_{CO_2} is raised to 35–40 mm Hg, light work is restricted. When the P_{CO_2} is raised to 60 mm Hg and higher, the individual at rest could remain in this AGA for some time, although he is incapable of work. The best way of removing the adverse effect of acute hypercapnia is to place victims in "normal" atmosphere.

The rapid transition from long periods in AGA with elevated P_{CO_2}, to breathing pure oxygen or air often causes deterioration of their well-being and general state. This phenomenon, expressed in acute form, was first detected in animals by Albitskiy [4], who termed it the reverse CO_2 effect. When hypercapnic syndrome develops, individuals must be gradually removed from CO_2-enriched AGA by reducing its P_{CO_2} [42, 138, 168]. Attempts to weaken the hypercapnic syndrome by administering alkalis, such as tris-buffered soda, did not give stable, positive results, in spite of partial normalization of blood pH [42].

The study of an individual's physiologic state and work function is significant when breakdown of the regeneration unit in an AGA will reduce P_{O_2} simultaneously with a rise in P_{CO_2}.

When breathing in a closed, small volume, there is a considerable CO_2 increase and a corresponding O_2 decrease [83]; this leads to abrupt deterioration of physiologic state and well-being when CO_2 in the inspired gas mixture is raised to 5–6% (P_{CO_2} = 38–45 mm Hg), even though O_2 reduction during this time is relatively small. A slow development of hypercapnia and hypoxia causes appreciable disturbances of work function and deterioration of the physiologic state when P_{CO_2} is raised to 25–30 mm Hg with a corresponding drop in P_{O_2} to 110–120 mm Hg. According to Karlin et al [170], in the third day of exposure to an AGA containing 3% CO_2 (22.8 mm Hg) and 17% O_2, the work function is markedly reduced. These data contradict results showing relatively small changes in work function even for considerable (up to 12%) O_2 decrease and a CO_2 increase to 3% in the AGA [134].

In simultaneous development of hypercapnia and hypoxia, dyspnea is the main symptom of toxic action. Pulmonary ventilation proves more significant than in equivalent hypercapnia. Such a significant rise in pulmonary ventilation is determined by hypoxia-elevated CO_2 sensitivity of the respiratory center, as a result of which the combined action of excess CO_2 and O_2 deficiencies in the AGA does not lead to an additive effect, but to synergism. Hence pulmonary ventilation is higher than the ventilation level that would have occurred with simple addition of the effects from reduced P_{AO_2} and increased P_{ACO_2}.

It can be concluded from these data and disturbances in the physiologic state that hypercapnia is dominant in the development of pathologic states when the regeneration system breaks down fully.

Chronic Effects of Hypercapnia

Study of the prolonged effect on humans and animals of elevated levels of P_{CO_2} in AGA established that clinical symptoms of chronic CO_2 toxic action is preceded by regular changes in the acid-alkaline equilibrium—development of respiratory acidosis leading to metabolic disturbance. Shifts occur in the mineral metabolism and evidently are adaptive, since the acid-alkaline equilibrium is preserved. These changes can be judged from the periodic rise of blood calcium and from changes in the marrow calcium and phosphorus. Calcium combines with CO_2; hence, the amount of CO_2 combined with calcium, in the bones, rises with increase in P_{aCO_2}. As a result of shifts in mineral metabolism, calcium salts form in the excretory system, a

TABLE 6. – *Toxic Effects of Elevated* CO_2 *Content in AGA*

No.	P_{CO_2} in AGA, mm Hg	Nature of manifestation of toxic action of CO_2 on human organism	Time at rest	Performance of physical load	Performance of mental work
1.	To 7.5	No unpleasant sensations; no functional changes detected	Up to 3–4 months	Possible (all kinds)	Possible
2.	To 15.0	No subjective symptomatics; some rise in minute respiration volume noted; development of limited acidosis	Up to 30 d	Of light and moderate intensity Heavy work is difficult	Possible
3.	To 25.0–30.0	State of discomfort; dyspnea especially during work; increase in minute volume of respiration 2–2.5 times the rest value; for exposure longer than 3 d, readily reversible changes in metabolic processes, followed by acidosis	Up to 7 d	Light work is possible Moderate work is restricted Heavy work is extremely difficult	Possible for formulated stereotype
4.	To 35.0–40.0	Dyspnea even at rest, "heaviness" in head, dizziness, increase in minute volume of respiration 3–4 times with relative stability of indicators of the functioning of the cardiovascular system; respiratory acidosis; disturbances of activity of cerebral cortex; disturbance of sleep	Up to 15 h	Light work is restricted Moderate work is extremely difficult Heavy work is impossible	Restricted even for routine mental work
5.	To 50.0	Dyspnea; headache, dizziness; disturbance of vision, disturbance of sleep, increase in minute volume of respiration of 4–5 times, respiratory acidosis, pronounced shifts of the functioning of the cardiovascular system; tachycardia, rise in arterial pressure; disorders of the activity of the central nervous system	Up to 3–4 h	Light work is difficult Moderate and heavy work are impossible	Difficult
6.	To 60.0	Intense rise in subjective and objective symptomatics	Up to 1 h	All kinds of work are impossible	Impossible
7.	Above 60.0, but not more than 75.0	Acute intensification of subjective and objective symptomatics	Up to 15 min	Excluded	Excluded

consequence of which can be kidney stone disease. Stones were detected in rat kidneys after a prolonged stay in an AGA with $P_{CO_2}=21$ mm Hg and higher, which validates this conclusion [178].

Metabolic changes caused by moderate gas acidosis were noted in humans who remained for long periods in AGA with P_{CO_2} exceeding 7.5–10 mm Hg, in spite of visible preservation of normal physiologic state and work capacity.

During Operation Hideout, subjects stayed 42 d in a submarine AGA containing 1.5% CO_2 ($P_{CO_2}=11.4$ mm Hg). The main physiologic parameters—weight, body temperature, blood pressure, and pulse rate—were essentially unchanged. However, in a study of respiration, acid-alkaline equilibrium, and calcium-phosphorus metabolism, adaptive shifts were detected. It was established that approximately from the 24th d in the AGA containing 1.5% CO_2, uncompensated gas acidosis occurred [179]. According to Zharov et al [213], no changes in blood pH were detected in a healthy young man after a month in an AGA with 1% CO_2, in spite of a small increase in P_{ACO_2} and an 8–12% rise in pulmonary ventilation, indicating a slight compensating gas acidosis. A decrease in blood pH, a rise in P_{ACO_2}, and a 20–25% increase in pulmonary ventilation were observed in subjects after prolonged periods (30 d) in an AGA with CO_2 elevated to 2%. Subjects felt normal when at rest; however, when performing intense physical work, some complained of headaches and rapid fatigue [213].

Subjects did not note a deterioration of well-being in an AGA with 3% CO_2 ($P_{CO_2}=22.8$ mm Hg). Blood pH changes indicated rapid development of uncompensated gas acidosis. A stay in this medium, although possible for many days, is always associated with increasing discomfort and a progressive reduction of work capacity.

From these studies it was concluded that remaining for many months in an AGA with P_{CO_2} above 7.5 mm Hg is undesirable because of chronic CO_2 toxic action [180, 213]. When an individual is in an AGA for 3 to 4 months, the P_{CO_2} must not exceed 3–6 mm Hg [123].

Shaefer [180] believes it desirable, when totally evaluating the effect of the chronic influence of hypercapnia, to single out three main levels of increased P_{CO_2} in an AGA which determine different individual tolerances to hypercapnia. The first level corresponds to raising P_{CO_2} in the AGA to 4–6 mm Hg, from which there is no significant effect on the organism. The second level corresponds to raising P_{CO_2} in the AGA to 11 mm Hg, when main physiologic functions and work capacity do not change appreciably. However, there is a slow development of shifts in respiration, acid-alkaline equilibrium regulation, and electrolyte metabolism, resulting in possible pathologic changes. The third level—elevating P_{CO_2} to 22 mm Hg and higher—leads to reduced work capacity, pronounced shifts in physiologic functions, and pathologic states after different time periods.

ARTIFICIAL GAS ATMOSPHERE (AGA)

History of AGA Development

The idea of producing an artificial atmosphere to protect man in high-altitude flights and during underwater immersions and swimming was first expressed by the famous French science fiction writer, Jules Verne. This idea received scientific commentary by the French physiologist Paul Bert [30], and the famous Russian chemist, D. I. Mendeleyev, who was the first to propose, in high-altitude flights, using sealed cabins with air pressure exceeding its pressure in the ambient environment [140]. Later, Tsiolkovskiy [194] pointed out the need for an AGA in spacecraft cabins.

This idea was applied to flight in the early 1930s. First in Switzerland (August Piccard in 1931), and then in the USSR and the US in 1933–1934, flights were made to altitudes of 15 500–22 000 m in stratosphere balloons equipped with sealed cabins. Flights in open cabins are not possible at such altitudes because the O_2 supply for the crew, at a pressure corresponding to ambient pressure, no longer prevents acute oxygen starvation. During preparation for these flights, variants of the AGA were examined and studies made with humans in sealed cabin simulators [8, 183]. Important information was obtained, not only on different

technical means of regenerating the AGA, but also on such physiologic parameters as O_2 requirement and CO_2 expiration of crewmembers.

Soviet and US investigators reached similar conclusions: to have stratosphere balloons in cabins in order to lighten their structure; maintain pressure below atmospheric (550–450 mm Hg); and increase O_2 in the AGA so that oxygen supplied to the crew would be wholly preserved. US and Soviet investigators rejected use of a one-gas oxygen medium, just as they rejected use of liquid nitrogen as the O_2 source, because of fire danger in such an AGA [8, 124, 183].

The short, hours-long duration of stratosphere balloon flights greatly simplified the AGA designing problem. The same problem as related to space flights, especially those of long duration, became considerably more complicated. It would not be advisable to forget the above studies, since for the first time, definite useful experience was obtained.

Thus, in working on the spacecraft AGA, Soviet and US scientists relied not only on sanitary investigations to set standards and design of a gas medium for living and production quarters, but also on investigation data in designing a submarine AGA, and experience in designing stratosphere balloon cabins AGA. Historically, Soviet and US investigators were guided extensively by common principles; however, in practice, designing the spacecraft AGA was solved quite unexpectedly.

Soviet investigators selected the AGA similar in parameters, pressure, and gas composition to standard terrestrial atmosphere (STA), thus developing suitable living conditions in normal flight regimes. US investigators, because of several technical advantages, use a one-gas AGA of oxygen at a total pressure of 258 mm Hg, suitable for astronauts. It is evidently convenient to use it when astronauts, in space suits, leave the cabin to enter very low total pressure [148, 149, 150].

These AGA, successfully used in flights, generally met the main physiologic principles of AGA design. During flight under normal gas exchange there was no appreciable stress of the adaptive mechanisms, therefore the adaptive reserve of the organism was not reduced.

Soviet and US specialists are continuing research on designing spacecraft AGA, indicating that the AGA currently used can scarcely be optimal for long-term flights. During work on this problem, variants of the AGA were discussed. Thorough examination and evaluation of AGA variants are best made according to some systematization of the possible AGA formulations. The basis of the AGA classification comprises chemical composition, physical properties, and main physiologic characteristics.

Physiologic evaluation of AGA in terms of gas exchange and P_{O_2} and P_{CO_2} levels in the internal environment (blood and alveolar air) can be classified into those equivalent to standard terrestrial atmosphere, and those not entirely equivalent, containing some excess O_2 and CO_2, or O_2 deficit. Chemically, AGA can consist of only one gas (O_2); two gases—O_2 and some biologically indifferent gas—or, finally, it can include, besides O_2, several indifferent gases (N_2, He, Ne, and Ar). Physical properties of an AGA depend not only on its chemical composition, but also on barometric pressure, which fluctuates widely.

Numerous AGA variants are theoretically possible for practical use in space flights. Only those which have attracted the greatest attention at present are considered, therefore are being studied in laboratory experiments, or have already been used in flights.

AGA Equivalent in Gas Exchange to STA and Composed of Two Gases (N_2 and O_2)

AGA can be considered as simulating the Earth's standard gaseous atmosphere which consists basically also of two gases, O_2 and N_2, and 1% of other gases. Simulating standard terrestrial atmosphere in spacecraft cabins means providing comfort according to standards set by hygienists for living quarters in geographic regions at sea level. Thus, reproduction of closely studied artificial conditions will be arbitrarily denoted STA.

In Soviet spacecraft cabins, the use of an AGA close to STA is entirely justified, it has been widely assumed [76, 118, 214]; biologically, it is entirely adequate for man who has been histori-

cally adapted to it. An AGA close to STA can be used in extended space flight as one of the most reliable AGA variants [76, 118]. Although STA was assumed applicable as an AGA in spacecraft cabins [68, 76], its use was not optimal in most cases. Thus, Gazenko and Genin argued: ". . . copying the terrestrial atmosphere unjustifiably limits the possibility of AGA variations that could prove desirable from the standpoint of engineering and human protection in an emergency situation" [68].

Selection of an AGA entails parameters: the higher the AGA pressure, the thicker the cabin walls and the greater the cabin weight. The adverse features of STA during emergencies have been pointed out [46, 76, 118]. A disturbance in cabin hermeticity causes significant barometric pressure drop which leads to detrimental action in explosive decompression. Low-pressure transition from STA to AGA, as when passing from one ship to another or when using space suits with low pressure, is fraught with development of altitude decompression sickness. Space suits with low pressure complicate not only the time spent by astronauts during emergencies, but can also adversely affect their egress into "free" space and on the surface of celestial bodies that are practically devoid of atmosphere or have an extremely rarefied one. Using STA in cabins only in limited cases has been recommended, besides possible emergency need. Long flights can cause functional organic shifts (asthenia—loss of conditioning) when the comfortable, quite stable parameters of STA prove far from optimal [71, 74, 76].

Soviet and US investigators [33, 46, 76] used a two-component AGA in spacecraft cabins, equivalent in gas exchange to STA, but with a barometric pressure lower than STA. Data in Table 7 and Figure 1 show maximum permissible reduction in AGA pressure to 190 mm Hg. To retain normal O_2 supply to the organism at low pressures, AGA gas composition must consist of O_2 only, i.e., no two-component gas. Accordingly, in examining AGA consisting of O_2 and N_2, four ranges of reduced pressure were used: 526, 405, 308, and 267 mm Hg, corresponding to 3000, 5000, 7000, and 8000 m of altitude.

Three of the above-listed AGA at 526, 405, and 308 mm Hg were successfully tested under laboratory conditions by Ivanov et al [95]. Studies at lower pressures were not carried out to prevent AGA which begins at altitudes of 7500–8000 m and to avoid fire due to increase of O_2 in the AGA.

Results showed that a month in AGA equivalent in O_2 to STA, at pressures corresponding to altitudes of 3000–7000 m, has no unfavorable effect. All three AGA variants tested proved equivalent from the physiologic standpoint. Changes in certain physiologic parameters were: 10–15% reduction in O_2 requirement, rise in heart rate especially in the orthostatic test, changes in diurnal periodicity of the EEG-frequency spectrum, and increase in the number of slow waves during the day. These changes did not depend on gas composition and AGA pressure, but were caused by hypodynamia and changes in work, rest, and sleep routines.

In continuing investigations by Kunetsov et al [117], subjects were kept for 2 months in an AGA with a total gas pressure of 308 mm Hg. Functional shifts were detected in subjects, caused mainly by hypodynamia. Considerable attention was given to developing an AGA with a total gas pressure of 300 mm Hg, but was not successful [33, 95, 117]. A pressure of 300 mm Hg is considered optimal, because it is still high and protects against decompression, therefore does not require desaturation of N_2 from the organism when N_2 is used in the AGA. It is also convenient to use space suits with low pressure, which preclude ADS. ADS develops only rarely in emergency depressurization during the first flight hours. The use of a two-component AGA with a pressure of 300 mm Hg is a probability, since it reduces cabin and AGA weight as such; but fire in this AGA is not more likely than when the STA is used (Tables 8 and 9).

On purely theoretical considerations, it is remarkable that as early as 1940, Spasskiy [187] considered an AGA with a total pressure of 260 mm Hg as promising for high-altitude aircraft cabins. The flight difference between this AGA and the above-considered AGA with a total pressure of 308 mm Hg eliminates detailed comparison. Small, mainly technical advantages of its use compared to the preceding AGA (308 mm Hg)

TABLE 7. – *Change of Barometric Pressure and* P_{O_2} *at Different Altitudes and Oxygen Conditions*

H altitude		Atmospheric pressure based on int'l st. atmosphere				Millibars	Partial pressure O_2 in dry air P_{O_2} (dry), mm Hg	Partial pressure O_2 in moist air P_{O_2} (moist), mm Hg	O_2 % providing respiratory conditions analogous to:			
m	ft	P mm Hg	Technical atmosphere kg/cm²	Physical atmosphere atm	(P_1S_1) lbs/in²				Terrestrial	2000 m	4000 m	5000 m
0	0	760.0	1.033	1.000	14.7	1014	159	150	21.0	16.2	12.25	10.5
500	1640	716.0	0.975	0.943	13.84	955	150.3	140.5	22.4	17.3	13	11.2
1000	3230	674.1	0.917	0.887	13.04	900	141.5	132	23.9	18.4	13.9	12.0
1500	4920	634.2	0.863	0.834	12.3	846	133	123.3	25.5	19.7	14.9	12.8
2000	6560	596.3	0.812	0.785	11.5	795	125	115.3	27.2	21.0	15.9	13.7
2500	8200	560.2	0.761	0.736	10.8	748	117.5	107.7	29.2	22.5	17.0	14.7
3000	9840	526.0	0.717	0.693	10.2	702	110.4	100.6	31.2	24.1	18.2	15.7
4000	13 100	462.5	0.63	0.609	8.94	617	97	87.2	34.3	27.3	21	18.1
5000	16 400	405.4	0.552	0.534	7.84	540.5	85	75.2	41.8	32.2	24.3	21.0
6000	18 700	354.1	0.482	0.466	6.85	472	74.4	64.5	48.8	37.6	28.4	24.5
7000	23 000	308.3	0.419	0.405	5.96	411	64.7	54.9	57.3	44.2	33.4	28.8
8000	26 200	267.4	0.364	0.352	5.17	356.5	56.1	46.3	68.0	52.4	39.6	34.2
9000	29 500	231.0	0.315	0.305	4.47	308	48.5	38.6	81.3	62.7	47.5	40.8
10 000	32 800	198.7	0.271	0.262	3.84	265	41.7	31.9	98.7	76.1	57.5	49.6
11 000	36 100	170.2	0.232	0.224	3.29	227	35.7	25.9	–	93.7	71	61.0
12 000	39 400	145.3	0.198	0.191	2.81	194	30.5	20.6	–	–	88.8	76.5
13 000	42 600	124.4	0.17	0.164	2.41	166	26.1	16.2	–	–	–	97.7
14 000	46 000	106.3	0.145	0.140	2.06	142	22.3	12.45	–	–	–	–
15 000	49 200	90.8	0.124	0.12	1.76	121	19.05	9.2	–	–	–	–
17 000	55 800	66.4	0.09	0.087	1.28	88.6	18.9	4.07	–	–	–	–
18 000	59 000	56.6	0.077	0.074	1.09	75.5	11.9	2.02	–	–	–	–
20 000	65 600	41.5	0.057	0.055	0.803	55.4	8.7	–	–	–	–	–
25 000	82 000	18.9	0.026	0.025	0.366	25.2	3.97	–	–	–	–	–
30 000	98 400	8.9	0.012	0.012	0.172	11.9	1.87	–	–	–	–	–
40 000	131 000	2.2	0.003	0.003	0.0426	2.94	0.46	–	–	–	–	–
60 000	164 000	0.6	0.001	0.001	0.0116	0.8	0.126	–	–	–	–	–
Working formulas	$\frac{M}{0.305}$	——	$\frac{P}{785}$	$\frac{P}{760}$	$\frac{P}{51.713}$	1.335 P	0.21 P	0.21 (P – 47)	$21\frac{760-47}{P-47}$	$21\frac{596-47}{P-47}$	$21\frac{462-47}{P-47}$	$\frac{21(405-47)}{P-47}$

Compiled by V. S. Yakovlenko.

TABLE 8.—*Flame Spread Rates for Materials in Various Atmospheres* [1]

Atmosphere	Air[2]		Air[3]		20% O_2 80% He		46% O_2 54% N_2		46% O_2 54% He		70% O_2 30% N_2		70% O_2 30% He		100% O_2 [3]		100% O_2 [2]	
Pressure	760 mm		760 mm		760 mm		380 mm		380 mm		258 mm		258 mm		258 mm		258 mm	
	cm/s	in/s	cm/s	in/s	cm/s	in/s	cm/s	in/s	cm/s	in/s	cm/s	in/s	cm/s	in/s	cm/s	in/s	cm/s	in/s
Wood	–	–	0.064	0.025	0.10	0.04	0.305	0.12	0.46	0.18	0.46	0.18	0.69	0.27	0.89	0.35	–	–
	–	–	±0.064	±0.025	±0.013	±0.005	±0.051	±0.02	±0.076	±0.03	±0.076	±0.03	±0.076	±0.03	±0.076	±0.03	–	–
Paper	–	–	0.076	0.03	0.76	0.30	1.07	0.42	1.60	0.63	1.4	0.55	1.9	0.74	2.28	0.90	–	–
	–	–	±0.025	±0.01	±0.15	±0.06	±0.051	±0.02	±0.13	±0.05	±0.13	±0.05	±0.15	±0.06	±0.18	±0.07	–	–
Cellulose acetate	0.0305	0.012	0.0076	0.003	–	–	0.28	0.11	0.38	0.15	0.51	0.20	0.46	0.18	0.76	0.30	0.71	0.28
			±0.0051	±0.002	–	–	±0.025	±0.01	±0.051	±0.02	±0.076	±0.03	±0.051	±0.02	±0.025	±0.01	±0.305	±0.12
Cotton fabric	0	0	0.25	0.10	0.43	0.17	2.28	0.9	2.8	1.1	4.6	1.8	3.05	1.2	8.1	3.2	3.8	1.5
			±0.025	±0.01	±0.025	±0.01	±0.76	±0.3	±0.025	±0.1	±0.76	±0.2	±0.051	±0.2	±0.51	±0.2	±0.13	±0.05
Foam cushion	0.48	0.19	0.36	0.14	0	0	6.9	2.7	5.3	2.1	0.25	0.1	15.2	6.0	33	13	31.5	12.4
			±0.051	±0.02	0	0	±2.0	±0.8	±0.76	±0.3	±1.3	±0.5	±1.3	±0.6	±2.5	±1	±1.3	±0.5
Plastic wire	0	0	0	0	0	0	0.64	0.25	0.89	0.35	1.1	0.48	1.52	0.60	2.13	0.84	0.84	0.33
	0	0	0	0	0	0	±0.025	±0.01	±0.051	±0.02	±0.025	±0.01	±0.051	±0.02	±0.076	±0.03	–	–
Painted surface	0	0	0	0	0	0	0.53	0.21	0.69	0.27	0.81	0.32	1.1	0.42	1.14	0.45	0.97	0.38
	0	0	0	0	0	0	±0.025	±0.01	±0.025	±0.01	±0.051	±0.02	±0.13	±0.06	±0.13	±0.05	±0.10	±0.04

[1] ± indicates average deviation.

[2] Previously reported SAM-TR-65-7S.

[3] This investigation.

TABLE 9.—*Energy Required for Ignition of Materials in Various Atmospheres*

(cal/cm²)

Atmosphere	Air	20% O_2 80% He	46% O_2 54% N_2	46% O_2 54% He	70% O_2 30% N_2	70% O_2 30% He	100% O_2
Pressure	760 mm	760 mm	380 mm	380 mm	258 mm	253 mm	258 mm
Wood	25±1	108±11	25±2	24±0.5	25±1	22±1	23±1
Paper	32±1	39±0.5	25±2	26±0.5	26±0.5	25±0.5	25±1
Cotton fabric	13±0.5	Nl	12±0.5	17±0.5	15±0.5	16±0.5	15±0.5
Plastic wire	20±1	Nl	16±1	Nl	17±1	46±1	16±1
Painted surface	30±1	Nl	56±5	70±4	81±3	57±5	36±1

cannot justify certain of its adverse qualities. At a pressure of 260 mm Hg, there is probability of ADS, and with reduction in reserve time, inevitable at lower AGA pressure, there is increased leakage of gases from the cabin.

AGA Composed of O_2 and He

Replacing nitrogen in an AGA with helium poses an important question. Is presence of N_2 in an AGA important and does it have the same biologic role in the STA to which man and animals have been adapted during their long evolutional development?

Man and animals can live normally in an AGA devoid of N_2, according to Soviet and US investigators [54, 76, 118, 130, 169]. Vertebrates and invertebrates develop normally in an AGA where N_2 is totally absent [35, 130, 206]. In man, the biologic role of N_2 is to fill body cavities, primarily the lungs—to sustain specific volume and prevent atelectases. Other inert gases, including He (to be discussed), can fulfill this role [2, 54, 85, 147, 151, 166, 167, 169, 177, 182]. Use of He as one of the main components of an AGA demands that it have no unfavorable effects.

Studies on animals and humans with nitrogen mixed with helium in AGA, at normal and reduced pressures, showed that helium had no toxic effect and like N_2, is a biologically inert gas [2, 16, 49, 54, 60, 165, 169]. Functional shifts caused by the heat-physical properties of He are: increase in oxygen requirements, reduction in erythrocyte count and hemoglobin level, and associated increase in diurnal iron requirements. Hamilton et al [84] detected such changes in rats in a helium-oxygen medium and Dianov [55] found changes in an animal's resistance to hypoxia.

After it was shown that He can replace N_2 in AGA, its replacement advisability was questioned. According to data of Yakobson, Dianov, and Kuznetsov [53, 207], when He is used, the onset of ADS and especially of its severe forms in astronauts after transition to conditions of low barometric pressure is somewhat reduced. This is based on the Bunsen coefficient of N_2 solubility in fat which is approximately four times higher than for He. In contrast, studies of US investigators Beard et al [19] established a more frequent appearance of the "bends"—the musculoarticular form of ADS in persons present in an AGA in which He was used. The incidence of severe ADS forms, when a He-containing AGA is used, is not settled.

Dianov et al have shown that when oxygen is breathed, the time of virtually complete desaturation of He from the organism is considerably less than for N_2 desaturation because of the low helium solubility in tissues and its high diffusion coefficient. This is an essential and indisputable advantage of using He in the AGA. Temperature increases in the cabin, due to He high thermal conductivity, will be much better tolerated by astronauts [33, 54, 55, 169]. In this medium, hypercapnia resistance, intense physical loads, and other influences leading to a significant rise in ventilation must also be increased [55, 115]. This effect is due to forced breathing of a helium-oxygen mixture, when resistance of air passages, owing to the low density of He, is less than when air is breathed. In normal,

quiet breathing this effect does not show up, since air passage resistance is now determined partially by inspired gas viscosity. The viscosity of He does not differ appreciably from that of N_2.

Nitrogen Replacement

Nitrogen replacement in an AGA with helium is justified by the high stability of the He atom to different kinds of radiation exposure. This advantageously differentiates He from N_2. The relatively high weight of N_2 determines its weak protective properties with respect to cosmic radiation; primary nucleons absorption and formation of secondary particles. According to data of Dmitriyev [58], excited nitrogen atoms and ions are formed by ionizing radiation in air. They enter into chemical reactions with O_2, resulting in formation of toxic compounds such as nitrogen oxide, nitrous oxide, and nitrogen peroxide. The advisability of replacing nitrogen in an AGA with helium also has an engineering justification. The density of He is approximately one-seventh that of N_2, hence use of a helium-oxygen atmosphere in spacecraft leads to reduction in launch weight, and in gas reserves weight necessary to replenish the craft atmosphere. This advantage of the helium-oxygen AGA cannot be manifested fully owing to high He fluidity. This is the reason for reducing reserve time if gases escape from the cabin when AGA nitrogen is replaced with helium, which must be considered as a disadvantage of this replacement. Replacement of AGA nitrogen with helium must lead to reduction in energy required to ventilate the cabin. In spite of the definite advantages of using He in an AGA, there are few experimental studies on humans. Soviet experiments [53, 187] dealt with an AGA consisting of O_2 and He at normal barometric pressure (1 atm).

Studies show that remaining in a helium-oxygen medium does not cause any essential changes in well-being, behavior, and work function. However, replacing nitrogen in the AGA with helium is still accompanied by some functional shifts which include changes in heat exchange, speech, and respiration [53, 54, 176]. Thus, remaining in a helium-oxygen AGA at temperatures that are comfortable under normal air atmosphere (18–24° C) was accompanied by appreciable cooling. At 21° C, subjects rapidly displayed unpleasant heat sensations when the mean-weighted skin temperature dropped nearly 2° in 2 h. In the helium-oxygen AGA, the zone of heat comfort shifted markedly toward higher temperatures and was 24.5–27.5° C during the day while at night it was 26–29° C. These data show considerable narrowing (by 3° C) of the heat comfort zone in the helium-oxygen medium compared with the similar zone in air [53, 54]. This effect of the helium-oxygen atmosphere is associated with the high thermal conductivity of He.

Replacing nitrogen in air with helium led to speech changes in subjects in the helium-oxygen AGA; the speech spectrum shifted toward high frequency by a value of 0.7 octave. Speech intelligibility deteriorated somewhat but was still retained at an acceptable level of 90–95%. The speech function was restored immediately after breathing ordinary air. The speed of sound in the helium-oxygen medium at a pressure of 1 atm and a temperature of 27° C is 1.85 times higher than in air, which explains speech distortion after nitrogen in air was replaced with helium [48, 120].

Functional changes of respiration in the helium-oxygen medium were manifested in an improvement of maximum possible ventilation of lungs, due to reduced resistance of the air passages. Thus, studies on air nitrogen replaced with helium showed the practical possibility of using this AGA. US investigators studied helium-oxygen AGA with a total pressure of 380 mm Hg [60, 155, 212], 360 mm Hg, and 258 mm Hg [2, 16, 89, 147, 166, 167, 182].

These studies suggest that prolonged (up to 56 d) stay in a helium-oxygen medium has no unfavorable effects on metabolism, respiration, blood circulation, and CNS. Pathologic shifts noted in these experiments were caused by various factors unrelated directly to the replacement of nitrogen in the AGA with helium. For example, in experiments by Zeft et al [212], irritation of eyelid mucosa (conjunctivitis) was due to the low humidity of the AGA (pressure of 380 mm Hg); when the humidity was raised, these disturbances disappeared. A decrease in one subject's orthostatic stability, as well

as in most investigations in cabin simulators, was evidently due to hypodynamia.

Mucosa dryness and development of conjunctivitis, noted in subjects after 56 days in a helium-oxygen AGA with a total pressure of 258 mm Hg (P_{O_2} = 175 mm Hg; P_{He} = 74 mm Hg; and P_{N_2} = 2 mm Hg), were also associated with low humidity. Abdominal pains cannot be related to He in the AGA, but were evidently due to other factors, possibly the unsuccessful diet. Only slight speech distortions and skin temperature changes when physical exercise was performed were related to He in the AGA. However, such changes have no significance, since speech distortions can be eliminated by technical means; also, unfavorable heat sensations in helium-oxygen media are easily remedied by raising the temperature of the artificial gaseous atmosphere.

In a comparative evaluation of helium-oxygen AGA with low pressure, when there is a slow leakage of gases from the cabin, the reserve time (during which the pressure drops to the critical value determining development of acute hypoxia) will be shorter for crewmembers, compared with AGA containing N_2, the higher the percent content of He in the AGA. Therefore, at the lowest total pressure (258 mm Hg), this difference between helium- and nitrogen-oxygen AGA will be relatively small [46, 174].

In conclusion, if in underground immersions the possibility of using He in AGA has been demonstrated, this question is still in the study stage for the AGA of spacecraft cabins.

One-Gas AGA

The advisability of using pure oxygen in cabins of high-altitude aircraft was discussed before World War II by Spasskiy [187], who assumed that O_2 might be used at a pressure of 230 mm Hg in hermetic cabins of high-altitude aircraft. He maintained that the pressure must not be reduced to lower levels since the probability of ADS and altitude meteorism are significant and even a small O_2 reserve during increased gas leakage in the cabin will be virtually absent.

Animals remaining for a long time in a one-gas AGA equivalent in gas exchange to STA and composed virtually of only oxygen ($P_{N_2} < 10$ mm Hg) with a pressure of 190–200 mm Hg was demonstrated [3, 56, 72, 130, 145]. It was established that in a single-gas medium equivalent to STA in terms of O_2, pulmonary atelectasis can develop in experimental animals. Pulmonary atelectasis in mice during the first 48 h in a one-gas atmosphere caused the death of several animals, although most animals spent the entire 59-d experiment without visible behavior disturbances or injury [130]. In later experiments on rats in this AGA [3, 72], atelectases developed in several animals during the first days, soon disappearing, after which the animals retained normal physiologic state for up to 100 d. There was moderate dehydration in the experimental animals caused by increased evaporation of liquid in the reduced (down to 200 mm Hg) AGA pressure.

In a one-gas AGA (P_{O_2} = 196 mm Hg), no atelectasis or other unfavorable effects were found in young growing rats [169]: only reduced urine excretion was noted during 24 d in this AGA. This effect is associated with increased fluid loss caused by evaporation in the rarefied atmosphere of the one-gas AGA.

Biologic Effects

A biological criterion was used to judge the influence of a single-gas medium – the capability of reproduction – in an experiment lasting 11 months. If a rat's lifetime is approximately 2.5 years, this experiment must be regarded as extremely long. According to the data, the one-gas medium has no unfavorable effect on the physiology and biology of the white rat. Pregnancy occurs normally and progeny grows and develops normally in this medium. The only puzzling result was the death of several animals born in the one-gas AGA after they had been transferred to STA 21 d after birth [169]. Death of animals in the STA probably was caused by side factors not directly associated with the one-gas AGA which they were in earlier. It can be concluded that the one-gas medium is biologically suitable, although there is risk of ADS and pulmonary atelectasis.

The effect on the human organism of an AGA mainly of O_2 with total pressure of 190–200 mm

Hg was studied in the US [143, 144, 145, 202], and in the USSR [72]. It was established that it is possible to use this AGA when necessary, but certain unfavorable effects were noted. Chest pains which developed in one subject in a medium with $P_{O_2} = 176$ mm Hg were possibly associated with pulmonary atelectasis. The pains disappeared when the AGA pressure was raised. Aural atelectasis developed in some subjects, and signs of dehydration were noted in all. In another investigation [145], pulmonary influenza was detected in six subjects, pain in joints in one, and a small drop (to 90%) in oxygen saturation of arterial blood was noted in two.

Thirty days in a one-gas atmosphere (N_2 content in the AGA was 5–10%) was tolerated well; subjects maintained physical and intellectual work at high level [72]. No atelectases developed in lungs or middle ear cavities, which, possibly, was due to subjects periodically performing physical exercise. Also, it is significant that N_2 content in the AGA was somewhat higher than in the experiments by Welch et al [202] and by Morgan et al [145]. Some adverse features were in the AGA tested. The necessity of prolonged desaturation of N_2 from the organism before beginning the experiment was noted. When desaturation time was less than 3 h, transition into the one-gas AGA usually led to ADS symptoms. Thus, investigations with humans showed that when preliminary desaturation and pulmonary atelectasis is prevented by physical exercises, one-gas AGA with a total pressure of 200 mm Hg can evidently be used in flights.

The advantages of using a one-gas AGA are that it provides for simplifying and carrying out more reliable regulation of life-support systems, and reducing the weight of the AGA and the cabin. Another advantage of this AGA is that low pressure reduces the probability of organic damage in the event of explosive decompression; using space suits at low pressure is also considerably simplified. At the same time, the one-gas AGA has several serious adverse features, which include increased fire danger (Tables 8, 9, 10). This is caused primarily by absence of diluent gases in the AGA (N_2, He, and Ne) reducing the combustion rate of various materials (Table 8). The great danger of fire breaking out necessitates limiting the use of several materials in the spacecraft cabin and necessarily imposes higher fire safety requirements.

Another serious disadvantage of a one-gas AGA with 200 mm Hg pressure is the near total absence of "reserve time" when there is increased leakage of gases from the cabin. The pressure drop of 70–80 mm Hg is a great danger to crewmembers. Such disadvantages of this AGA require lengthy desaturation of N_2 at launch, anticipating the possibilities of pulmonary and middle ear atelectases and rapid dehydration of the organism in the event of reduced moisture in the AGA.

Hyperoxic AGA was examined partially in the discussion of O_2 toxic effects on the organism. Again, the one-gas AGA with 258 mm Hg total pressure was investigated and successfully tested in US flights of 2 weeks' duration. Its further use in flights of longer duration is an object of discussion. With longer time spent in this medium, the probability of the O_2 toxic effect on respiratory organs and blood system, as well as its high fire danger, will possibly eliminate use of this AGA for lengthy interplanetary flights [33, 46, 76].

Based on a comparative evaluation of AGA variants (shown in a general way in Table 10), it is held that a two-gas AGA consisting of O_2 and N_2 or He (possibly also Ne) with total pressure of 300–400 mm Hg will have definite advantages on certain occasions [76, 118]. These considerations evidently led to the fact that a two-gas atmosphere consisting of 70% O_2 and 30% N_2 at a total pressure of 258 mm Hg was used in Skylab in flights up to 86 days.

Active AGA

In examining AGA variants, most investigators fear preeminently that a particular AGA variant could affect the organism and cause adaptive changes (Table 10). It is assumed that the more inert the AGA from the biological point of view, the more suitable it is. In opposition is the idea that one of the factors preventing signs of asthenization during lengthy flights can be an AGA which actively stimulates adaptive reactions to different unfavorable flight conditions. Such an AGA acquired the term *active AGA*.

TABLE 10. – *Comparative Estimate of AGA Variants*

No.	Evaluation criteria	Artificial gas atmosphere (AGA)							
		P = 760 mm Hg O_2 – 21% N_2 – 79%	P = 760 mm Hg O_2 – 21% He – 79%	P = 405 mm Hg O_2 – 42% N_2 – 58%	P = 405 mm Hg O_2 – 42% He – 43%	P = 308 mm Hg O_2 – 57% N_2 – 43%	P = 308 mm Hg O_2 – 57% He – 53%	P = 258 mm Hg O_2 – 100%	P = 200 mm Hg O_2 – 100%
I.	Possible damaging action:								
	Disturbance of tissue structure, pulmonary atelectases, hemolysis of erythrocytes, and so on	–	–	–	–	–	–	±	±
II.	Danger of ADS developing:								
	a) at launch	–	–	–	–	–	–	+	+++
	b) in flight with use of pressurized space suit (200–170 mm Hg)	++++	+++	±	±	–	–	–	–
III.	Necessity of desaturation	+++	+++	±	±	–	–	+	+++
	a) at launch	–	–	–	–	–	–	+	+++
	b) in flight with egress from cabin	++++	+++	±	±	–	–	–	–
	c) desaturation time	6–8 h	2–3 h	?	?	–	–	4 h	6–8 h
IV.	Danger of damage from ADS	++++	+++	++	++	+	+	+	+
	a) severity of gas embolism	+++	+++	++	++	+	+	–	–
V.	Extent of damage when gases leak from cabin	±	++	++	+++	++	++++	+++	++++
VI.	Resistance to high temperatures	4	1	3	2	3	2–3	3	2
VII.	Resistance to ionizing radiation	2	2	2	2	3	2–3	3	2
VIII.	Danger of fire and explosion	±	±	+	+	++	++	++++	+++
	a) manifestation of toxic products	+	–	+	–	+	–	–	–
	b) rate of combustion of tissues and plastics	±	+	+	+	++	+++	++++	+++
IX.	Weight of AGA	5	3	3	2	3	1–2	2	1
	a) weight and capacity of fan	5	3	3	2	3	1–2	2	1

NOTE: The following symbols were used for a comparative evaluation of the estimate of probable degree of danger of damaging effects: No (–), extremely slight (±), low (+), moderate (++), high (+++), highest (++++). A 5-point scale was used for the comparison of AGA variants: 1. highest, 2. good, 3. moderate, 4. poor, 5. worst.

In nearly all studies in cabin simulators, when remaining for a long time in AGA regardless of its variants, the possibility of asthenization developing was noted, as the result of reduced motor activity [95, 117, 203]. The signs were: reduction in physical work capacity and orthostatic stability, and reduced resistance to influences such as acceleration and hypoxia [110, 198]. In lengthy flights also, weightlessness aggravates the adverse effect of hypodynamia, indicated from investigations where physiologic effects of weightlessness were simulated by immersing subjects in liquid or restricting them to bed rest. Substantial disturbances in blood circulatory regulation were noted, with reduction in orthostatic stability and disturbed regulation of motions, changes in the support motor apparatus, and shifts in protein and mineral metabolism.

In 1964, Genin in the USSR [71, 74], and (independently) Lamb in the US [121] proposed using a purposefully altered AGA to prevent asthenia during lengthy space flights. Lamb noted that biochemical and physiological shifts during adaptation to a moderate degree of hypoxic hypoxia must prevent several adverse effects of weightlessness; therefore, he proposed using a hypoxic AGA. This idea was implemented [129, 188] by investigating a lengthy stay with strict bed rest during two gradually increasing degrees of hypoxia.

Soviet investigators noted that change in AGA gas composition is only one of the possible ways to condition subjects; it is also possible to use changes in other parameters of the medium for the same purpose: fluctuations in AGA temperature, for example. Significance of the actual hypoxic conditioning regimen was also shown. Vasil'yev et al [197] made a comparative evaluation of hypoxia conditioning, establishing that the highest effectiveness of the stepwise "fractional" regimen is in ascents to increasingly higher altitudes, remaining in an O_2 deficit atmosphere for 6 h followed by 18 h in an AGA with normal P_{O_2}. Later, animals secured in special cases to severely restricted motions were exposed to AGA variants. Tests were made of AGA with O_2 content reduced to different levels, with excess CO_2 content, and with simultaneously reduced P_{O_2} down to 70–80 mm Hg and P_{CO_2} elevated to 30–38 mm Hg. Data indicated that the AGA used were stimulating in different intensities on blood, respiration, and the cardiovascular system of experimental animals, and promoted increased resistance to G-loads and acute hypoxia [199].

In pressure-chamber experiments with humans restricted to bed rest, a daily 6-h conditioning session (ascents to gradually increasing "altitudes" from 2500 to 4500 m) brought milder symptoms of hypodynamia. However, initially it caused short-term moderate discomfort in some persons due to the effect of hypoxia. Conditioning prevented reduced resistance to G-loads considerably; it even increased resistance somewhat to acute hypoxia. It was thought that to prevent asthenization, an AGA with nonstationary, cyclically varying gas composition should be used. This idea is based on spending time in this AGA which should not form stable adaptation to the altered gas medium. At the same time, changes in the AGA can be selected in time so that work function is increased. It should be added that use of these AGA can also prove useful to retain normal periodicity in processes of vital activity, which can be substantial in lengthy flights [76].

A deficiency of motions was experienced in nonstationary AGA with significant fluctuations in P_{O_2} (from 110 to 320 mm Hg) on different days of the investigation. This showed a possible marked purpose for influencing various functional systems through the use of these AGA [77]. The rational selection of all parameters for use of these AGA to prevent asthenia in crewmembers on long flights is far from resolved; further intensive experiments are needed.

In conclusion, space flights of many months and many years impose new requirements on criteria for evaluating the AGA. It will be necessary in the future to evaluate the quality of an AGA, based not only on accepted physiologic-hygienic parameters, but also in regard to general biologic indicators that delineate the effect of the AGA on lifespan, aging, reproduction, and other body processes.

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Chapter 2

TOXICOLOGY OF THE AIR IN CLOSED SPACES

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Spacecraft engineering and design for life-support services is restricted to meeting the minimum biologic needs of the astronauts. These restrictions arise from the mass, volume, energy, and associated cost requirements for providing more than minimal life-support services.

This chapter is concerned broadly with providing man's minimal physiologic requirements without significant impairment of health or functionality. The more specific concern is to identify those factors of spacecraft construction and operation that may interfere with meeting man's minimal atmospheric needs. The qualitative and, wherever possible, quantitative description of the quality of the atmosphere in the spacecraft are discussed. In particular, this chapter is devoted to a consideration of those atmospheric contaminants which may have an adverse effect on the health and functionality of astronauts.

The sources and compositions of these contaminants in the atmosphere of the craft will be identified. Their potential effects on the human body will be considered individually and collectively insofar as the data permit. The establishment of acceptable concentrations for toxic agents in the artificial gaseous atmosphere (hereafter referred to as AGA) of the spacecraft is a matter of balanced judgment of their risks, benefits, and costs. Finally, this chapter will summarize experience so far with the establishment of acceptable concentrations, and call attention to areas of uncertainty needing further investigation.

In 1966, V. V. Parin [77] pointed out that in spite of large-scale achievements and the great volume of experimental data collected, space biology and medicine were only at the initial stages of development. The increased tempo of space flights has placed greater demands on space biology and medicine, resulting in intensified study of man's reactions to space flight. The results of some of these studies will also be discussed.

The isolation of people and equipment in hermetically sealed environments can result in gradual accumulation of airborne contaminant chemicals and microflora up to toxic or infectious magnitude. Experience with such environments is not totally lacking. The situation in submarines and other underwater habitats resembles in many ways the conditions in spacecraft. There are at least three important differences: (a) the amount of space and energy available per person is much less in the spacecraft, (b) the ability to return rapidly to a normal environment is greater in a submarine, and (c) the completely unknown effect of weightlessness is a factor in space flight.

[1] With contributions from V. P. Savina and S. N. Zaloguev, USSR, and E. M. Roth, USA.

SOURCES AND IDENTIFICATION OF CONTAMINANTS IN THE ARTIFICIAL GASEOUS ATMOSPHERE (AGA)

The spacecraft AGA is a dynamic mixture of the gas or gases which might be deliberately provided for respiration such as oxygen, nitrogen. water, and carbon dioxide. There are other components considered contaminants which are undesirable, if not potentially dangerous, and which must be controlled. Even those essential gases added deliberately must be controlled within limits to avoid adverse effects. The contaminants have several origins including biologic (man and microorganisms), materials (construction and supplies), processes (electrical, life support), and external (electromagnetic and heavy particle radiation); they may be produced during normal operations or emergencies (leaks). These contaminants have been reviewed by Ross [84]. The nature, and especially the amount of AGA contaminants from these sources, will vary with the duration of the space flight.[2]

The concentration of contaminants at equilibrium and the time to reach this concentration are determined by the variables of Equations (1) and (2) [86]. These are key factors in establishing the rate of removal needed to attain a given equilibrium level in the atmosphere.

$$C = \frac{W}{b}\left(1 - e^{\frac{-bt}{a}}\right) \qquad (1)$$

where,

C = mg/m^3 of contaminant at time t;
W = mg contaminant generated/day;
b = m^3 atmosphere leaked/day at x psia;
t = days elapsed time;
e = 2.718

This equation suggests that an equilibrium level of contaminant will be reached. The time to reach 99% of equilibrium concentration after closure can be estimated by the equation:

$$t_{\text{days}} = 4.6a/b \qquad (2)$$

where,

a = m^3 total effective volume
b = m^3 leak/day at x psia

In evaluating the buildup rate, important secondary factors to be considered for each contaminant are the kinetics of sorption along adsorption beds and the breakthrough curves for such gas bed systems. These curves also determine the nature and timing of secondary chemical reactions which can occur on the bed and thus the alteration in the nature of the trace contaminants to be considered.

Biologic Sources—Microflora

The growth of microorganisms can be expected in spacecraft on surfaces in addition to those of the human body. Bacteria, fungi, and possibly algae will grow on surfaces of the spacecraft if there is sufficient adsorbed nutrient and water. Experiments have been described with men in chambers simulating certain factors of space flight under different regimes of work and rest. Along with physiological, psychological, and clinical investigations, attention was given to the microflora of the chamber and skin of the occupants, and the immunologic reactiveness of the men. Significant changes and interactions were found in the microbial system [12].

Popov and coworkers utilized small, closed rooms which had been disinfected, had practically no influx of dust, with controls for composition, temperature, and circulation of air. They found that contamination of skin and clothing of the occupants was only minimally affected by dust from clothing, footwear, furniture, and other equipment. Possible sources of contamination were: food residues, untrapped urine and feces, and bacterial aerosols. The important and continuously active source of skin contamination to the occupant's skin was the skin itself [12].

Table 1 illustrates the increase of microbial content in the air and the effect of an air purification system in a sealed chamber occupied for 120 days. The level of microbial contamination of air depends on the duration of man's stay, number of crewmembers, conditions of their work, filtering capability and cycling of the

[2] The numerous valuable contributions of Kustov and Tiunov are worthy of note and several are cited in this chapter [43, 44, 46, 100, 101].

mechanical system of purification from chemical substances, and regeneration of air. It also depends on the presence of special disinfectant apparatus, and gas composition of the atmosphere. Along with the increase of general bacterial contamination of the air, there are shifts in the yeasts and other specific microflora present with an increase in the proportion of pathogens. For example, a small but significant increase in the population of *Candida* sp has been noted as well as saprophytic white staphylococci, diphtheroids, bacilli, and sarcinae. The skin microflora vary among individuals, which is to be expected, but these differences soon disappear upon confinement in real or simulated spacecraft [59, 70, 73, 113].

Since animals have been flown in spacecraft, it is important to consider their microflora also. Sitnikova's observations on animals in experimental chambers revealed that the quantity of microorganisms in the air increased fivefold, and there was a shift to predominance by types of organisms more resistant to the effects of the air such as spores, aerobes, and molds. It has also been suggested that animals in sealed chambers might develop a reduced resistance to virus infections [12, 70].

The effect of the air composition on the microbial population, as noted above, has also led to the suggestion by Borsenko et al [70] that the AGA might be adjusted to produce a decrease in bacterial contamination of the air. However,

TABLE 1.—*Average Microfloral Contents of Air, Skin, and Pharynx of Subjects Tested at Different Periods of a 120-Day Experiment* (After [70])

Index (total count)	Before experiment	Experiment period, days								Days after experiment		
		1–15	16–30	31–45	45–60	61–75	76–90	91–105	106–120	1–15	16–30	31–60
In 1 m^3 air	1500	7500	12 000	14 000	7500	17 000	14 000	30 000	3000[1]			
On 1 cm^2 skin	30	56	66	66	60	53	53	66	30[1]	39	30	31
In 1 cm^3 pharynx washings	34	66	74	37	10	102	58	168	33[1]	30	28	30

[1] On days 106–120 of the experiment, the low level of microbial infestation is related to the development and use of a system in the hermetic chamber for purifying air from microorganisms.

According to the Soviet experience, the following rules seem to characterize the microbial content of the AGA:

1. There are periodic increases in the number of microflora.
2. Each quantitative increase is accompanied by a change in the qualitative composition.
3. The skin microflora indicate development of the phenomenon of dysbacteriosis.
4. Each periodic increase includes an increase in the proportion of skin microflora having pathogenic properties or increased resistance to antibiotics of the penicillin and tetracycline groups [12, 49, 70].

this subject has not received much study. Similarly, little attention has been given to contamination of the AGA by gases released by the microflora. Korotaev and coworkers [43] have established that the algae, *Chlorella*, release toxic materials including carbon monoxide. The CO formation is related to oxidation of the tetrapyrrole nucleus in the chlorophyll molecule.

Biologic Sources—Man

All the excretory products of man contribute to the gaseous pollution of the AGA in the spacecraft, which are released into the spacecraft from lungs, gastrointestinal tract, urinary tract, skin, hair, and mouth [12, 86].

Respiratory. The lungs release water, carbon dioxide, and carbon monoxide predominantly. The rate of carbon monoxide exhalation from normal degradation of hemoglobin by one person is about 0.4 ml/h. Analysis of the exhaled air of healthy young adults showed these minor contaminants present: ammonia, formaldehyde, acetaldehyde, acetone, methylethyl ketone, methanol, propanol, butanol, formic acid, acetic acid, propionic acid, methane, ethane, and higher hydrocarbons [71, 94, 100, 109].

Gastrointestinal. The gastrointestinal excretions are feces, flatus, and urine. Their gaseous components include indole, skatole, carbon dioxide, hydrogen, hydrogen sulfide, methane and other hydrocarbons, nitrogen and its oxides, aliphatic acids, phenols, oxygen, and various mercaptans. The latter depend to a great extent on the diet. Nearly 150 specific compounds have been identified in urine, very few of which are volatile until degraded by bacteria, whereupon the principal air contaminant is ammonia. Details of the amount and composition of feces, flatus, and urine have been tabulated by Roth, Wheaton, and Grace [12, 109].

Integument. The skin and its sweat glands are the sources of volatiles such as ammonia and phenols along with numerous trace materials. The skin and the hair are also sources of particulate matter that will be suspended in the air. These desquamated scales consist of proteins and lipids and carry numerous microorganisms. Their particle size is too large to be of any health significance but they may create mechanical problems in the spacecraft's equipment [109].

In view of the contaminants described, it is clear that man in a sealed environment becomes an important source of toxic contaminants. These impurities in the AGA must not be permitted to accumulate above safe levels.

Materials

Materials currently being used in US manned spacecraft were listed at the NASA Manned Spacecraft Center in Houston, Texas [33]. Kustov and Tiunov have reviewed the experience with USSR spacecraft materials [46].

Compounds of relatively high vapor pressure are outgassed from solid materials and from the hydrocarbon lubricants and operating fluids of machines. They originate from such sources as plastics, toilet articles, lubricating compounds, insulations, paints, adhesives, and residual solvents from degreasing treatments.

The rate and composition of outgassing for various spacecraft materials have been studied [19, 74, 81]. The oxygen content and temperature of the atmosphere alter the rate and composition for the products. Intermittent purging of the atmosphere is also a variable to be considered in predicting contaminant outgassing and accumulation rates. Compounds continue to be outgassed after 90 days' exposure to space cabin atmospheres. The outgassing characteristics and other design parameters for nonmetallic components of US spacecraft have recently been incorporated in a handbook available from the Manned Spacecraft Center [73].

A special panel, convened in 1967 under the Space Science Board of the US National Academy of Sciences, was concerned with outgassing products in confined spaces. Their report tabulates more than 300 compounds detected in various US spacecraft and flight simulations [66].

Processes

The numerous processes carried out aboard a spacecraft are another significant source of AGA contaminants, many of which are in the form of solid or liquid aerosols.

Cooking may release such gases as acrolein, carbon monoxide, and formaldehyde along with solid particulates as smoke. Personal hygiene procedures, including washing and shaving, produce aerosols. Ozone may be produced by electrostatic precipitators used to remove particles from the air. It may also be produced by ultraviolet radiation used for controlling microorganisms. Any electrical apparatus having a corona or spark discharge will also form ozone.

Many of the proposed systems for recovering oxygen from carbon dioxide during long flights operate at elevated temperatures. If the AGA contains halogenated organic compounds they may be partially or totally decomposed when passing through the oxygen regenerators. The

decomposition products are often more toxic than the original impurity. Alkaline processes for removing carbon dioxide can generate sufficient heat to create similar problems.

One reaction of this type is of special concern in the spacecraft. Its starting materials are the halogenated solvents used for degreasing equipment prior to assembly or for solvents in paints and other coatings. Traces of these often remain to be outgassed later during space flight and may then be decomposed as:

$$Cl_2C{=}CHCl \xrightarrow[\text{alkali}]{\text{heat and/or}} ClC{\equiv}CCl{+}HCl$$

The trichloroethylene is considered moderately toxic, the HCl is an irritant, but the dichloroacetylene is extremely toxic. This problem has been reviewed in detail [66].

Spacecraft contain numerous heat transfer systems which involve fluids having detectable vapor pressures. Small leaks of these fluids can produce a gaseous contaminant as well as an aerosol.

Aerosols

In view of the numerous sources (bacteria, man, materials) and aerosols (solid or liquid), it is of value to consider some of the properties of aerosols in relation to their behavior in the weightlessness condition of space flight.

Even *nontoxic* particulates may be a hazard in space operations because of the zero-gravity environment [9]. In reviewing toxic hazards, there must be concern that aerosols can act as adsorbents or condensing nuclei for toxic gases [90]. This facilitates entrance into the lower respiratory tract of materials which, because of their high water solubility, are generally trapped in the upper respiratory tract. It also provides for local areas of extreme irritation due to concentration of the toxic gas at the locus of impaction.

The problem, which is unique in the closed living space, is the tendency of aerosol particles to increase with time in numbers and mean diameters.

Theoretical considerations of the role of zero gravity in the properties of aerosols imply that the amount of particle or droplet contamination inhaled in orbit could be increased over the amount inhaled in a similar situation under $1{-}g$ environment [10]. The following data and conclusions are taken directly from the Busby and Mercer study [10].

> The predicted characteristics of particle and droplet deposition in the respiratory passages for the weightless environment show that in space, as on Earth, the nose or mouth should continue to operate as highly efficient filters, protecting the lower respiratory passages from all particles and droplets above about 10 μm diam. Fortunately, this size is considerably less than that of particles and droplets of most contaminants which might be introduced into the spacecraft cabin atmosphere. Theoretical *deposition curves* predict that fewer inhaled particles and droplets, having diameters between about 0.5 and 10 μm, will be deposited in lower respiratory passages in a weightless environment, than in one of unit gravity. Substitution of helium or another gas for nitrogen would, in this pressure range, alter viscosity by only a few percent, hence should not alter these deposition curves significantly. There are no definitive empirical data to support these theoretical curves.

Under conditions of Earth gravity, retention of particles in diameter size 0.2 to 5 μm varies between 20 and 90%. Of the particles gaining entrance to the lower respiratory tree, maximum retention is for 1-μm particles and minimum retention is at 0.4 μm. The disposition of these deposited particles depends on their solubility. Those which are water-soluble are rapidly absorbed into the blood stream and a toxicologic effect may occur in a short time. Less soluble substances and those deposited on the upper airways are moved by the flow of mucus and by ciliary action to the pharynx, where they enter the gastrointestinal tract. An excellent review of the deposition, clearance, and retention of inhaled particulates was prepared by Middleton and his committee, concerned with an air pollution standard [54].

Ionized aerosols have been discussed often as a cause of behavioral changes during various

meteorological phenomena [45]. Other biologic effects, such as those on tracheal cilia and on lower biologic forms, have also been reported. The concentration of aerosol ions in the natural or submarine atmospheres has always been small, averaging about 450 (+) ions and 250 (−) ions/cm^3 [42]. No data have been obtained in operating space cabins. In view of the low concentration of aerosol ions in submarines and the uncertain significance of the experiments with isolated tracheal preparations, the potential significance of these aerosols in space cabins is not clear. The problem has been discussed by Nefedov [69].

Malfunctions and Emergencies

In addition to materials present during normal operations, the toxic atmospheres resulting from fire or equipment failure must be considered. Accidents in the launch and preparation areas, as well as on board future spacecraft where extravehicular maneuvering units may be serviced, can lead to exposure to vapors and aerosols of rocket fuels and oxidizers from spills or leaks. Such exposures may lead to acute toxicity from relatively large doses of the compounds. Their toxic effects have been recently summarized [39].

Equipment malfunctions, especially those of electrical equipment, may cause overheating and thermal degradation of insulation. Fire in a spacecraft will produce combustion products along with decomposition products of any fire extinguishing materials used. In these situations, a variety of compounds of different degrees of toxicity will be formed, depending on the materials involved and the conditions of decomposition.

When high molecular weight materials are decomposed by heat, two general mechanisms are involved: depolymerization and fragmentation; both probably occur in all instances but in varying proportions. Monomer production is high from polytetrafluoroethylene, polymethylmethacrylate, and polymethylstyrene. The monomers and chain fragments may also react at high temperatures to form new materials, such as methanol, carbon monoxide, halogen acids, aldehydes, hydrogen cyanide, octafluoroisobutylene, and carbonyl fluoride. If metals are involved in overheating, for example selenium rectifiers, fumes of the metal and its oxides will be formed. Each material and each potential malfunction must be considered carefully in selecting items for spacecraft construction [1, 36, 90, 109].

The proposed transfer of spacecraft occupants from one ship to another poses special problems. What will be the effect on new personnel entering a ship whose environment is already contaminated with the gaseous, particulate, and microbial effluvia of a preceding crew? Will a period of double occupancy be required while the new crew becomes adapted sufficiently to assume control of the ship? Will a crew moving from a contaminated ship to a clean one or back to Earth experience any difficulties [72]?

Analysis and Monitoring

Qualitative and quantitative analyses of the vital gases and contaminants in the AGA are essential to protect the health of the astronaut. The variety of compounds and low concentrations of many challenge the sensitivity and accuracy of existing analytical equipment, especially those compatible with spacecraft. Consequently, the data obtained from space flights are limited and subject to inaccuracies.

The reproducibility of levels of toxic materials found in space cabin simulators has been recorded [14]. Detailed analyses of these materials illustrate the variability of data from sample to sample and laboratory to laboratory. At the present state of the art of analysis and sampling, any data on "the highest concentration" found in sealed cabins must be viewed with the appropriate level of skepticism suggested by these data.

Procedures are continually being improved and gas chromatographic techniques are commonly used. Current studies of infrared spectroscopy interferometry, double resonance microwave spectroscopy, mass spectrometry, and other new techniques, offer some promise for ground-based and possibly in-flight sampling and analysis [8, 14, 57, 83, 92, 99, 102]. The techniques and procedures used by the USSR have been described by Nefedov et al, who have also pointed

out the need to monitor the AGA for microbial contamination [70, 71].

External Contaminants

Spacecraft and their occupants are subject to electromagnetic and heavy particle radiation, especially on exposure to a solar flare. These effects have recently been discussed by Grahn [67], and Lebedinskii [48].

Experience from both manned and unmanned Moon landings so far indicates that contamination of the craft by extraterrestrial materials will not present any new or magnified health hazards. This observation does not necessarily apply to human landings on other targets.

Odors

The human olfactory sense permits detection of vapors of many organic substances at concentrations of 10^{11} to 10^{13} mol/cm^3 air, and some at concentrations as low as 2×10^{9} mol/cm^3 [17, 21]. There are also indications that substances at one-tenth the threshold may influence the odor quality of other odorants present at concentrations well above the threshold [40]. The use of the olfactory sense in detecting and diagnosing malfunctions in equipment systems has been thoroughly reviewed [31].

Fortunately, the human olfactory sense adapts to odors quite rapidly. Experiences in space cabins and space cabin simulators suggest that crews are not bothered by odors in the cabin which may overwhelm additional crew who are unacclimatized.

POTENTIAL BIOLOGIC EFFECTS OF SPACECRAFT AIR CONTAMINANTS

All compounds have an adverse effect on the body at some quantity or concentration. Upon absorption into the body, toxic substances may be processed in one or more of several ways. They may be retained or excreted unchanged; or biotransformed by oxidation, reduction, hydrolysis or conjugation to products less or more toxic. Through these processes, the body has the ability to accept a finite amount of any substance without injury, according to present knowledge. When the capacity of these processes is exceeded, there is an adverse effect, the magnitude of which is related to the amount of excess material absorbed. The relationship between causative dosage and resultant effect is not necessarily a constant proportionality over the entire range. This lack of proportionality in dosage-effect relationships makes extrapolations beyond the range of available data unreliable [61].

In most instances the body can repair the damage with no residual effect, although sometimes there is a permanent change, such as a scar. In such cases, the total permanent change from single or repeated exposure may be sufficient to cause detriment to the body. In a few, relatively rare circumstances, the initial injury can alter the body's physiological processes in specific tissues so that they function abnormally long after the causative agent has disappeared, examples of which are changes in hormone excretion or cellular proliferation to produce tumors [111].

The study of these effects, which constitutes the science of toxicology, is complicated by many variables such as differences due to sex, age, and species. These factors and others have been reviewed and discussed extensively [35, 86].

The present state of toxicological knowledge is not adequate for reliable prediction of the effects of most substances on an individual at any given dose. This is especially true for the space program for two reasons: the increased use of multi-ton quantities of high-energy physiologically reactive compounds with inherent increased possibility of accidental exposure; and the contemplated long-term space mission within a closed system, in which, unlike submarine conditions, unlimited power is not available for complete control of the atmosphere. For adequate toxicological information in both situations, the greatest need is for inhalation data. This has led to construction of numerous experimental laboratories with sealed chambers for studying the effects of toxic substances on man and animals. One of these has been described in detail [37].

Exposure or dose may be expressed in several ways. One describes the quantity in terms of

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weight or volume of material per unit weight of the animal, for example, mg/kg. When referring to the concentrations of a gas or particulate in the air, the terms parts per million (ppm), which is a volume-volume ratio, or mg/m^3 are generally employed. In air exposures, the time of contact in minutes or hours is included. In the space cabin environment with an altered partial pressure of the atmosphere, it has been suggested that μmol/m^3 or mmol/25m^3 may be a more reasonable way to express the data [66]. The latter unit gives a numerical value which, at 1 atm pressure and at 25°C, is the equivalent of ppm by volume (the units used for submarine standards and occupational exposures to gases and vapors). At the same time it expresses the molar concentration per unit of space volume and is, therefore, equivalent to partial pressure of the contaminant. Unfortunately, the toxicological literature does not yet make use of these latter expressions as standard terms.

The dose-response data from toxicity studies result in a sigmoid graph with the actual data being more or less scattered about a smooth curve because of variability between test animals. The least variability is at the dose producing 50% response. Abbreviations used are: lethal dose (LD) and lethal concentration (LC); the percent of animals affected is expressed by subscript 0, 50, 100, and so forth. When subscripts are not used, the value has probably been based on limited observations and lacks statistical validity. When time is a factor, such as for inhalation exposure, it must be given. For example, LC_{50}/4 h means the concentration most likely to be lethal to 50% of the animals upon exposure for 4 h.

Quantitative relationships of dose and response are exceedingly important in the theoretical and practical evaluations of toxic action. In general, the greater the dose, the more severe the response or more rapid its onset. With some substances, time is an equally important factor in determining effect. Mathematical modeling of these relationships has been discussed by Roth [86].

Acute Toxicity

The term acute toxicity refers to the adverse effects from single or multiple doses delivered in a short time, such as by inhalation for a few hours. These are relatively high doses. Data on the acute toxicity of spacecraft contaminants are needed for several purposes. They serve as a quick and inexpensive screening procedure for estimating degree of toxicity and nature of the toxic effect. Such data provide a useful guide to selection of materials for use in space. Acute toxicity data are vital to planning for long-term toxicity studies and are directly useful when planning for emergency situations.

The concepts and methods of acute toxicity determinations, reviewed by a US National Academy of Sciences committee under the chairmanship of Lehman [60], describe in some depth the various factors that can affect the outcome of acute toxicity testing.

A brief review. The significant acute toxic effects of AGA contaminants will be reviewed, but space will not permit detailed discussion of their action, such as effective concentrations. Their action may be noted over the entire range of a few parts per million to several percent by volume. The alcohols produce narcosis and are irritants to the eyes and respiratory tract at high concentrations. Methanol is unique for its specific injury to the optic nerves. The esters of acetic acid have properties similar to those of the corresponding alcohols. They are metabolized to the alcohol. The ketones also are irritants and depressants of the central nervous system, and their odors can cause nausea at high concentrations. The aldehydes are strong irritants, generally stronger than the related ketones or alcohols and esters.

The acute toxicity of acetone for man in a sealed chamber has been reported by Mikhailov [56]. Concentrations of 0.44 and 0.55 mg/m^3 produced changes, respectively, in the electrocortical reflex and in the light sensitivity of the eye. Physiological compensatory changes for these effects were noted and it was concluded that short-term exposures up to 10 mg/m^3 are safe for man. Similar effects might be expected from many other oxygenated compounds at different concentrations.

The saturated alicyclic and aliphatic hydrocarbons are relatively mild in toxic action. High concentrations lead to narcosis. There is a possi-

bility that very high concentrations may also affect the cardiovascular system. The toxic action of acute exposure to aromatic hydrocarbons is primarily depression of the central nervous system. Many compounds of this class are irritating.

Halogenated aliphatic compounds vary widely in the nature and severity of their acute toxicity; most cause narcosis and many injure the kidneys. Several are especially powerful agents for producing cardiac arrhythmias.

The heterocyclic compounds have few physiologic actions in common; the majority have distinct odors but toxic effects are diverse.

The inorganic gases encountered in spacecraft are respiratory irritants with the exception of carbon oxides. The action of most inorganic gases is exerted in the upper part of the respiratory tract, but a few, such as phosgene, penetrate deeply into the lungs. The carbon oxides, CO and CO_2, produce significant effects in acute exposures and deserve more detailed discussion.

Carbon dioxide is a normal component of air and a constituent of expired air resulting from metabolism. At concentrations above the normal physiologic range it stimulates the respiratory center and causes increased respiration. Concentrations of 7 to 10% by volume may produce unconsciousness, even if oxygen content is maintained at normal levels.

When carbon monoxide is inhaled, it reacts with hemoglobin to form the relatively stable compound, carboxyhemoglobin (COHb). This reaction utilizes the same bonding sites in hemoglobin as those for transporting oxygen from lungs to tissues. The result is anoxia at the cellular level throughout the body. It is more convenient and reliable to relate atmospheric CO to the percent of hemoglobin converted to COHb, which in turn can be related to toxic action. The heart and central nervous system are most sensitive to this effect. The cardiac effects are, of course, more critical during periods of heavy exercise or heat stress and may be significant at levels as low as 5% COHb. It has been suggested that subtle central nervous system effects result from COHb concentrations around 10%. A recent review of the toxicity of CO [68] includes a computer program developed by Roslinski for the equation introduced by Coburn [13], which relates CO exposure to bodily uptake. This equation correlates closely with experimental data.

The Coburn equation includes the CO produced endogenously by metabolism of hemoglobin, but does not directly allow for increased endogenous CO resulting from radiation-induced hemolysis. It has been shown that a dose of 600 R will produce an increase of $10.7\% \pm 1.3$ in the blood carboxyhemoglobin with concomitant decrease in the oxygen transport capacity [69].

The actions of microflora on spacecraft crews, a form of acute toxicity, should be considered. The normal bacterial flora in man's skin, mucous membranes, and intestines have been thoroughly reviewed [82] with special emphasis on differences in flora of various body sites. The microbiological changes in sealed chambers have already been discussed. The tendency toward increased total skin flora, especially in axillary, groin, and other fold areas [20, 23, 26, 82], is augmented by wearing a space suit and by high humidity [22]. The increasing bacterial population tends to reach a plateau after variable periods in a given environmental situation [12]. There is an exchange of fecal and skin flora among enclosed subjects with no tendency for pathogens to become predominant [32, 72]. Throat flora are exchanged less rapidly [23]. Little is known about the viral population in sealed systems. Subtle interactions between the gaseous environment and host may alter viral infectivity [28].

Chamber studies so far indicate no tendency toward decreased body resistance to pathogens [50]. Pathogens have been transferred from subject to subject with no outbreak of infection [23]. Presence of 100% oxygen at 5 psia does not appear to alter greatly animals' susceptibility to pathogenic infections [58]. It would be expected that the isolated spacecraft environment would eliminate exogenous infectious disease. However, radiation and subacute stress may alter response to enable normal flora to become pathogenic in future missions, but no problems have arisen so far. In nuclear submarines with large crews, there tends to be a flurry of infectious disease of primarily respiratory type in the first few weeks of a cruise, but this incidence drops

rapidly as *herd immunity* develops [110]. This pattern may be expected in future large space crews. The problem of microbial shock in space missions of long duration is still a hypothetical one [51].

New personnel, introduced into spacecraft that have been occupied for some time, may require a period of adaptation. Another consideration that affects crew safety is the effects of microbial flora on equipment. Filter beds clogged after prolonged exposure may be another, more subtle engineering problem, and fungi can cause the deterioration of electronic components [86].

Chronic Toxicity

Chronic toxicity usually refers to adverse effects of chemicals on the organism from repeated or continuous exposures lasting months or years. The quantities involved at any one time are relatively small. Occasionally it also refers to delayed effects from which recovery is slow. Unless otherwise indicated, this discussion applies to the first meaning.

The concepts and methods of chronic toxicity determinations were reviewed by the US Food and Drug Administration in 1959 [5]. The methods described are essentially those used today. An extensive, diverse literature on more recent methods will probably be consolidated by one or more authors in the near future. Animal responses to continuous exposure as measures of human response may not be entirely correct in all instances [34].

First consideration for chronic toxicity must be the AGA itself, especially its vital component oxygen. Our knowledge of oxygen toxicity indicates that excursions of only a few percent above the normal partial pressure can cause serious effects to the central nervous system as well as other vital tissues. These physiologic principles were reviewed by Roth in the *Bioastronautics Handbook* [109]. Golberg has provided a more recent, although brief, review [30]. Marked cardiovascular effects were described by Wood in 1972 [112].

Comments on the chronic toxicity effects of specific compounds in the AGA (which follow) are intended to identify possible critical problems but in no way are complete discussions of the materials' toxicity.

Alcohol concentrations which might be encountered continually in spacecraft AGA are probably low enough to be fully metabolized to CO_2 and H_2O with no adverse effects. Precautions are necessary to avoid accumulation of alcohols that will produce absorbed levels greater than the metabolic capacity of the body. This level is limited for methanol by the excretion rate of formic acid, the end product of methanol metabolism. Excess formic acid upsets the body's acid-base balance. It has been postulated that blindness caused by high doses of methanol is due to specific action of formic acid on the optic nerves [111]. Liver enlargement is also found in such circumstances.

Higher molecular weight alcohols, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, and tert-butyl, upon chronic exposure, lead to liver and kidney damage usually at concentrations well below those producing narcosis and below those found irritating [8].

Esters of these alcohols with acetic acid are found. The first noticeable effect of chronic exposures with increasing concentrations is hypotension and irritation followed at higher concentrations by pulmonary edema, liver and kidney damage, and narcosis [78].

The chronic toxicity of ketones seems related to their irritancy with little or no cumulative toxic effects since they are readily metabolized at low concentrations [111]. The same may be said of the aldehydes; however, their control level must be lower than that of the corresponding ketones to avoid pulmonary edema [78].

The aliphatic and aromatic hydrocarbons, with the exception of benzene, are only slightly toxic at low concentrations of chronic exposures. Mild irritation of vital organs and narcosis are found at higher levels. Benzene is well-known for its ability to damage the bone marrow leading to anemia and leukemia. Benzene should be rigidly controlled because of the seriousness and irreversibility of its effects [27].

The chlorinated hydrocarbons, $CHCl_3$, $ClCH_2—CH_2Cl$, $Cl_2C{=}CCl_2$, CH_3CCl_3, have all been detected in the AGA of spacecraft. Chronic exposures can lead to liver and kidney

injury, which does not appear to happen with the chlorofluoro-hydrocarbons $ClCF_3$, Cl_2CF_2, $FCCl_3$, and Cl_3CCF_3 which have also been found in spacecraft. The latter compounds have very low chronic toxicities. All halogenated hydrocarbons should be considered as capable of causing cardiac arrhythmias and each should be studied carefully for this factor. These compounds have another feature in common: thermal decomposition to toxic products, a degradation enhanced by alkaline conditions. The products include the halogenated acids, HCl, and HF, which are irritants, and most importantly may also include the highly toxic chlorinated acetylenes. The latter attack the nervous system, especially the trigeminal nerve causing paralysis [89].

Among the heterocyclic compounds, a variety of chronic toxic effects is found. Skatole can be a depressant of the circulatory and central nervous systems [87]. Furan will produce reversible liver changes [96]. Liver and kidney injury has been found from both dioxane and indole but more importantly, both compounds have been reported to produce cancer in animals [4, 18].

Of the inorganic gases and vapors found in the AGA of spacecraft, ammonia is perhaps the most innocuous. Its ready solubility in the moisture layer of the upper respiratory tract and prompt metabolism lead to the conclusion that it is unlikely to cause any systemic toxicity problems. Its odor at low levels, to which a person may well adapt, and its irritancy at high concentrations appear to be limiting factors for continuous exposure in spacecraft. However, note the following Soviet results.

Mikhailov [55] studied the chronic toxicity of ammonia, a product of the activity of man, in experimental animals. At 7.2 to 8.1 mg/m^3 there seemed to be a cumulative action as expressed by increased organ/body weight ratios, decreased oxygen consumption, decreased weight gain, decreased lifespan.

There is little probability that occupants of spacecraft will experience chronic exposure to the strong irritant gases, HCl, HF, COF_2, SO_2, or NO_2, since they are usually formed only in emergencies. If such conditions should develop, the toxic effects would be chronic irritation of the respiratory tract which might cause bronchitis, tracheitis, pulmonary edema, or emphysema.

Methanethiol, CH_3SH, and other alkylmercaptans originate from feces and may be found at low levels in spacecraft. At these levels, odor control is the primary objective. Higher levels can have serious effects on the central nervous and circulatory systems [88].

Acetonitrile at high concentrations for acute exposures produces cyanosis. Chronic exposures at lower concentrations cause lesions in the brain, lung, liver, and kidneys [80]

p-Dichlorobenzene may be found as an off-gassing product and thus presents a chronic exposure problem. It is a strong eye irritant and has been reported once to cause cataracts [6].

Carbon dioxide chronic exposures at about 2 or 3% by volume or greater produce a reversible, compensated acidosis characterized by increased bone deposition of carbonates. At levels below those producing respiratory stress there seems to be little, if any, effect on performance capability of submarine crews under these conditions [91].

Carbon monoxide by chronic exposure will reach an equilibrium level of hemoglobin saturation within 24 h or less in accordance with Coburn's equation [13]. There is evidence of compensatory increases of hematocrit and hemoglobin content of the red blood cells following prolonged, continuous exposures to carbon monoxide. If the burden of CO is great, the body's compensation can elevate the viscosity of the blood which may cause enlargement of the heart [52, 65, 106].

An extensive review was conducted by Soviet scientists on problems created by man's endogenous production of CO in a sealed environment. Considering the biochemical and physiological indices for man as affected by CO at 110 mg/m^3, they concluded that the minimum physiological shifts observed could not be due totally to carboxy hypoxemia, and that there was probably significant action by CO at the tissue level [46]. This is not unexpected considering that many tissues, such as muscle, contain other globin proteins having the tetrapyrrole moiety similar to hemoglobin.

Programs have been established to provide specific toxicologic information on selected

propellants and to study the effects of long-term, continous exposure to possible trace contaminants at reduced atmospheric pressures and under the influence of one- and two-gas systems (oxygen or oxygen/nitrogen) [2, 66, 99]. These studies include definitive measurements of physiologic changes evidenced by clinical chemistry, changes in behavioral patterns, and gross and microscopic pathology, which, it is hoped, will permit more definitive evaluation of the space cabin problem.

Chronic effects on man have been noted as a result of the microbiological contamination of the AGA in closed systems. The indices of intellectual and physical ability to work deteriorated as microflora in the air increased and changed in composition [72]. In the flight simulation studies extending to 4 months by Borsenko, reduced responses of the central nervous sytem were noted accompanied by general suppression of activity and other physiologic functions such as resistance to the microflora [7].

Increased incidence of skin autoinfections was observed in submarine crews and flight simulation volunteers, which was attributed to nervous psychic fatigue and limited sanitary facilities [12]. The increased microfloral content of the AGA was also accompanied by reduced leucocytic phagocytosis and decreased lysozyme content of the saliva [70].

Possible use of algae (*Chlorella* sp) for converting CO_2 to O_2 led to a study of the effects of trace contaminants of the AGA on algal metabolism. Small amounts of ammonia, carbon monoxide, or acetone increased the average cellular consumption of CO_2. Hydrogen sulfide and air exhaled by man decreased the CO_2 utilization [44].

Combinations of Contaminants

Nearly all of man's encounters with contaminants in air involve more than one pollutant simultaneously. This is true in closed systems such as spacecraft and submarines as well as the open systems of occupational and public exposures. It is surprising to find very few studies on the toxicity of mixed contaminants; one reason may be the overwhelming number of possible combinations and permutations that might be investigated. It would be highly desirable to be able to predict with reasonable reliability whether the components of a mixture would act upon man independently, as oxygen and nitrogen, or interdependently. If they should act interdependently, would they be antagonistic, simply additive in their effects, or synergistic to produce a greater than additive effect? Even a plausible theory or hypothesis would be useful as a guide for choosing combinations for experimental study.

This problem has been discussed specifically in relation to space flight by Tiunov and Savateev [101], who suggest that mathematical equations can be developed for calculating the combined effects of contaminants in the AGA. It is necessary to know the kind of interaction between the components, if it is additive, antagonistic, or synergistic, in order to select the proper equation.

A mathematical approach to mixed gas exposures has been developed for occupational exposures by the Threshold Limit Values (TLV) committee under the chairmanship of Stokinger for the American Conference of Governmental Industrial Hygienists [3]. The mixture of gases and particulates from thermal decomposition of polymers has been analyzed and their acute toxicity determined [36, 99].

Experimental evaluation of the chronic toxicity effects of a mixture of gases was reported by Sandage [88]. The mixture consisted of hydrogen sulfide (20 ppm), methylmercaptan (50 ppm), indole (10.5 ppm), and skatole (3.5 ppm). Monkeys, rats, and mice were exposed continuously for 90 days. It is clear from their findings that the problem of mixed exposures is far from simple additivity. The observed effects were:

1. Sulfhemoglobin was formed to a significant degree in rats and monkeys, but ten times as much appeared in the blood of rats.
2. A low-grade hemolytic process appeared to exist in all animals, although there was no evidence of impairment of hematopoietic function.
3. There were marked species differences in response to the chemicals. Lung pathology was observed in 75% of the mice, but was not significant in the other

two species. Liver pathology was not significant in rats and monkeys but existed in 60% of the mice. Weight loss was significant only in the mice. On the other hand, stress tests revealed significant decrease in endurance of rats, but not of mice.

4. The real cause of death in monkeys is obscure. In mice and rats, however, the cause of death was probably anoxia and secondary respiratory infection, both of which are compatible with the lung pathology observed.
5. Rats and mice exposed to the mixture of compounds displayed a higher mortality rate than when exposed to the single compounds. There are a number of reasons for believing that this difference reflects significant differences among individuals with regard to sensitivity to toxic compounds. There is also evidence of adaptation to the toxic atmosphere if the animals are able to survive the first severe effect.

Data have been reported on the physiologic changes resulting from space flight. This study of actual manned space flights included the stress of weightlessness along with exposure to numerous contaminants of the AGA [25].

EXISTING AIR QUALITY STANDARDS

Individuals vary widely in responses to stresses by physical, physiologic and psychologic conditions. These variations, which occur among individuals and in any one individual from time to time, represent differences in genetic makeup and life history. Accordingly, the ideal method of avoiding excessive stress is to observe each person closely and to remove or limit the stresses when his response reaches an acceptable level, prior to that considered undesirable. The goal should be to develop standards for response limits rather than for stress limits. Unfortunately, knowledge of the multitude of response mechanisms in the human body is meager and means of observing them are quite limited, especially in spacecraft. It is expected that the Skylab experiments will provide data on this problem. The indirect approach must be taken to protect individual spacecraft occupants by limiting stresses, using engineering methods designed to maintain conditions that will not produce adverse responses in the *average human.* Variations from the average human are wide, making it necessary to incorporate safety factors when setting standards for design and operation of the engineering systems involved. This requires monitoring the health of each individual in space for changes.

Occupational Standards

One of the most comprehensive sets of standards (and best known) for safe exposures to air contaminants is the Threshold Limit Values (TLV) [3]. These standards for occupational exposures to more than 500 compounds "represent conditions under which it is believed that nearly all workers may be repeatedly exposed day after day without adverse effect." Other guidelines are available to the space toxicologist—the maximal allowable concentrations of the American Standards Association's Z–37 Committee [105]. Soviet toxic hazard standards for industrial exposure have been published [75, 107]. Much of the toxicologic basis for their standards is in a series of publications, the most recent of which is by Letavet and Sanotskiy [49a].

It has been suggested that these occupational values used for exposures of 8 h/d, 5 d/wk might be converted into values for continuous exposure in space. However, experience with submarines capable of continuous submersion up to 90 d has shown the necessity to reevaluate the data used for TLVs to establish safe air concentrations of the submarine air contaminants [11, 93]. Animal toxicity studies comparing 90-day continuous exposures with intermittent exposures of 8 h/d, 5 d/wk for 90 days at the TLV showed that the mathematical extrapolation of the TLV was most dangerous [88]. These tests in animals during 90 days at the Threshold Limit showed effects ranging from no mortality or other untoward effects to moderate toxicity, to almost complete lethality.

In our present state of knowledge it can be concluded that none of the industrial air limits

can be used with certainty, either directly or by extrapolation, for space cabin environments. Although such an extrapolating equation has been proposed [97] in which all variables likely to affect toxicity were included, subsequent experimental animal work [99] showed that such a procedure could not be relied on in any given case. Unpredictable variations in the rate of metabolism under conditions of continuous exposure relative to intermittent exposure appear to be overriding. It should be noted that animal studies are not capable of revealing the magnitude of several of the factors included in any extrapolation equation [34]. Soviet and US scientists have independently reached the same decision [101].

Public Health Standards

Worldwide concern for environmental pollution has prompted many countries to develop air quality standards. Such standards are set in the US by the Environmental Protection Agency and by various States to protect the most sensitive segments of the population including infants and the aged. The standards incorporate large safety factors. A careful selection for spacecraft personnel, including excellent health, makes it clear that public air standards are not necessarily applicable to spacecraft AGA.

Submarine Standards

Experience in submarines, especially those capable of continuous operation for up to 90 days, is useful for spacecraft operation. Applicability to spacecraft of standards currently in use by the US Navy (shown in Table 2 [103, 104]) has been discussed by committees of the US National Academy of Sciences (NAS) [63, 66]. Even the 90-day exposure limits set for submarines are not directly applicable to spacecraft because of many differences [11, 97]. Efforts to use these values when mixtures of toxic materials are involved (which is almost always in aerospace situations) are not only meaningless but also may be dangerous.

Submarine standards give values for 1 h, 24 h, and 90 d. Standards for shorter times—ceiling values which should not be exceeded without risk of significant health effects—are designed to be applied to emergencies. Such limits represent the maximum allowable concentrations permissible under operational conditions and are not to be construed as permissible limits for repeated short-term exposures. It is envisioned that sufficient time between these peak exposures will have elapsed to allow complete recovery of the exposed individuals. In some cases, there may be minor symptomatology.

Spacecraft Standards

Preliminary recommendations of limits in space to the above compounds for 1 h, 24 h, 90 d, and 1000 d have been given for a few of the compounds in Table 2 [63, 66]. Summary tables of the toxic mechanism of these compounds, sites of attack on the body, and groupings in regard to

TABLE 2.—*Limits for Atmospheric Constituents in Nuclear Submarines*
(Limits in ppm by volume unless otherwise noted) (After [104])

Chemical substance	90-Day limit	24-Hour limit	1-Hour emergency exposure limit	Remarks
1. Acetone	300	2000	(*)	
2. Acetylene	6000	6000	6000	Set at approximately 1/4 of lower explosive limit of 2 1/2%
3. Acrolein	(*)	(*)	(*)	
4. Ammonia	25	50	400	
5. Arsine	0.01	0.1	(*)	
6. Benzene	1.0	100	(*)	See item 15 (a)
7. Carbon dioxide	3.8 mm Hg	7.6 mm Hg	19 mm Hg	Equivalent to 1/2, 1, and 2 1/2% at 760 mm Hg

TABLE 2.—*Limits for Atmospheric Constituents in Nuclear Submarines*—(Continued)
(Limits in ppm by volume unless otherwise noted) (After [104])

Chemical substance	90-Day limit	24-Hour limit	1-Hour emergency exposure limit	Remarks
8. Carbon monoxide	25	200	200	
9. Chlorine	0.1	1.0	(*)	
10. Dichlorodifluoromethane (Refrigerant 12)	200	1000	2000	Set by decomposition products formed in $CO-H_2$ burner
11. Dichlorotetrafluoroethane (Refrigerant 114)	200	1000	2000	Set by decomposition products formed in $CO-H_2$ burner
12. Ethanol	100	500	(*)	
13. Formaldehyde	(*)	(*)	(*)	
14. Freon refrigerants	—	—	—	See items 10, 11, and 37
15. Hydrocarbon solvents				Principal sources include: paint thinner, lighter fluid, mineral spirits, etc
(a) Benzene	3 mg/m³	3 mg/m³	(*)	Equivalent concentrations in ppm are listed under item 6
(b) Total aromatics (less benzene)	10 mg/m³	(*)	(*)	
(c) Total aliphatics (less methane)	60 mg/m³	(*)	(*)	
16. Hydrogen	10 000	10 000	10 000	Set at approximately ¼ of lower combustible limit of 4%[1]
17. Hydrogen chloride	1.0	4.0	10	
18. Hydrogen fluoride	0.1	1.0	8	
19. Hydrogen sulfide	(*)	(*)	50	
20. 2-Propanol	50	200	(*)	
21. Mercury	0.01 mg/m³	2.0 mg/m³	(*)	
22. Methane	13 000	13 000	13 000	Set at approximately ¼ lower explosive limits of 5.3%
23. Methanol	10	200	(*)	
24. Methylchloroform (1,1,1-trichloroethane)	2.5	10	25	Based on decomposition in $CO-H_2$ burner
25. Monoethanolamine (MEA)	0.5	3.0	50	
26. Nitrogen dioxide	0.5	1.0	10	
27. Oxygen	140–160 mm Hg not exceeding 21% by volume	140–160 mm Hg not exceeding 21% by volume	(*)	Physiological lower limit, fire safety upper limit
28. Ozone	0.02	0.1	1.0	
29. Paint thinner	—	—	—	See hydrocarbon solvents, item 15
30. Phosgene	0.05	0.1	1.0	
31. Phosphine	(*)	(*)	(*)	
32. Stibine	0.01	0.05	(*)	
33. Sulfur dioxide	1.0	5.0	10	
34. Triaryl phosphate	1.0 mg/m³	50 mg/m³	(*)	
35. 1,1,1-trichloroethane	—	—	—	See item 24
36. Trichloroethylene	(*)	(*)	(*)	
37. Trichloromonofluoromethane (Refrigerant 11)	5	20	50	
38. Vinylidene chloride	2.0	10	25	

*Limit has not been established.

[1] During battery charges, the H_2 limit shown above may be exceeded as discussed in Chapter 62, NAVSHIPS Technical Manual 0901–000–0020.

sources and chemical classifications have also been published [16].

The latest recommendations for air standards in spacecraft are given in Table 3 [63]. Similar to the submarine standards, the short-term limits are designed to allow time to cope with emergencies and represent ceiling values. If the limits are exceeded, alternatives must be considered such as wearing full space suits, masks, and helmets or opening the craft to discharge the contaminated air, or there may be significant health effects beyond minor discomfort anticipated at certain emergency exposure limits. These limits are based on the principles developed by the National Academy of Sciences-National Research Council (NAS–NRC) Committee on Toxicology for establishing emergency inhalation limits for military and space chemicals [95]. These principles were reviewed and expanded in 1968 by a NAS committee chaired by Nelson [66]. The committee utilized these criteria for trace contaminant control in manned spacecraft:

1. Contaminants must not produce significant adverse changes in the physiological, biochemical, or mental stability of the crew.
2. The spacecraft environment must not contribute to a performance decrement of the crew that will endanger mission objectives.
3. The spacecraft environment must not interfere with physical or biological experiments nor with medical monitoring.

In utilizing those criteria for development standards, these premises were adopted:

1. Any contamination of the spacecraft atmosphere *may* be detrimental.
2. Zero contamination level of the spacecraft atmosphere is impossible.
3. Data do not exist that will permit one to predict with precision the maximum contaminant concentration that will not cause degradation of the mission.
4. Provisional limit values can be established from some contaminants to serve as guidelines for design, development, and testing of future space systems.
5. These provisional limit values can ultimately be transformed into fixed limits if sufficient data about the effects of continuous exposure to a single compound and to multiple compounds can be obtained.

Of the 200 to 300 materials identified in hermetically sealed systems, the Committee selected 11 for immediate consideration and provisional recommendations. For purposes of these provisional criteria, the Committee assumed a spacecraft atmosphere ranging from 760 to 258 mm Hg total pressure, containing nitrogen as a diluent gas, oxygen sufficient to maintain normal (sea-level equivalent) alveolar partial pressure, and carbon dioxide below 5 mm Hg. Temperature and relative humidity are expected to be within the comfort zone for the total pressure selected. A detailed discussion is included in the report of the information studied for each substance. The shortcomings of the data and the needs for research are also discussed, which have since been reviewed and expanded by another NAS committee under the chairmanship of Stokinger. Spacecraft air quality standards were recommended for 52 compounds at these exposure times: 10 min, 60 min, 90 d, and 60 mo [63]. The compounds and recommended concentrations in the AGA are shown in Table 3 on the following three pages.

Soviet scientists have a similar approach to developing standards for spacecraft AGA. Gazenko and Genin considered the possibility of using submarine experience and recommended establishment of maximum levels for all harmful impurities in spacecraft [24]. Kuznegov recommended that pure oxygen atmosphere at 193 mm is dangerous, that a mixed gas should be used [47]. Nefedov and others called attention to interactions among spacecraft occupants, and to physiologic changes in occupants from this interaction [72].

Standards for contaminants were suggested by Gorodinskii, Levinskii, and Serbakov for 24-h continuous exposures [32]. Lebedinskii, Levinskii, and Nefedov suggested maximum values for more than 4 months' space flight [49], which are shown in Table 4.

TABLE 3.—*Atmospheric Contaminant Limits for Manned Spacecraft*
ppm (mg/m³) (After [63])

Compound (molecular weight)	10 Min, special area[8]	60 Min	90 Days	6 Months	Footnotes
Alcohols					
1. Methyl alcohol	— —	200	40	40	
(32.04)	— —	(260)	(52)	(52)	
2. Ethyl alcohol	2000	2000	50	50	(6)
(46.07)	(3800)	(3800)	(95)	(95)	
3. n-Butyl alcohol	— —	200	40	40	
(74.12)	— —	(600)	(120)	(120)	
4. Isobutyl alcohol	— —	200	40	40	
(74.12)	— —	(600)	(120)	(120)	
5. sec-Butyl alcohol	— —	200	40	40	
(74.12)	— —	(600)	(120)	(120)	
6. tert-Butyl alcohol	— —	200	40	40	
(74.12)	— —	(600)	(120)	(120)	
7. n-Propyl alcohol	— —	200	40	40	
(60.11)	— —	(500)	(100)	(100)	
8. Isopropyl alcohol	400	200	40	40	
(60.11)	(1000)	(500)	(100)	(100)	
Esters					
9. Methyl acetate	— —	200	40	40	
(74.0)	— —	(600)	(120)	(120)	
10. Ethyl acetate	— —	300	50	50	
(88.10)	— —	(1080)	(180)	(180)	
11. Butyl acetate	— —	200	40	40	
(116.16)	— —	(940)	(188)	(188)	
12. Propyl acetate	— —	200	40	40	
(102.1)	— —	(840)	(168)	(168)	
Ketones					
13. Acetone	— —	1000	300	300	(6)
(58.08)	— —	(2400)	(720)	(720)	
14. Methylethylketone	— —	100	20	20	
(72.1)	— —	(290)	(58)	(58)	
15. Methylisobutylketone	— —	100	20	20	
(100.08)	— —	(410)	(82)	(82)	
16. Methylisopropylketone	— —	*100	*20	*20	(5)
(86.77)	— —	(350)	(70)	(70)	
Aldehydes					
17. Acetaldehyde	— —	50	10	10	(1)
(44.05)	— —	(90)	(18)	(18)	
18. Acrolein	— —	0.2	0.1	0.1	
(56.06)	— —	(0.5)	(0.2)	(0.2)	
19. Formaldehyde	— —	1.0	0.1	0.1	
(30.03)	— —	(1.0)	(0.1)	(0.1)	

See footnotes at end of table.

TABLE 3.—*Atmospheric Contaminant Limits for Manned Spacecraft*—(continued)
ppm (mg/m³) (After [63])

Compound (molecular weight)	10 Min, special area[8]	60 Min	90 Days	6 Months	Footnotes
Alicyclics					
20. Cyclohexane	— —	300	60	60	
(82.14)	— —	(1020)	(204)	(204)	
21. Cyclopentane	— —	300	60	60	
(70.13)	— —	(870)	(174)	(174)	
22. Methylcyclohexane	— —	500	*15	*15	(5)
(98.14)	— —	(2000)	(60)	(60)	
23. Methylcyclopentane	— —	300	*15	*15	(5)
(84.1)	— —	(1029)	(51)	(51)	
Halogenated aliphatics					
24. Chloroform	— —	100	5	5	
(119.39)	— —	(490)	(24.5)	(24.5)	
25. 1,2-Dichloroethane	— —	200	10	10	
(98.97)	— —	(800)	(40)	(40)	
26. Dichloromethane	— —	100	25	25	
(85.94)	— —	(340)	(87.5)	(87.5)	
27. Methylchloroform	— —	300	50	50	
(133.4)	— —	(1620)	(270)	(270)	
28. Tetrachloroethylene	— —	100	5	5	
(165.85)	— —	(680)	(34)	(34)	
29. R-11. Trichlorofluoromethane	— —	5000	100	100	
(140.5)	— —	(28 500)	(570)	(570)	
30. R-12. Dichlorodifluoromethane	— —	5000	100	100	
(124.0)	— —	(25 500)	(510)	(510)	
31. R-113. Trichlorotrifluoroethane	— —	500	50	50	
(192.5)	— —	(3950)	(395)	(395)	
Aromatics					
32. Benzene	— —	100	1.0	1.0	
(78.11)	— —	(320)	(3)	(3)	
33. Ethylbenzene	— —	200	20	20	(4)
(106.16)	— —	(860)	(86)	(86)	
34. Styrene	— —	50	*10	*10	(5)
(104.1)	— —	(215)	(43)	(43)	
35. Toluene	— —	200	20	20	
(92.1)	— —	(760)	(76)	(76)	
36. 1,3,5-Trimethylbenzene	— —	25	*3	*3	
(120.2)	— —	(123)	(15)	(15)	
37. Xylene(o-, m-, p-)	— —	100	20	20	
(106.12)	— —	(430)	(86)	(86)	
Halogenated aromatics					
38. Dichlorobenzene, (mixed o- and p-)	— —	50	5	5	
(147.01)	— —	(300)	(30)	(30)	

See footnotes at end of table.

TABLE 3.—*Atmospheric Contaminant Limits for Manned Spacecraft*—(continued)
ppm (mg/m³) (After [63])

Compound (molecular weight)	10 Min, special area[8]	60 Min	90 Days	6 Months	Footnotes
Heterocyclics					
39. 1,4-Dioxane	— —	100	5	5	(7)
(88.0)	— —	(360)	(18)	(18)	
40. Furan	— —	2	0.04	0.04	
(68.07)	— —	(5)	(0.1)	(0.1)	
41. Indole	1.0	1.0	0.1	0.1	(5)
(68.07)	(4.8)	(4.8)	0.5	0.5	(partially).
42. Skatole	1.0	1.0	0.1	0.1	(4)
(131.1)	(5)	(5)	(0.5)	(0.5)	(partially).
Inorganics					
43. Ammonia	100	100	25	25	
(17.03)	(70)	(70)	(17.5)	(17.5)	
44. Carbon dioxide	40 000	30 000	10 000	10 000	
(44.01)	(72 000)	(54 000)	(18 000)	(18 000)	
45. Carbon monoxide	— —	125	15	15	(2, 3)
(28.01)	— —	(144)	(17)	(17)	
46. Hydrogen chloride gas	— —	5.0	1.0	1.0	
(36.46)	— —	(7.5)	(1.5)	(1.5)	
47. Hydrogen fluoride gas	— —	5.0	0.1	0.1	
(20.0)	— —	(4)	(0.08)	(0.08)	
48. Nitrogen dioxide	— —	2.0	0.5	0.5	
(46.01)	— —	(4)	(1.0)	(1.0)	
49. Phosgene	— —	0.5	0.05	0.05	
(98.92)	— —	(2.0)	(0.2)	(0.2)	
50. Sulfur dioxide	— —	5.0	1.0	1.0	
(64.1)	— —	(13)	(3)	(3)	
Miscellaneous					
51. Acetonitrile	— —	40	4.0	4.0	
(41.05)	— —	(68)	(6.8)	(6.8)	
52. Methylmercaptan	1.0	1.0	0.1	0.1	(4)
(48.11)	(2)	(2)	(0.2)	(0.2)	(partially).

[1] Based on eye irritation.

[2] The 60-min limit is based on requirement that the carboxyhemoglobin level not exceed 10%, assuming heavy work activity (30 l/min respiration) and conformity to Coburn's equation. If the assumption of heavy work activity in the weightless situation proves unreal, then a value of 300 ppm (330 mg/m³) is recommended.

[3] The mg/m³ limits are also specified for the 70% O_2, 30% N_2 atmosphere at 5 psia (1/3 ATA).

[4] Long-term limits based principally on odor.

[5] Estimated levels bear an asterisk; more inhalation data with animal models would be desirable.

[6] Not to be included in group limits.

[7] These levels for dioxane are subject to drastic revision downward (< 1 ppm) if future research proves that the compound is carcinogenic in animal models at low (< 100 ppm) inhalation concentrations.

[8] 10 Min, special area. A proposed separate compartment in long-term spacecraft which has a higher ventilation and air purification rate than the rest of the craft. It will house the commode and may also be used for procedures involving air contaminants such as degreasing prior to soldering.

TABLE 4.—*Suggested Spacecraft Air Standards* (After [32, 49])

Contaminant	Duration	Standard
SO_2	24 h	1.5%
NH_3	24 h	5 mg/m³
Total organic oxygen demand	24 h	150 mg O_2/m³ in air
CO	24 h	15 mg/m³
CO	>4 mo	5 mg/m³
CO_2	>4 mo	0.2–0.3%

Khalturin and coworkers noted that water condensed from the AGA is a source for drinking and food preparation, and pointed out that almost all trace impurities in air are in greater concentrations in the condensation moisture [41]. Also, the microflora of the AGA possibly could chemically contaminate the water supply. If there is unavoidable microbial contamination of water supplies, organic halogen compounds may be used for sterilization [53]. Optimum concentrations of the agents and modes of dispensing depend on the level of reducing agents present along with the bacteria and thus require empirical study for specific spacecraft application.

This effect of trace contaminants in the air on the water quality of spacecraft calls for mention of recent recommendations by a NAS panel under the chairmanship of Housewright [62, 64]. They suggest quality standards for potable water and for wash water to be used for personal hygiene, which are in Tables 5 and 6.

CRITERIA FOR ADDITIONAL SPACECRAFT AIR STANDARDS

It is clear from the foregoing that air quality standards for trace contaminants in sealed environments must be developed with due regard to the specific system under consideration. The dual interaction between components of the system and the AGA must always be kept in mind. The air standards affect the choice of materials and systems just as the materials and systems selected affect the standards developed and the cost of meeting the standards. These considerations have been amply discussed here, and in the literature [46].

The principles and criteria from which the actual standards are developed are perhaps best described by those effects that are excluded or avoided. Unacceptable effects are: (1) any permanent adverse health effects; (2) any effects, even temporary, impairing the ability of the individual to carry out assigned tasks; and (3) any effects that will interfere with the purpose of the mission. Special circumstances must also be considered:

(a) Some degree of tolerance might develop in the course of prolonged space flights.
(b) Elements of additional hazard might be imposed on man by changes in the new generation of red blood cells formed after the first 90 days which could lead to potentially altered levels of susceptibility to toxicants.
(c) Increased sensitivity of specific tissues might develop, for example, in bone marrow, liver, and kidney, through changes in the subcellular components such as metabolizing enzymes which normally permit changes in response to environmental burdens.
(d) Restriction of movement and fatigue may add further stressful conditions to the environment and alter to a degree, as yet unknown, the response to toxic agents in humans [76].
(e) The effects of 5 psia, 100% oxygen may be profound, especially on those agents which can destroy the antioxidant defenses [2, 85]. As an example, reduction in levels of tocopherol in the plasma of Gemini astronauts has been reported along with a hemolytic process. There is some indication that in animals, oxygen at 5 psia will synergize with systemic toxic agents such as CCl_4 [99]. Species differences are quite marked, the primates being relatively resistant. The synergistic factors for specific agents in humans is still not known.

This rigorous approach for personnel safety is also consistent with scientific requirements. The NASA Space Medicine Advisory Group and the Respiratory Physiology Group of the NAS Space Science Board's 1966 Summer Study have

TABLE 5.—*Physical Standards For Potable Water in Spacecraft* (After [64])

Physical property	90 Days	6 Months	3 Years
1. Turbidity (Jackson unit) not to exceed	10	5	5
2. Color (platinum-cobalt units) not to exceed	15	15	15
3. Taste	Unobjectionable	Unobjectionable	Unobjectionable
4. Odor	Unobjectionable	Unobjectionable	Unobjectionable
5. Foaming (allowable persistence in s)	15	5	5
6. pH	— —	7.0 to 8.0	7.0 to 8.0

Proposed Permissible Limits for Inorganic Chemical Agents (mg/l or ppm) for Potable Water in Spacecraft

Agent	Mission Duration		
	90 Days	6 Months	3 Years
Ammonium	ns [1]	5.0	5.0
Arsenic	0.5	0.5	0.1
Barium	2.0	1.0	1.0
Bismuth	ns [1]	0.05	0.01
Boron	5.0	1.0	1.0
Cadmium	0.05	0.01	0.01
Chloride	450	250	250
COD (dichromate method)	100	100	100
Chromium (hexavalent)	0.05	0.1	0.05
Cobalt	ns [1]	0.02	0.01
Copper	3.0	1.0	1.0
Fluoride	2.0	2.0	2.0
Lead	0.2	0.05	0.05
Manganese	ns [1]	0.1	0.05
Iron	ns [1]	1.0	0.3
Mercury (alkyl)	ns [1]	0.005	0.005
Mercury (other)	ns [1]	0.05	0.01
Nickel	ns [1]	0.1	0.05
Nitrate (as N)	10.0	10.0	10.0
Nitrite	10.0	0.1	0.1
Selenium	0.05	0.05	0.01
Silica	ns [1]	10.0	10.0
Silver	0.5	0.1	0.05
Sulfate	250	250	250
Solids (Total)	1000	500	500
Zinc	ns [1]	5.0	5.0

[1] ns—No standard.

reaffirmed the principle that engineering exigencies should not dictate the environment; the environment must be supplied to provide the best medium for the experimental effort and it might also be added, the best medium for the mission profile. Thus, if one of the goals of prolonged manned space flight is to ascertain man's adaptability and response to the weightless environment, it is necessary to design manned spacecraft so that the Earth atmosphere or a reasonable simulation be provided in order not to prejudice the study of the one facet of space flight that cannot be duplicated on Earth—weightlessness [29].

TABLE 6.—*Tentative Standards for Wash Water Specifications* (After [62])

Physical/chemical/ microbiological standards	Specification
Color	≦ 15 cobalt units
Conductivity (specific, 25°C)	≦ 2000 μmho/cm
Foaming	Nonpersistent above 15s
Odor	Nonobjectionable
Carbon (total organic)	≦ 200 mg/l
Lactic acid	≦ 50 mg/l
Nitrogen (ammonia)	≦ 5.0 mg/l
Sodium chloride	≦ 1000 mg/l
Solids (dissolved, after evaporation, 180°C).	≦ 1500 mg/l
Urea	≦ 50 mg/l
Detergents	Not specified
Oxygen (demand, chemical)	Not specified
pH	5.0 (min.), 7.5 (max.)
Microorganisms (standard 48-h plate)	≦ 10/ml

The first step in recommending an acceptable concentration for exposure to an atmospheric contaminant is to describe the dose-response relationship. What effects will result from exposure to various concentrations for various periods? Such descriptions of exposure versus effects are sometimes called air quality criteria. In theory, with sufficient experimentation they can be determined quite precisely. In practice, at any given moment, use must be made of information available from a review of the literature, published and unpublished, even though not completely adequate.

The second step in recommending a concentration for human exposure to an atmospheric contaminant is to determine the acceptable level of effect which can then be matched against the dose-response curve to establish the concentration. The acceptable level of effect is almost completely dependent upon the circumstances of exposure. Will the exposure occur while strolling down the street? (In this case an objectionable odor might be limiting.) Or will it occur during armed combat? (In this case reversible hypertension might be acceptable, but temporarily decreased visual or auditory acuity would not.)

Let us consider briefly how others have defined an acceptable effect and proceed to what might be acceptable for 100- and 1000-day space flights. Then we will return to the first step of dose-response relationship and discuss some of the critical variables [108].

There is a wide spectrum of acceptable effects from air contaminants. At one extreme, Emergency Exposure Limits are recommended by the NAS Committee on Toxicology [95] or by an American Industrial Hygiene Association committee [38]. Both committees accept any reversible effect that (a) will not interfere with the performance of tasks to be accomplished during the emergency, (b) not significantly reduce vision or visibility or interfere with breathing or prevent self-rescue, and (c) not expose the individual to additional risks such as fire and explosion.

At the other end of the spectrum, criteria and standards are being developed to protect the public from adverse effects of air pollution, which require identification of the most sensitive segment of the population. Standards are then set at levels low enough to protect those sensitive individuals. Some of the principles involved have been discussed by a committee of the National Academy of Sciences [61].

When developing standards for specific circumstances of human exposure to toxic materials, a fundamental principle must be carefully observed:

> The *toxicity* of a substance is its intrinsic capacity to produce injury when tested by itself. The *hazard* of a substance is the likelihood it will produce injury under the circumstances of exposure [15].

Thomas [98] has classified the chemical toxicants that may be encountered in spacecraft into four categories according to the probable responses to low-level continuous exposure: (1) equilibrium (intake-excretion): (2) adaptation, desensitization, cross-tolerance; (3) cumulative damage; and (4) all or none (carcinogens, sensitizers).

A final factor must be included in criteria for developing AGA standards—the concern about the *total* health of the spacecraft occupants. We are not only looking at the health hazards of airborne materials but also all hazards regardless

of route of entry. The total body burden must be considered when setting air limits for those materials which might also be ingested in food, water, or medication, or absorbed through the skin. The concern for total health of the individual in space again implies that each must be his own normal base for comparison for monitoring the effects of the spacecraft contaminants. A thorough preflight determination of each individual's physiology, metabolism, and reactions to stresses of various kinds is needed to make sure that an adequate margin of safety has been used in setting a standard [49].

It has been suggested that two numerical standards might be set for each contaminant. One would be an "alert" standard that would require intensive monitoring and perhaps special control procedures. The second would be an "abort" level requiring drastic action.

The recommendations for alert and abort levels and TLV_{space} in the classifications of Cox [16] and Hine [35] must still be looked on with some skepticism, because of the complexity of variables already discussed. The well-documented rationale by Hine is a good source for basic data; the concept was put into practice in a 90-day flight simulation in 1970 [79].

Committees such as those which have been discussed usually find the available data not entirely adequate for recommending standards, so that safety factors must be used. These safety factors should be of a magnitude commensurate with (1) the severity of the response; (2) degree of hypersusceptibility related to preexisting (such as respiratory) disease, heredity, and nutritional state; (3) extent of physical exertion; and (4) uniqueness of man's response, e.g. hypersensitivity of the respiratory tract [61]. Microbial infestation of spacecraft will be an increasing problem as the duration of flight and number of occupants increase. This will be reflected primarily in the quantity and quality of microflora on astronauts' skin and clothing. Particular concern is expressed for proliferation of fungi and yeast (*Candida* sp) which may be pathogenic to man [7]. The difficulty in treating diseases caused by such organisms further enhances the need for concern. The possibility cannot be excluded of microbes existing in the extreme conditions of space and planets. These microorganisms may be pathogenic for man, thus represent danger not only for crewmembers but also for the Earth's population upon return of the craft and equipment [7]. There is also considerable value in averting the uncontrolled drift of Earth types of life into space.

It is not easy to develop efficient methods of antisepsis for these various aspects of microbial growth. The methods selected must not have a negative influence on crewmembers in the complex medium of spacecraft. The methods must be compatible with the numerous and varied mechanical systems of space flight, be fire- and explosion-proof, and of minimum weight, volume, and energy requirements [7].

Therefore, the use of antimicrobial methods developed for other types of hermetically sealed rooms is not possible, especially when considering the possibility that microflora from cosmic space and other planets may be adapted to exist in extreme conditions, and thus may not be sensitive to such factors as ultraviolet radiation, vacuum, and high or low temperatures [7].

If resorting to chemical means for controlling the microflora, two other potential problems arise. The chemicals, such as phenol, may be a health hazard to the occupants, or the microorganisms may develop strains resistant to the chemical controls, which has occurred with hexachlorophene. Extensive research, development, and evaluation for new control methods are clearly needed.

Emergency Standards

In addition to the concerns already discussed, to be included in criteria for chemical and microbial contaminants during normal space flight, there must also be criteria developed for emergency situations, in order that they can be prevented, reduced in severity, or planned to be taken care of adequately when they do occur.

As Gazenko and Genin [24] have pointed out, it is necessary to consider the possibilities of emergency situations in space flight when maintenance of the optimum parameters of AGA will not be possible. These emergencies can be grouped as—medical, thermal, mechanical, and

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chemical—quite aside from those emergencies affecting the operation of the spaceship. They will require a high tolerance from man for several kinds of divergences from the optimum parameters.

Medical emergencies would include organ malfunctions, infectious diseases, dental problems, and similar. The medical significance and treatment of emergencies to the respiratory tract, skin, and eye from particulates in space cabins have been reviewed [9]. Other medical emergencies are beyond the scope of this chapter. Similarly, the physiologic emergencies—loss of control of heat or humidity in the craft and mechanical trauma and anoxia associated with partial or total loss of pressure—are beyond the scope of the present discussion.

Chemical emergencies which might arise from equipment failure require development of criteria and principles for control. A NAS panel chaired by Smyth [95] developed a basis for establishing emergency inhalation exposure limits applicable to space chemicals. The emergency limits for these compounds contain no safety factor and are considered tolerable for a single emergency during the duration of the mission.

These principles have been utilized for subsequent development of Emergency Exposure Limits (EELs) for specific compounds under specific conditions of exposure, which are listed in Table 7. It must be noted that none of these carries any safety factor and therefore they should *not* be applied to situations differing significantly from those for which they were developed. Potential new applications should be referred to the Committee on Toxicology of the US National Academy of Sciences in Washington, D.C.

The Emergency Exposure Limit for short-term exposure to an airborne contaminant is a concentration which, when inhaled for a specified single brief period (rare in an individual's lifetime), is believed not to result in a period of disability or interfere with the performance of his assigned task. In no event shall the value so selected produce danger from flammability of combustible aerosols, or result in substantial impairment of vision or visibility, or the ability to breathe. Transient effects may be experienced. The limits are intended to guide the informed specialist. It is believed that he can be more competent in protecting people if he is furnished

TABLE 7.—*EELs Recommended by NAS/NRC Committee on Toxicology* (After [95])

Compound	Time		
	10 Min	30 Min	60 Min
Acrolein	—	—	0.2 ppm
Aluminum fluoride	25 mg/m³	10 mg/m³	7 mg/m³
Aluminum oxide	50 mg/m³	25 mg/m³	15 mg/m³
Ammonia (anhydrous)	500 ppm	300 ppm	300 ppm
Boron trifluoride	10	5	2
Bromine pentafluoride [1]	3	1.5	0.5
Carbon disulfide	200	100	50
Carbon monoxide:			
(normal activity)	1500	800	400
(mental acuity)	1000	500	200
Chlorine pentafluoride [1]	3	1.5	0.5
Chlorine trifluoride	7	3	1
Diborane	10	5	2
1,1-Dimethylhydrazine	100	50	30
Ethylene oxide	650	400	250
Fluorine	15	10	5
Formaldehyde [1]	—	—	3
Hydrazine	30	20	10
Hydrogen chloride	30	20	10
Hydrogen fluoride	20	10	8
Hydrogen sulfide	200	100	50
JP-5 Fuel [1]	5 mg/l	5 mg/l	2.5 mg/l
Monomethylhydrazine (MMH)	90 ppm	30 ppm	15 ppm
Nitrogen dioxide	30	20	10
Oxygen difluoride	0.5	0.2	0.1
Perchloryl fluoride	50	20	10
Sodium hydroxide	4 mg/m³	4 mg/m³	2 mg/m³
Sulfur dioxide	30	20	10
Sulfuric acid	5 mg/m³	2 mg/m³	1 mg/m³
Tellurium hexafluoride	1 ppm	0.4 ppm	0.2 ppm
1,1,2-Trichloro-1,2,2-trifluoroethane (Refrigerant 113)	—	—	1500 ppm
Unsymmetrical dimethylhydrazine	100	50	30

[1] Tentative.

with a limit which, in the best judgment of a group of toxicologists, is the greatest concentration justified by the experimental evidence, provided the absence of any arbitrary safety factor is made known generally. This realistic limit would be analogous to the strength of material data used by the structural engineer in designing. The safety factor is applied in his operation of design, in proportion to the precision with which stresses to be withstood are known to the designer.

Emergency Exposure Limits cannot be promulgated without adequate experimental toxicological studies. The minimum information required is:

1. Beyond reasonable doubt, the identity should be known of the most sensitive target organ or body system whose integrity is menaced by short inhalations of the substances, and at what level effects on this target are insignificant.
2. It is necessary to have time versus concentration response data extending in both directions beyond the time intervals for which limits are to be promulgated, and sufficient observations to verify complete reversibility of effect. Data on two species, one a nonrodent mammal, are recommended as absolute minimum.
3. Certain human exposure data for orientation purposes are essential in estimating the emergency limits. These data can be obtained experimentally or by careful observation of any accidental exposures during commercial development.

UNCERTAINTIES OF STANDARDS

The development and promulgation of any standards for human exposure to atmospheric toxicants is fraught with many uncertainties. It is the intention in this section to point out a number of these uncertainties to develop skeptical caution, and suggest fruitful lines for further investigation.

The use of data from animal testing for predicting the effects of a substance on humans carries several sources of uncertainty, which include:

(a) differences among individuals of the same animal species,
(b) differences among animal species,
(c) extrapolation of data from animals to humans,
(d) differences among humans,
(e) nonuniformity of the contaminated air masses in gas leaks.

Chemical toxicants are rarely present alone, although most toxicity studies use pure materials. The difficulty in evaluating the milieu of contaminants in a spacecraft is the interaction among the components which has been discussed. The interaction may be physical, such as in the adsorption of gases on solid particulates; it may be chemical, as in the poisoning of catalysts in life-support systems; it may be biologic, where the toxic effects are modified either in degree or nature, as it in thickening of the alveolar barrier by NO_2 [61].

The dynamics of the spacecraft AGA pressure and composition are reflected in changing body burdens of the contaminants. Cumulative effects at any one time in such a variable exposure history are most difficult to assess. In addition to the usual effects which may be predicted in the average individual, there are also the unusual responses of allergic sensitization, idiosyncratic reactions, and adaptive tolerance. Nutrition plays an important role and specific dietary deficiencies may modify susceptibility.

Interpretation of information derived from animal experiments requires mature, experienced, scientific judgment from a variety of professional disciplines. The evaluation should consider all the variables mentioned and more, including conditions under which the data were obtained and, in particular, their relevance to the conditions of human exposure. Were data from human exposures available, they might result in standards of considerable reliability. Obviously, reliable human information is preferred, and should be obtained and utilized whenever possible. The research needs appear to be almost endless.

In spite of all the foregoing problems and uncertainties, the scientific community may well be proud of the advice it has provided to the space engineers on matters of toxicity and health hazards. The successes of the Soviet and US manned space programs are testimony to the skill of the astronauts and their supporting scientists and engineers.

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Chapter 3

THERMAL EXCHANGES AND TEMPERATURE STRESS

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Space flights for human passengers have been conducted in the blandest thermal environment man can devise. Since temperature, gas movement, and humidity of the artificial atmosphere in spacecraft can be totally controlled, thermal comfort can be engineered for astronauts within the vehicle. Certain variations from standard air-conditioning practice are necessary in artificial atmospheres if the pressure is lower than 1 atm or where the gas composition is not that of air; precise and positive control of temperature and humidity is necessary in these small atmospheric volumes, but the physiologic comfort state, where metabolic heat is dissipated at minimal physiologic cost, has been achieved. Because the volume of the artificial atmosphere in a spacecraft is small compared with the ocean of air on Earth, the men within this sealed small volume become important sources of both heat and water vapor. Along with the thermal energy generated by equipment, they constitute the primary loading of the environmental control system.

When astronauts leave the spacecraft for extravehicular activity (EVA), either during flight or on the lunar surface, their full pressure suits contain artificial atmospheres of even smaller volume. Now the astronaut is the dominant thermal load as he generates heat and water vapor that are frequently in large amounts. Neither the spacecraft nor the astronaut in a full pressure suit exchanges much heat with the space environment. Both are essentially isolated in the airless void, where energy transfer takes place primarily by electromagnetic (thermal) radiation. But because of the high thermal energy from direct sunlight and the low effective radiant temperature of space, and because the vehicle or the astronaut may move unpredictably into full sunlight or full shadow, the surfaces of spacecraft or space suits have been treated so that incoming radiant energy is largely reflected, and out-going radiant energy largely prevented from escaping.

Since men within spacecraft or wearing spacesuits during extravehicular activity are major sources of heat and water vapor, it has become increasingly important to know in detail the characteristics of metabolic heat generated under various conditions of human activity, particularly those connected with space flight. Metabolism might be expected to decrease somewhat during prolonged confinement, restricted activity, and weightlessness; during extravehicular activity, of course, it is vital to know what levels the metabolic heat production will reach, how long high levels can be sustained, and what the relationships are between heat produced in the body and heat dissipated from its surface.

Metabolic heat production can be extremely high during extravehicular activity, which made it necessary to develop a special method for transferring heat from the man's body to the heat sink in his portable life-support system. The method developed was the water-cooled garment, which proved to be far more effective for remov-

ing heat than the gas-cooling used in early pressure suits. Should a failure occur in the astronaut's portable life-support system during extravehicular activity, loss of the heat sink would soon lead to serious trouble from body heat storage [1] and rising body temperatures. This has led to renewed interest in the limits of heat storage, particularly when the source of the stored heat is internal rather than external to the man.

For many years there has been strong interest in those conditions of supersonic flight in the atmosphere when external heat loads are not negligible, but, quite the contrary, are far higher than anything in man's normal climatic experience. During reentry of the spacecraft into the Earth's atmosphere, enormous thermal energy is generated at the leading surface of the spacecraft, most of which is dissipated by ablation of the heat shield. But should some failure occur, there might be a rapid increase in cabin temperature, making important man's tolerance for what has been called slow heat pulses.[2] It was recognized that human limits for these extreme temperatures were set by surface pain rather than by heat storage, but heat storage limits are also important if the temperatures are less severe. Any supersonic flight by aircraft or spacecraft carries the possibility, however remote, that cabin cooling could fail and high cabin temperatures would lead to serious storage of body heat. A great amount of work has been done on the effects of stored body heat which is of external origin, both in laboratories of the Soviet Union and the United States.

Cold, as a thermal stress, has not been of major concern. However, in some early lunar landings the astronauts complained of being overcooled while resting within the lunar module and wearing water-cooled garments. There is a potential cold problem if returning astronauts land in cold ocean waters or in winter terrain and rescue should be delayed. (The problem of survival in cold will not be treated in this chapter.)

Discussions in this chapter will be on the major topics: human comfort, metabolic heat production, rates of heat dissipation and water loss, the water-cooling technique for extravehicular activity, tolerance for extreme heat and heat storage, and, finally, biothermal models used in the space program.[3]

THERMAL COMFORT DURING SPACE FLIGHT

Definitions of thermal comfort for humans are disappointingly imprecise, because the comfort state is subjectively defined and because there are many different combinations of clothing, activity, temperature, sunshine, humidity, barometric pressure, and wind that are judged to be comfortable. The standard definition of comfort among heating and air-conditioning engineers in the United States is "that condition of mind which expresses satisfaction with the thermal environment."

In the introductory section of this chapter it was suggested that comfort is a state of heat balance, the maintenance of which requires minimal physiologic effort—that is, all metabolic heat should be readily transferred to the immediate environment without imposing major physiologic responses such as sweating and shivering. Heat balance can be maintained with these thermoregulatory responses in climatic levels of heat and cold, but if these responses are prolonged, fatigue accumulates over a period of hours and the exposure may have to be terminated. Fanger [21] shows that there are three necessary conditions for optimum thermal comfort: that a state of heat balance exists; that the mean skin temperature stays at a level related to metabolic heat production; and that the sweat rate is no more than that appropriate for a particular metabolic activity level. Comfort conditions are shown by the curves in

[1] The accumulation of heat in the body leading to a rise in body temperature.

[2] Conditions where wall temperatures rise at rates of 30°–60°C/min, leading to skin pain and burning when wall temperatures exceed 110°C.

[3] The valuable contribution made by E. Ya. Shepelev of the Institute of Biomedical Problems, Moscow, is gratefully acknowledged. His review of Soviet research, especially in the field of human thermal tolerance, was an important addition to the materials used in preparing this chapter.

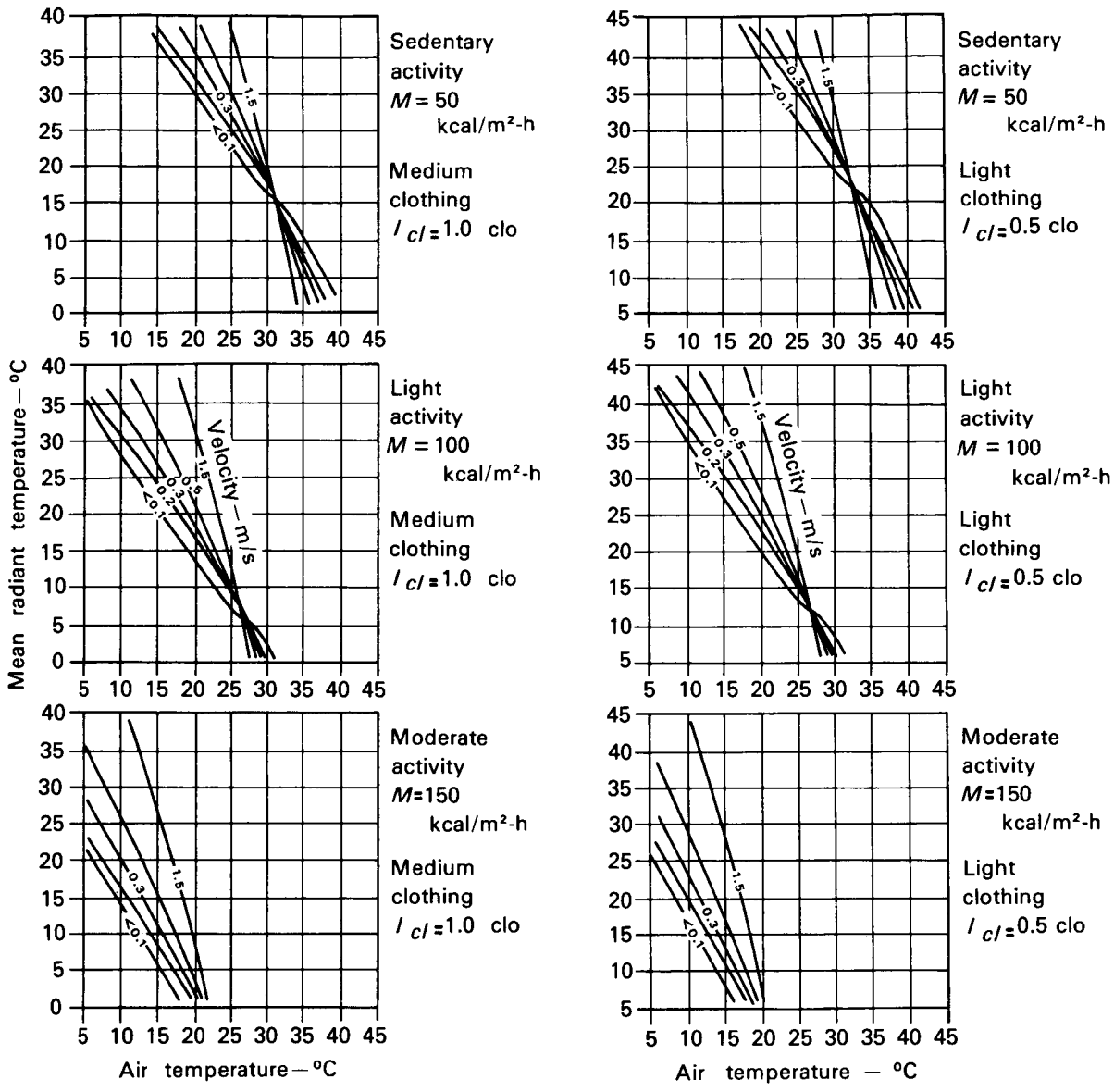

FIGURE 1.—(Left) Comfort lines for a range of air velocities, air temperatures, and mean radiant temperatures for men in light clothing and for three activity levels. RH is 50%. (Right) Men are in medium-weight clothing; charts are the same as in left column.

Figure 1 for three activity levels and two clothing weights.

To define comfort for spaceflight missions is relatively simple, because some of the major variables that must be considered on Earth are usually constant in a space vehicle. For example, metabolic activity is generally close to the resting level, at times lower than normal and at others slightly higher; the clothing assembly is known and constant; gas pressure, gas temperature, and gas velocity are essentially constant; and humidity and wall temperature are controlled. An accurate calculation of the thermal characteristics of the environment can be made in advance. Thus, the internal environment of a spacecraft is totally controlled and not subject to the kind of daily and seasonal variations to which we are accustomed on Earth.

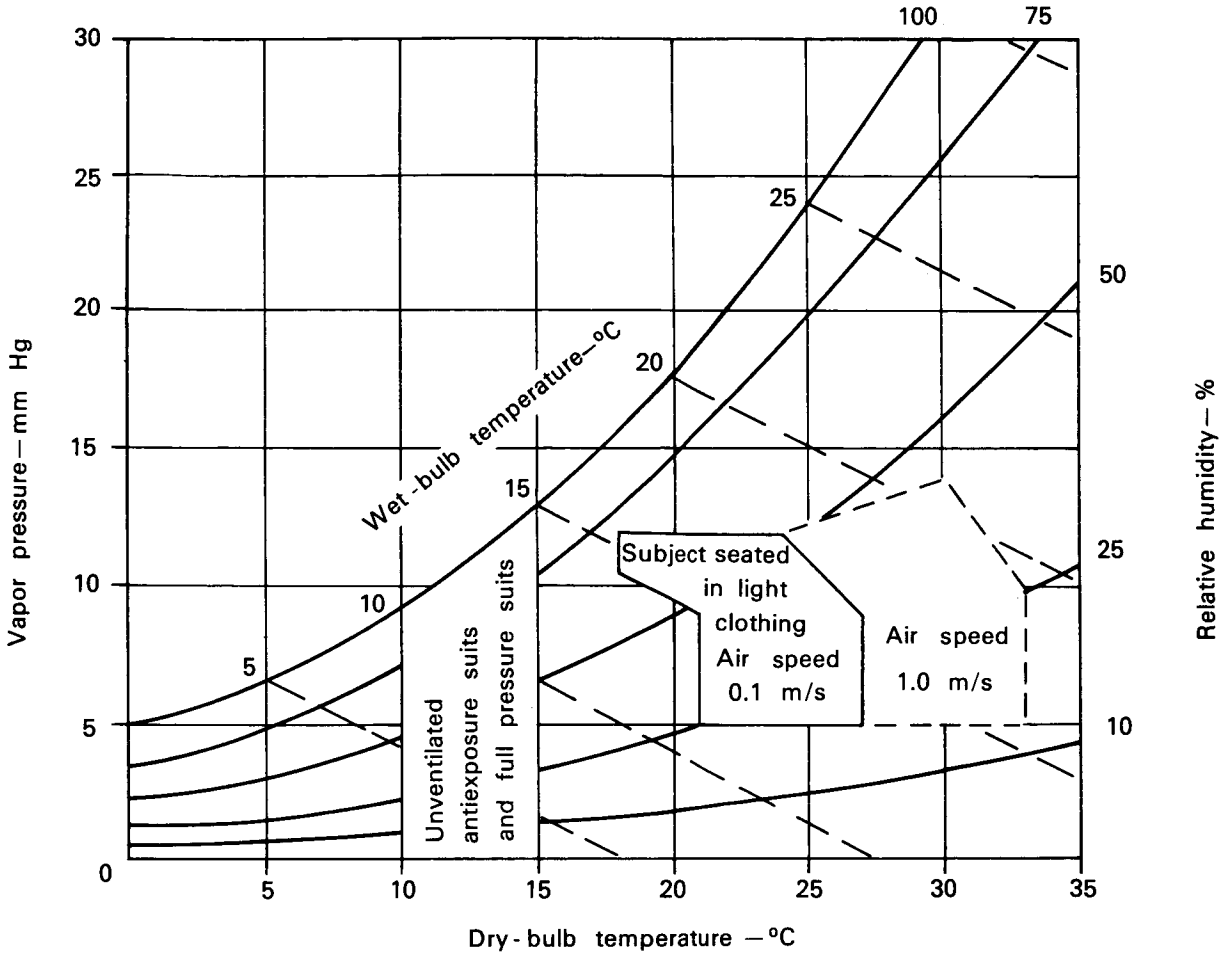

FIGURE 2.—Simple definitions of comfort for the conditions shown. Light clothing has an insulating value of 0.5 clo.

If it is clear that thermal comfort can be obtained with many combinations of environmental temperature, humidity, pressure, air motion, clothing, and activity, we can examine the major environmental conditions that affect comfort. In Figure 2, a comfort zone is defined in terms of the temperature and the absolute humidity of air for men at rest wearing lightweight clothing (insulation 0.5 clo) and where the air pressure is 1 atm absolute (ata), as it is at sea level. Certain variations in temperature and humidity are permissible if the air velocity changes, shown in Figure 2 by the extension of the comfort zone (indicated by a dashed line). Below the primary comfort zone is a different area which shows what is comfortable for a man not wearing standard clothing, but wearing insulated and impermeable clothing typical of flight clothing worn in high-performance aircraft. Above the comfort zone, within a limited range of temperatures and humidities, it is possible for men to maintain heat balance for up to 12 hours, but at a considerable physiologic cost characterized by raised cardiac output and heavy sweating.

A different way of defining human comfort under Earth conditions has been used in the United States for many years by the heating and air-conditioning engineers. The comfort chart of the American Society of Heating, Refrigeration, and Air Conditioning Engineers is reproduced as Figure 3; it is based on the familiar scale of Effective Temperature, which relates the thermal effects of temperature, humidity, and air motion into combinations that produce

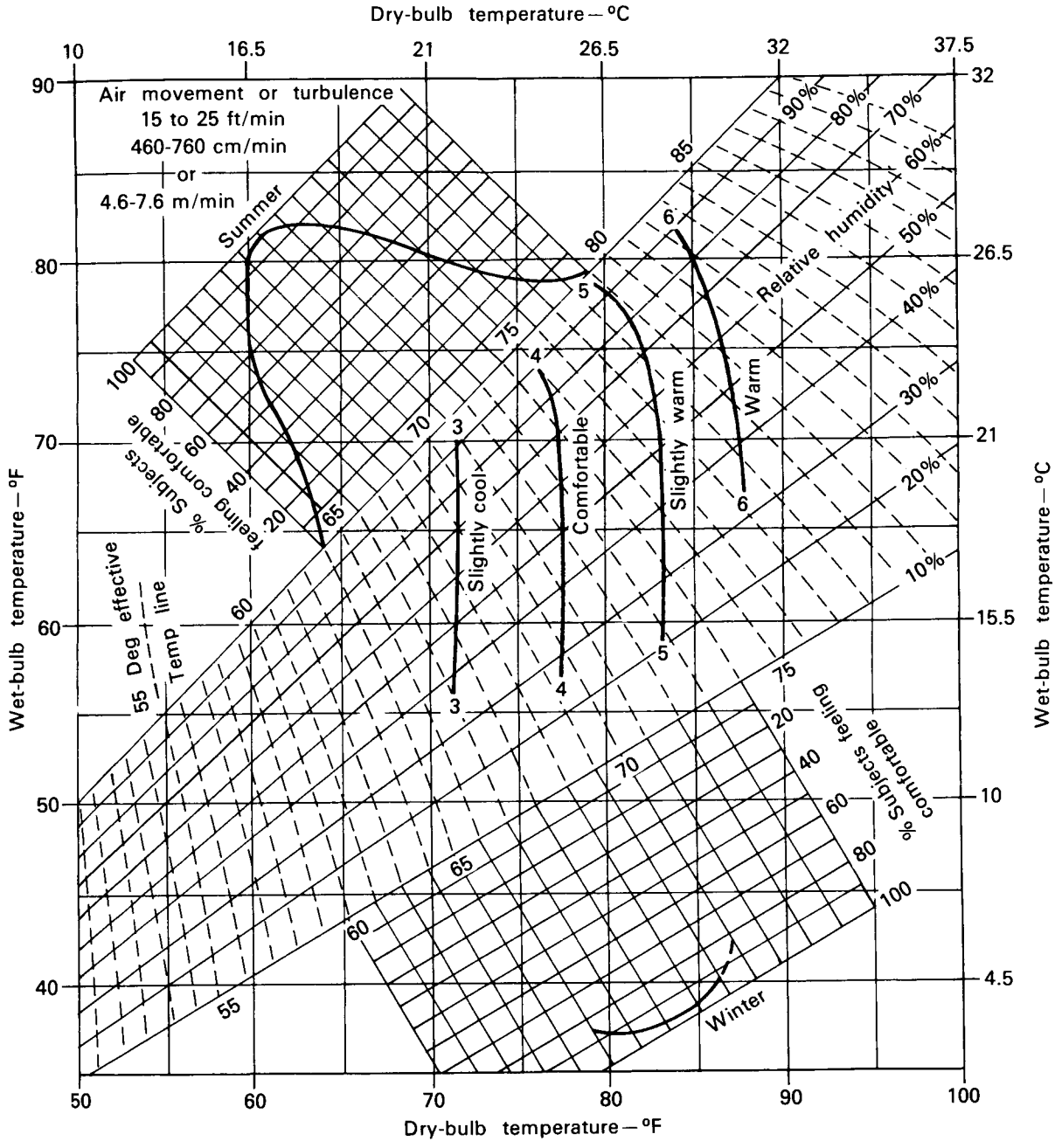

FIGURE 3.—Comfort and near-comfort conditions of air temperature and humidity (wet bulb temperature or relative humidity), indicated by the nearly vertical lines labeled "slightly cool," "comfortable," "slightly warm," and "warm." A secondary scale of Effective Temperature is given as a band of dashed lines. Note that this Effective Temperature scale is only for air motion of 15–25 fpmin (4.6–7.6 m/min). (From ASHRAE *Handbook of Fundamentals*, p. 122, by permission)

the same feeling of warmth. Comfort was defined by numerous people who cast votes upon whether they felt a given environment to be comfortable, slightly warm, warm, or slightly cool, which is shown in the central, more or less vertical lines, on the diagram. These lines are related to Effective Temperature, which is shown on a scale using wet and dry bulb temperatures at a given low-air movement. In addition to the nearly vertical comfort lines, distribution curves show the percentage of subjects who felt comfortable at various temperatures, both in summer and winter. Preferences in summer are for slightly higher Effective Temperatures than those preferred in winter.

Since the data in Figures 1–3 are based upon Earth conditions at 1 ata, and with resting subjects normally clothed, it is evident that one cannot apply these data directly to the spacecraft environment. The composition of the artificial atmosphere may be similar to that of air, or it may contain very different gases—for example, pure oxygen in many American spacecraft. In addition, the natural movement of gases in Earth gravity is very different from their movement in subgravity states of orbital flight, or on the lunar surface. Next, we consider estimates of the effect these changes have on the comfort conditions in the environment.

Berenson [4], using equations for heat transfer between the man and the environment, calculates comfort temperatures for a mildly active nude man in a cabin where the total pressure is 310 mm Hg and in which all gas motion is by forced convection. This curve is shown in Figure 4, with one derived from Fanger's comfort charts [21] when the air pressure is 760 mm Hg. In both cases, comfort is defined similarly in terms of heat balance, skin temperature, and sweat level.

The conventional heat balance equation is

$$M = E \pm R \pm C \pm K \pm W \pm S \text{ kcal/m}^2\text{-h} \quad (1)$$

where M is metabolic heat production; E is evaporative heat loss; R is heat loss or gain by radiation; C is heat loss by convection; K is heat loss or gain by conduction; W is mechanical work; and S is heat storage. In the comfort

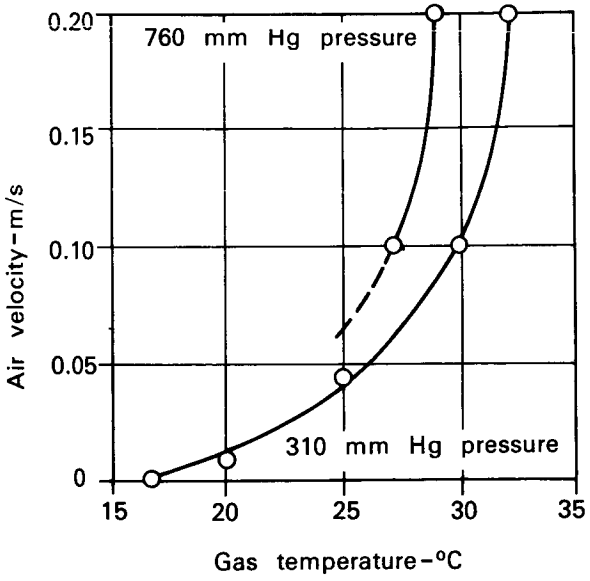

FIGURE 4.—Comfort temperatures at two different barometric pressures as a function of forced gas velocity. (Based on Fanger [21] and Berenson [4])

state, storage is zero; for rest and most activities, W is zero, and M is taken at some standard value—e.g. 70 kcal/m²-h in the examples shown in Figure 4. Heat transfer by conduction is usually negligibly small. The remaining heat exchange terms (E, R, and C) can be estimated for given environments by the following equations, adapted from Berenson [4].

$$E = 0.126\,\mathrm{W} T_a A_b K_e \left(\frac{v}{P}\right)^{0.5} (P_{ws} - P_{wa}) \quad (2)$$

where W is the ratio of the body surface that is wet to the whole body surface area (not greater than 0.25 for comfort or mild activity); T_a is air temperature in °C; A_b is body surface area in m²; K_e is a fluid property that depends on diffusivity of water vapor in the gas mixture and on transport properties of the gas mixture (for air, $K_e = 1$); v is velocity of the gas in m/s; P is barometric pressure in mm Hg; P_{ws} is the saturation vapor pressure in mm Hg for water at skin temperature; and P_{wa} is the vapor pressure of air. Note the enhancement of evaporative heat loss by low barometric pressure, a factor which will be noted in later discussion.

$$R = \sigma A_r (\bar{T}_s^4 - \bar{T}_r^4) \quad (3)$$

where σ is the Stefan-Boltzmann constant; A_r is the radiation area of the body in m^2; $\bar{T}_s$ is mean skin temperature in °K; and $\bar{T}_r$ is the mean radiant temperature in °K.

$$C = 0.21 k_c P v A_b (\bar{T}_s - T_a) \quad (4)$$

where k_c is a factor that varies with the transfer properties of the gas mixture (and for oxygen-nitrogen mixtures $k_c = 1$).

It is possible to make calculations of thermal comfort and heat exchange in gas compositions different from those of air and for various total pressures. A complete analysis by Bottomley and Roth [10] gives equations for the effects of various inert gases on convective transfer and evaporative heat loss. Table 1 summarizes empirical tests on unusual gas mixtures at several barometric pressures.

It has been common practice to test any special artificial atmosphere with prolonged exposure in ground-based simulators, a practice which will probably continue until sufficient empirical data are at hand to write comfort equations for such special conditions.

TABLE 1.—*Temperatures Selected by Subjects in Space Cabin Simulators* [10, 29]

Gaseous environment, mm Hg		Selected temperature, °C
Helium	509	24.5–27.5 (awake)
Oxygen	171	26–29 (asleep)
Other gases	80	
	760	
Helium	220	
Oxygen	160	24–25
	380	
Helium	93	
Oxygen	160	24–25
	253	
Helium	230	
Oxygen	150	24
	380	
Helium	74	
Oxygen	175	24
	249	
Nitrogen	206	
Oxygen	165	23
	371	
Oxygen	258	22
Oxygen	191	21

Studies on the physiologic effects and convective heat loss in helium-oxygen atmospheres over a range of barometric pressures were reviewed by Hiatt and Weiss [29]. They summarized animal experiments which at first had suggested a metabolic stimulating effect of 20°C helium-oxygen environments, but then showed that the effect was thermal, since oxygen consumption was the same in helium-oxygen as in air when the temperature was raised to 27°–30°C. Human experiments at normal pressure and at $^1/_2$ atm showed little effect on oxygen consumption, but a modest increase in skin cooling. The convective heat transfer at 1 atm pressure in helium-oxygen was about twice that for air, while at $^1/_2$ atm the helium-oxygen mixtures used to simulate space-cabin environments were equal to air or perhaps a little less effective as cooling media. But both Soviet and American studies in space cabin simulators (at pressures from $^1/_3$–1 atm) showed that the comfort temperatures for men during prolonged habitation were higher than for air, with a narrower temperature range (see Table 1). There was evidence that at least some of the effect was due to a decreased insulating value for the clothing when it was soaked in helium-oxygen instead of air. The authors concluded that there was little advantage in substituting helium for nitrogen in space cabin or space suit atmospheres.

What are the problems that arise if comfort conditions are not maintained? In a review on thermal comfort and health, Hardy [27] shows that the greater the departure from comfort conditions and the longer the duration of such exposure, the more serious the effects. Within the comfort zone, small variations in temperature are consistent with sensations of comfort and pleasure, and in this zone, body temperature is regulated by vasomotor activity in the skin. With a moderate departure from the comfort zone there is increased sensation of thermal effect and increasing sensations of discomfort, accompanied by measurable physiologic strains on the cardiovascular, respiratory, and other systems involved

in thermoregulation. With large departures from comfort and with long exposure, the thermal sensations become intense and often painful, there may be failure of thermoregulation and acute discomfort, excitability, restlessness, depression, and fatigue. Severe cold exposure, of course, leads to tissue injuries such as frostbite, while prolonged and severe heat exposure may lead to heat prostration or heat stroke and death.

Finally, comfort conditions in space flight involve not only the low metabolic levels prevalent within the cabin but also the high levels produced by extravehicular activity. It is possible to keep a man comfortable under these conditions, which has been shown in the laboratory by Webb and Annis [58]. They demonstrated that for activities up to six times the resting level, enough cooling can be supplied so that sweating is not needed to dissipate metabolic heat. Cooling was supplied in two forms: by cold air moving at a velocity great enough so that metabolic heat was removed from the body surface at low sweat levels; and by a water-cooling garment worn under an insulated and impermeable suit. As might be expected, the harder the work, the lower the skin temperature had to be in order that a sufficient temperature gradient existed to remove the large quantities of metabolic heat produced. Such data are shown in Figure 5, where the final mean skin temperature after an hour or more of the indicated physical activity had reached a near-equilibrium level. Final heart rates and final rectal temperature data are shown on the same figure. A curve has been added from a formula by Fanger [21] for the desirable or comfortable skin temperature recommended as a function of metabolic activity. Notice that the slope and location of the Fanger curve nearly coincide with that from the Webb and Annis data when air cooling was used. The slope for the skin temperature with water cooling is shallower. This probably reflects the effectiveness of the coupling between the water-cooling tubes and the skin. The steady-state levels of heart rate and rectal temperature, reached near the end of each experiment, are those for exercise without thermal strain. There was no evidence of continuing heat storage, and the physiologic cost was

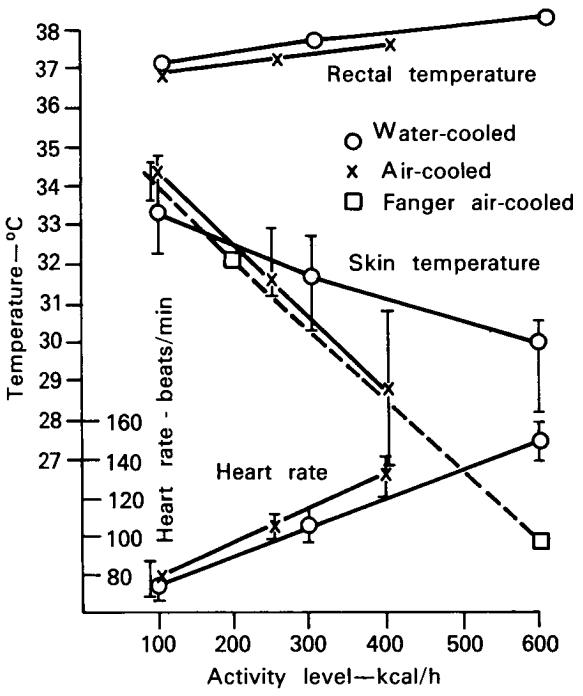

FIGURE 5.—Final steady-state values for heart rate, skin temperature, and rectal temperature for a range of metabolic activities when subjects worked in cooling environments which kept sweating below 100 g/h. (From Webb and Annis [58]; added dashed line for skin temperature from an equation from Fanger [21])

evidently minimal in terms of heat dissipation. Incidentally, the criterion for minimal sweating was that the total weight loss be no greater than 100 g/h under any of the conditions of exercise.

Thus, the principles of designing for thermal comfort in the artificial atmosphere of spacecraft are understood, and thermal comfort has been achieved in the first decade of Earth orbital and lunar flights.

HEAT PRODUCTION OF MAN DURING SPACE FLIGHT

Heat production from metabolism and muscular activity is a matter of special concern during space flight. The machinery that controls thermal conditions of the artificial atmosphere must be capable of responding quickly and accurately in order to maintain the heat balance of the astronauts. Unlike the situation on Earth where the ocean of air dissipates metabolic heat easily,

the small and confined volume of artificial atmosphere could, if not properly controlled, permit rapid increase of heat and humidity, quickly leading to uncomfortable conditions—possibly to the tolerance limit of stored body heat.

The heat balance equation was given in the preceding section as Equation (1); in this section the emphasis is on the heat-production term, *M*. Since there is seldom a sizable heat load or heat drain during space flight, the man's own heat production is of dominant concern in calculating the conditions necessary for heat balance. The general level of *M* during flight, whether the men are awake, asleep, or active within the vehicle, and especially the level of *M* during activity outside the vehicle, defines the load placed upon the environmental control system.

The heat generated by astronauts during flight inside the vehicle has been estimated from oxygen consumption and CO_2 production using the classical values for the caloric equivalent of oxygen as influenced by the respiratory quotient (RQ). In Table 2, the first set of data is that reported by Voronin et al [51] for four Soviet astronauts in the Vostok spacecraft. The second set of data is that given by Berry and Catterson [6] for American flights lasting 4–14 days; these estimates are based on the amount of CO_2 absorbed in the chemical purifying beds of the spacecraft. The third set of data is from Voronin et al [51], who studied astronauts in sealed cabin simulators on the ground for various periods of time; note that the ground-based estimates are slightly higher than those from actual flights. The fourth set of data is that reported by Jackson et al [30], based on a study of four men in a sealed cabin simulator during a 90-day period. These values are still higher. They come from the first American experiment with a mixed gas in a sealed space, where total pressure was 517 mm Hg, and nitrogen was the major constituent of the atmosphere. Of course, no ground simulator can produce the effect of weightlessness on metabolic processes, which ought to be to decrease metabolism.

Estimates from ground-based simulators, as well as estimates made from the classical physiologic literature, seem conservative—that is, they cause more-than-adequate supplies of oxygen to be carried and more-than-adequate heat removal capacity. This has caused no serious weight penalty in space vehicles designed to operate for 2 or 3 weeks. However, more precise data on heat generation, hence oxygen supply and CO_2 removal, will be needed for flights of longer duration. More extensive flight data on metabolic activity will be very useful in planning for longer flights. This topic is discussed further in Volume III, Part 2, Chapter 1.

Heat production is not constant within a 24-hour day, even when the subject is at rest and

TABLE 2.—*Metabolic Heat During Flight Inside the Spacecraft, or in Ground Simulators*

Vehicle	Average O_2 consumption l/min	Average CO_2 production l/min	Respiratory Quotient	Average heat production	
				W	kcal/min
Vostok spacecraft [51]					
A. G. Nokolayev	0.293	0.250	0.85	99	1.42
P. R. Popovich	0.333	0.283	0.85	113	1.62
V. V. Tereshkova	0.288	0.235	0.82	97	1.39
V. F. Bykovskiy	0.292	0.242	0.83	98	1.41
Gemini spacecraft [6]					
Gemini 4					1.67
Gemini 5					1.40
Gemini 7					1.54
Simulators of Vostok and Voshkod spacecraft 12–13 d exposures [51]	0.333–0.368	0.271–0.299	0.81	112–123	1.60–1.77
NASA/McDonnell-Douglas space station simulator, 4 men for 90 d [30]	0.443	0.333	0.75	146	2.10

in a constant environment. Aschoff and Pohl [1] discuss the rhythmic variations in energy metabolism in animal forms, including man. Their preliminary data on oxygen consumption of a woman subject during 24-hour periods suggested a definite circadian pattern related to the established diurnal curve of body temperature. More recently, Webb [57] reported definite circadian cycles in oxygen consumption, heat dissipation, and body temperature in two subjects who were studied for 24-hour periods by direct and indirect calorimetry. Since these experiments were conducted in Earth laboratories under carefully controlled conditions, there can only be speculation about the effects of space flight on the circadian pattern of metabolism. But the cycles appear to be independent of diurnal patterns of physical activity.

So far we have discussed the low heat production levels of men during space flight, including the possibility that these estimates are generally too high for very prolonged weightless flight. But there is a very different picture of heat production when astronauts wearing space suits are active outside their vehicles. This was first suggested during the first walk in space by the Soviet astronaut Leonov, who showed surprisingly high heart rates and considerable fatigue following 20 min in the vacuum, 10 of which were spent outside the vehicle. During the first four American space walks, made on Geminis IV, IX–A, X, and XI, not only were heart rates sustained at a high level for much of the ½–hour to 2–hour periods, but also the work planned for these periods of extravehicular activity had to be modified or terminated [16, 35]. In Gemini IX–A, the activity of the astronaut was so high that he became hot, sweated profusely, and fogged the faceplate of his helmet. In Gemini XI, high heart rate was coupled with high respiratory rate, which may have been due to excessive buildup of carbon dioxide, and the astronaut became tired and had to reenter the vehicle before completing his assigned tasks. In the final outside excursion of the Gemini series (Gemini XII), a 2–hour extravehicular activity was completed successfully by using better restraints to help the astronaut to do his work and by changing the workload so that the man could handle it readily. Only once did his heart rate rise above 140 beats/min. Although no direct measurements of heat, oxygen consumption, or CO_2 production were made, it was clear that the high metabolic heat production of most of the space walks was more than could be removed by the cooled, recirculated gas in the suits. It appeared that gas-cooling of space suits could not handle the high heat production to be expected during nonlimited extravehicular activity.

When lunar landings were made, the astronauts left the vehicle in space suits that were directly and positively cooled with water-cooling undergarments. It was possible to estimate metabolic heat from heart rate, from the decay of the pressure in the oxygen supply cylinder, and, even more convincingly, from the heat extraction by the liquid-cooled garment. Data of this sort have been reported by Berry [5] for the first lunar landing, the flight of Apollo 11. In 2.5 hours of lunar exploration on foot, one astronaut generated 565 kcal of heat and the other, 763 kcal, as shown in Figures 6 and 7. This means that heat production averaged 281 W (watts) and 354 W for the two men, respec-

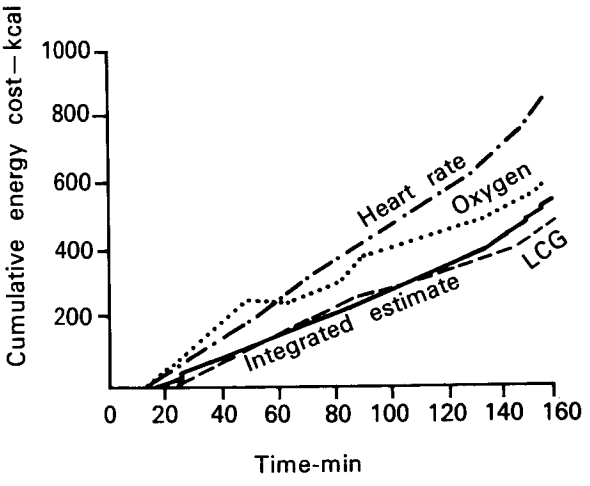

FIGURE 6.—Cumulative energy cost during lunar extravehicular activity for the Apollo 11 commander based on three different methods of estimation, plus a fourth (solid) line representing the best integrated estimate from these and other data. "LCG" is data from the Apollo liquid-cooled garment. (From Berry [5])

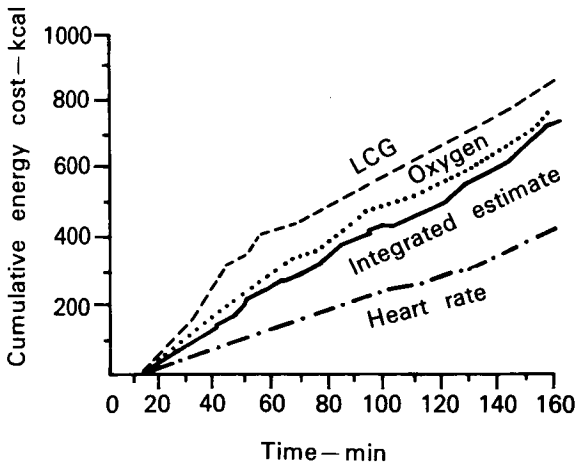

FIGURE 7.—Cumulative energy cost during lunar extravehicular activity for the Apollo 11 lunar module pilot. (From Berry [5])

tively, or roughly three times the resting level of heat production. The men could have worked at a higher level, but they were not permitted by the ground controllers to work at their maximum rates. Longer periods of lunar exploration have since been accomplished, but the data on heat production have not yet been published.

Men who are in good physical condition can sustain work levels at 80% of their maximum capacity for an hour or longer without resting, and some champion athletes can sustain even higher levels for 3 to 4 hours at a time. A man weighing 70 kg with a maximum oxygen consumption of 60 ml/kg, or 4.2 l/min could then be expected to sustain 80% of this level for an hour, which is 3.36 l/min or 16.8 kcal/min, or 1171 W. (Experimental data of this kind will be found in Åstrand and Rodahl's *Textbook of Work Physiology* [2].) This great increase in heat production is generated in the active skeletal muscles. A rise in muscle temperature occurs exponentially over a 10-min period, as was reported by Saltin et al [43]. In addition, as soon as work begins there is an exponential rise in oxygen consumption and heart rate, the rise being essentially complete in about 3 min. However, the excess heat being produced does not appear on the body surface immediately. The sequence of events is shown in Figure 8, where subjects were working in water-cooled suits controlled to prevent

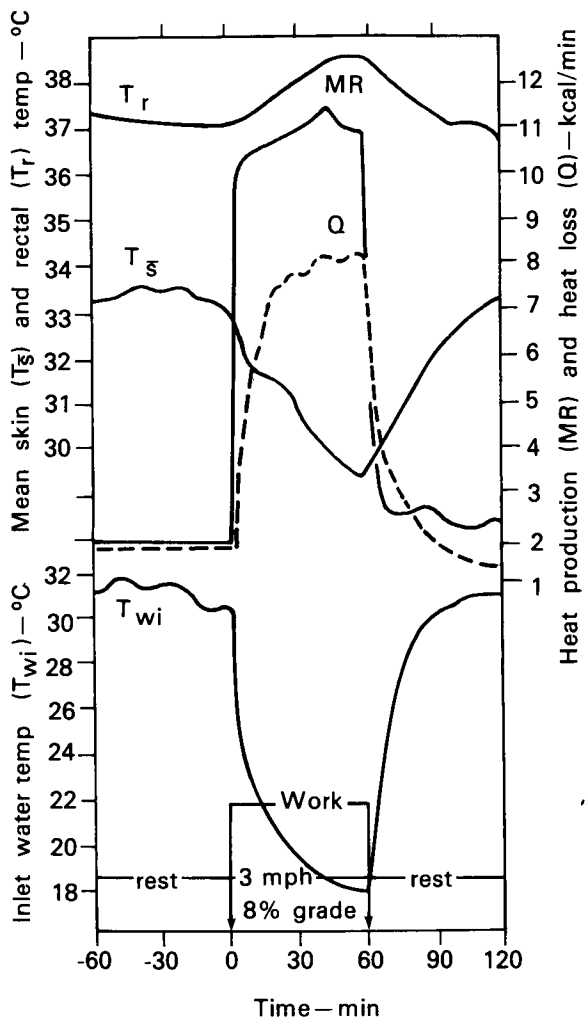

FIGURE 8.—Averaged rectal temperature (T_r), metabolic rate (MR), and heat removal (Q) from six experiments where subjects were cooled by controlling the water inlet temperature (T_{wi}) to a water-cooled suit while subjects rested, then worked at 10–11 kcal/min for 1 h. (From Webb and Annis [58])

significant sweating. The curve labeled Q is heat extraction, which rises exponentially but much more slowly than the curve labeled MR, which is metabolic rate from oxygen consumption. Notice that during the early part of work the rectal temperature rises, suggesting that there is an obligatory heat storage despite the presence of adequate cooling.

Metabolic heat is generally produced at a low resting level during space flight, but can rise to very high levels during the vigorous activity of

men who leave the space vehicle wearing space suits. The quantity of heat involved and the time course of its dissipation from the body surface following the start of work are both of great interest in the design of cooling control, which is discussed in a later section. Further data on the low levels of heat produced during long, quiet flight are to be hoped for in future missions.

WATER LOSS AS A MEANS OF DISSIPATING HEAT

The body loses heat steadily by water evaporation from the skin and from the moist linings of the respiratory tract. Each gram of water lost in this way carries with it 0.58 kcal as latent heat of evaporation, and under normal comfort conditions this steady loss of water, the so-called insensible perspiration, represents approximately one-fourth of the resting metabolic heat production. In the small sealed artificial atmosphere of a space cabin or space suit, the water produced by the man must be removed constantly to avoid causing high vapor pressure and loss of the thermal comfort state. Therefore, the environmental control system for the artificial atmosphere must be designed to remove water vapor at the rate generated by the astronaut. Just as the direct heat loss of the body surface must be removed as fast as it is generated in the small sealed atmosphere, so must water vapor if intolerable thermal conditions are to be prevented. It is appropriate to consider man as a source of water vapor and also the effect of high vapor pressures on comfort and thermal tolerance.

A small continuous obligatory loss of water has long been called insensible perspiration; it consists of water lost by diffusion through the skin and in the exhaled air. Both losses are affected by the vapor pressure of the air around the man—the higher the vapor pressure, the smaller the loss. Under most conditions with which we are familiar on Earth, the vapor pressure of air around us does not vary over a wide range; hence, we are accustomed to thinking of insensible water loss as relatively constant at about 30 to 50 g/h.

The rate of water diffusing through the skin is determined by the difference in the vapor pressure under the skin and that of ambient air, and is limited by the diffusion resistance of the skin as a barrier. The rate is also influenced by the total pressure of the environment, since diffusion is inversely proportional to the square root of pressure. The major factor is the vapor pressure gradient between tissue fluid under the skin and the ambient vapor pressure. It is usually assumed that the vapor pressure under the skin is that of water at skin temperature; thus a skin temperature of 33°C would give a vapor pressure of 38 mm Hg. Ambient vapor pressures are nominally around 10 mm Hg in spacecraft; thus the gradient would be 28 mm Hg. It has been shown by Buettner [14] that diffusional transfer stops when the ambient vapor pressure equals 90% of the saturation vapor pressure at skin temperature, thus defining the diffusion resistance of the

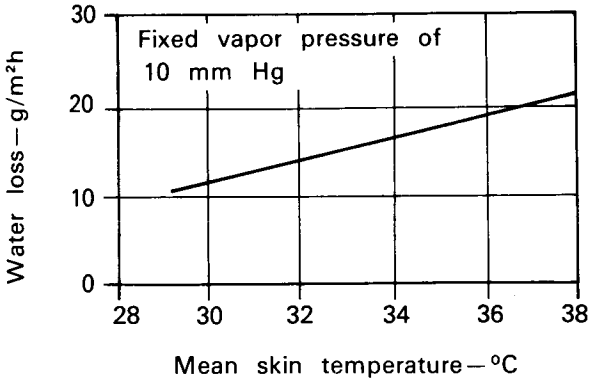

FIGURE 9.—Diffusional water loss through skin as a function of skin temperature, at ambient vapor pressure of 10 mm Hg.

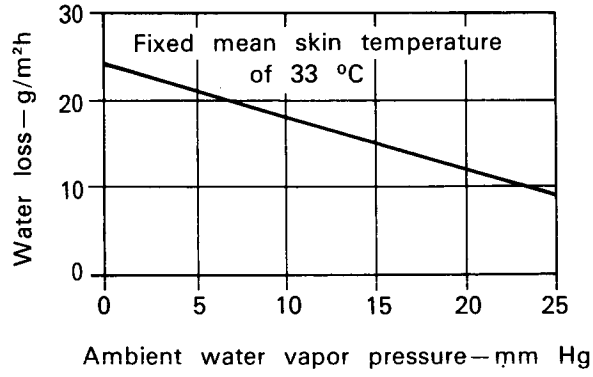

FIGURE 10.—Diffusional water loss through skin as a function of ambient vapor pressure at a fixed mean skin temperature of 33°C.

skin. In a review of this topic and other water exchanges in space suits and capsules, Webb [55] summarized water loss by diffusion through the skin, as shown in Figures 9 and 10. These two figures show the effect of a change in skin temperature when the vapor pressure of the ambient air is fixed, or, if the skin temperature is fixed, the effect of a change in the ambient vapor pressure.

Water loss through the skin is higher at low ambient pressures, as shown by Hale et al [25]. They reported that diffusional water loss from the arm increased from a rate of 10 g/m²-h when the barometric pressure was 760 mm Hg to approximately 17 g/m²-h when the barometric pressure was 253 mm Hg. Unpublished observations by the author showed an even greater effect on weight change of nude men in an altitude chamber where sweating was prevented by administration of atropine; in this case the rate was 15 g/m²-h at 760 mm Hg, and 38 g/m²-h at 253 mm Hg.

The rate of water lost from the respiratory tract is primarily determined by the respiratory ventilation rate. Ambient vapor pressure and total pressure also have an influence. Data of this sort are summarized in Figure 11, from the review

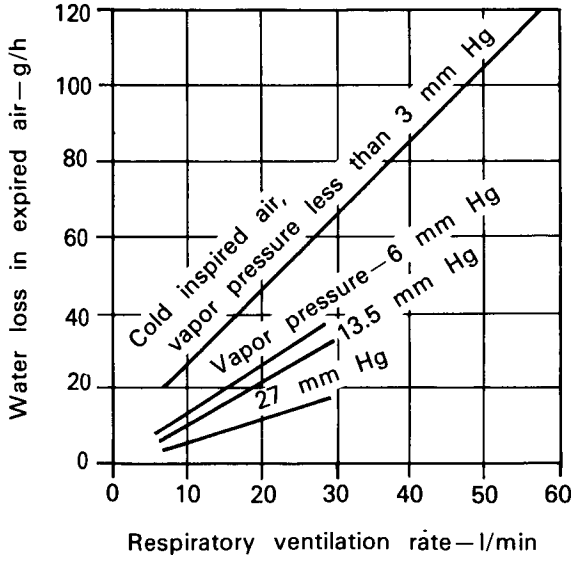

FIGURE 11.—Water losses in expired air as a function of respiratory ventilation rate, for several vapor pressures of the inspired (ambient) air. (From Webb [55])

of Webb [55]; in this figure one may determine the respiratory water loss in g/h as a function of respiratory ventilation rate, and at a number of ambient vapor pressures from low (3 mm Hg) to high (27 mm Hg). Since respiratory minute volume increases with the activity of the subject, so respiratory water loss increases as a function of metabolic level.

For most purposes it is sufficient to take a standard value for insensible water loss, since it represents only a relatively small part of the metabolic heat dissipation and a relatively small water load on a well-designed environmental control system. Such a standard value is usually given as 900 g/d, or 37.5 g/h. This represents 14 kcal/h, or 16 W. If the artificial atmosphere is at considerably less than 1 atm pressure, then this value might increase by 50% or 100%, but it still represents only a small part of the total metabolic heat dissipation.

Water is actively secreted by the sweat glands for the purpose of cooling the skin. There is also a nonthermal or psychogenic activity of the sweat glands, but quantitative data on the amount of nonthermal sweating is scarce. Perhaps the clearest set of experimental data on the rate of nonthermal sweating is that of Brebner et al [11]. They observed that subjects in a cool room who required no sweating for thermal balance were losing water at higher than diffusional rates from the face, hands, soles of feet, axillae, and groin. These rates were two to four times higher than the rate of insensible water loss measured over the rest of the skin surface. Such rates would not necessarily prevail throughout 24 hours, but would be most likely during the waking hours, especially when the subjects were alert, anxious, or excited. This sort of sweating could be expected in astronauts during the busier periods of space flight.

Thermal sweating is a major physiologic response to the need for heat dissipation. It occurs when ambient conditions are not cool enough for dissipation of metabolic heat. The rates of sustained thermal sweating can be very high, as much as 2000 g/h and higher. There is a great amount of literature on the rate of sweating as a function of environmental conditions and ac-

tivity. One summary of such data is shown in Figure 12. The studies, from which this figure was drawn, were made of men lightly dressed in shorts and shoes, rather than in the space-related conditions of low barometric pressure and wearing space suits. However, the principle remains the same: sweating increases as ambient conditions are warmer and as the metabolic heat generated is higher. Sweat rates can be high when activity is undertaken in space suits of limited mobility, illustrated by the report of Harrington et al [28], also by the early days of extravehicular activity in the Gemini program, reported by Burns et al [16].

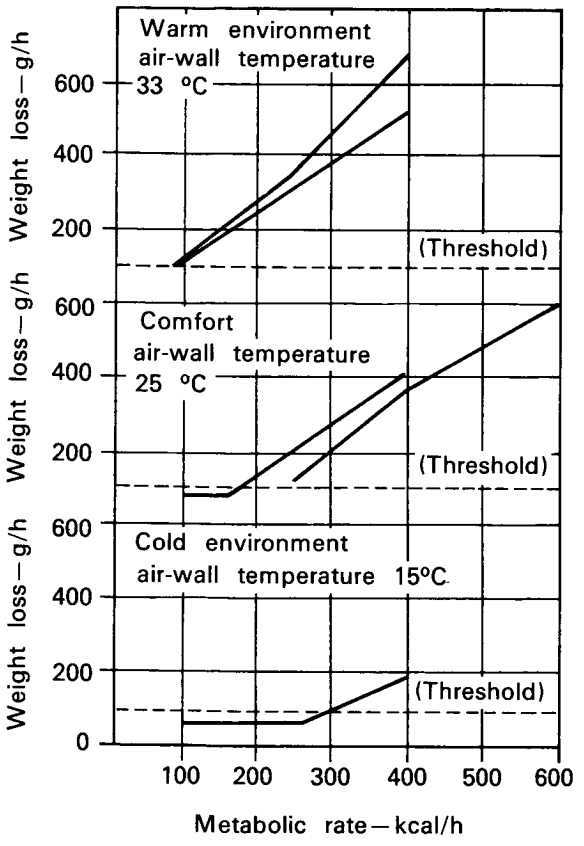

FIGURE 12.—Sweat production (from weight loss) as a function of metabolic rate for men wearing only shorts and shoes in three different environments. Threshold level for thermal sweating is indicated by a dashed line at 100 g/h. The curves were derived from three separate studies; there were two sources of data at 33°C, and two sources at 25°C, hence two similar curves in these two parts of the figure. (From Webb [55])

To illustrate the critical nature of high rates of sweating if the gas-conditioning system in a space suit cannot keep up with the amount of water evaporated, consider the following example. Suppose that the free volume of the artificial atmosphere in the suit is 300 l and has an initial vapor pressure of 10 mm Hg (10 mg/l water). Suppose further that the man is working hard enough to produce 10 g/min sweat, all of which evaporates, and that the portable life-support system removes 8 g/min from the recirculated gas. The net addition of 2 g/min water vapor over a 5-min period will add 10 g water to the atmosphere for a total of 13 g in the 300 l. This is equivalent to air saturated at a temperature of 37°C or a vapor pressure of 47 mm Hg. In such an atmosphere, no sweat would evaporate and all cooling by this route would have ceased. Under such conditions there would be rapid storage of body heat.

The preferred value for the water vapor pressure in an artificial atmosphere is 10 mm Hg. As little as 5 mm Hg is acceptable, but lower than that may cause uncomfortable drying of the mucous membranes of the respiratory tract. Probably an upper limit is 15 mm Hg, for beyond this level the evaporation of sweat is reduced and thermal discomfort begins.

Heavy sweating in space suits and overloading of the environmental control system during the earlier days of extravehicular activity led to the development of a more direct means of cooling whenever high metabolic activity was expected. It became important to prevent the high sweat rates during high metabolic activity. This new means of cooling, the liquid-cooling garment, will be discussed next.

WATER-COOLED GARMENTS

Perhaps the most significant development in thermal control to come from the space program is the water-cooled garment, which has been used during extravehicular activity in the Apollo lunar landing program. This method of removing heat directly from the body surface, using water as a heat transfer fluid, is a powerful method of maintaining thermal balance during high metabolic activity; the method can be readily con-

trolled either by the astronaut or automatically. It has also proved a reliable means of measuring heat loss calorimetrically, both in the laboratory and during lunar excursions.

Despite the successful use of air-ventilated suits for men in industry, when in sealed clothing and seated in aircraft under hot conditions, gas cooling proved totally inadequate for men working in pressurized full-pressure suits [23, 32, 36, 41, 53]. This became evident both in laboratory studies [28], and in the extravehicular activities of the Gemini program [16, 35]. The problem was essentially that of an engineering limitation due to the power needed to circulate a very high volume of the relatively thin gas, oxygen, at 0.25 ata, to carry heat and water vapor from the skin to the life-support system. Estimates were that 1000 to 2000 l/min of this thin gas would be needed to remove the metabolic heat from a man exercising at five times his resting level in a space suit, where there was little external heat load. An electric motor to drive a blower to move this much gas would require several hundred watts, which would mean an excessively large and heavy battery pack.

The water-cooling garment was first proposed by Billingham [7], in a theoretical paper on thermal problems of men on the Moon. In 1962, the first water-conditioned suit was made at the Royal Aircraft Establishment in Farnborough, England, as reported by Burton and Collier [17]. Their intent was to provide thermal comfort for pilots who were confined to a closed cockpit while the aircraft waited on the runway and heat from sunshine accumulated. Experimental evidence showed that comfort conditions could be maintained despite high external heat loads. It was also evident that the power required to pump the water through the suit was far less than the power required to circulate sufficient cool air to do the same job. Soon after, the water-cooled suit was adopted in the United States by the National Aeronautics and Space Administration as the means of removing heat in the Apollo space suit. This development was described by Jennings [31], and physiologic evaluations of the suit have been reported [18, 49, 52, 58]. The major Soviet study is that of Barer et al [3].

It was demonstrated by Crocker et al [18] and Webb and Annis [58] that as much heat could be extracted by the suit as was being generated by men working hard in insulated sealed clothing. Waligora and Michel [52] demonstrated the quantity of cooling required for men working in space suits in the laboratory; and Veghte [49] showed that under conditions of high external heat load, water cooling was far more effective than gas cooling in full pressure suits.

A water-cooled suit consists of a network of small plastic tubes whose total length is about 100 m. The network lies against the skin or is held in tunnels of thin cloth sewn to a suit of underwear. Water is circulated through the tubing network at a flow rate of 1–2 l/min, and the flow is usually constant. Increased cooling is achieved by lowering the temperature of the water entering the suit. An excellent review of the development of water-cooled suits and the various designs which have emerged is that of Nunneley [39]. She points out that applications have been found in industry as well as in aircraft and space-flight situations. Shvartz [45] has also reviewed the subject recently, comparing the effectiveness of cooling applied to different parts of the body.

The distribution of cooling tubes over the skin has been designed in several different ways. One approach has been to proportion the number of tubes according to either the mass of a given body segment or to its area. In both cases, the torso received the greatest amount of cooling, the legs next, and the arms least. Head, hands, and feet are omitted in these suits. This design seems to make sense when the heat load is largely external, such as when a pilot is seated in a hot cockpit. This function of the cooling garment is essentially to block heat leakage from outside the clothing rather than to remove metabolically produced heat.

A second design approach, which seems to work better when the heat load is principally internal (metabolic), is to distribute the cooling in relation to where most of metabolic heat appears. The head is one such site, and the legs an even more important one if the subject is using his leg muscles during work. The hands and feet should be included if possible, since

these are major sites used by the body when thermoregulation demands a variation in heat dissipation. As an example of this design approach, Webb et al [59] proportioned their cooling tubes as: legs and feet, 50%; arms and hands, 23%; torso, 19%; and head and neck, 8%. But flow through these tubes was proportioned as: legs and feet, 40%; arms and hands, 26%; head, 22%; and torso, 12%.

A vital part of the design of these garments is the means to assure good fit and continuous contact of the cooling tubes with the skin. One approach was to use an open-mesh garment made with elastic fibers to which the cooling tubes are attached, and another, a diamond pattern of tubing which stretches open as the garment is put on. Both designs appear to work satisfactorily, since experiments with both types have shown that skin temperature can be lowered at will, even during exercise, with water flow rates of 1–2 l/min and inlet temperatures between 5° and 30°C.

The flow rate of water has been most often reported as 1.5 l/min [56–60] or 1.82 l/min [5, 52]. This amount of flow permits satisfactory heat removal during rest or hard work, and at reasonable water temperatures.

The application of water-cooled garments was successfully demonstrated in the Apollo lunar landing program [5]. In all lunar landing missions in the Apollo program, the water-cooled garment has proved capable of removing metabolic heat as it is generated while the astronaut works. In fact, as predicted from laboratory findings, there was more than enough cooling since the astronauts, who had a manual control valve with three positions, felt overcooled if they used the maximum cooling available. As the lunar exploration program developed, longer and longer extravehicular activities were possible, partly because of the success of water cooling. There was no evidence of metabolic heat storage despite that, on the lunar surface, there was little or no heat loss to the airless lunar environment. Fairly high work rates were occasionally undertaken by the astronauts in their enthusiasm over lunar exploration, as evidenced by high heart rates, but there was no report of heavy sweating, heat storage, or similar signs of inadequate heat removal.

Physiologically speaking, it is important that a powerful means of cooling has been developed which permits a man to work at nearly any level without need for sweating. A new means was found for insuring thermal comfort even during work. When work levels are high, and heat dissipation to the environment is severely limited, as it is in space suits worn in the vacuum of space, the water-cooled suit can be controlled so that skin temperatures are reduced and heat dissipation is made easy. There is very little physiologic cost to heat dissipation under these conditions.

With such a powerful means of heat removal at hand, a new problem arose: how to control the cooling in relation to the need for heat dissipation. After a number of experiments of the type illustrated by Figure 8, Webb et al [60] found that immediately following the onset of work, physiologic responses changed exponentially, each response with a characteristic time course. Oxygen consumption and heart rate rose rapidly, while heat dissipation rose with a much slower time course, during which time the rectal temperature rose and reached a plateau level. The time constants for each of these variables given by the authors are shown in Table 3. They proceeded to develop automatic

TABLE 3.— *Values for Metabolic Time Constants* [60]

Metabolic variable	Time constant, min
Heart rate	0.4
Oxygen consumption	0.5
Mean skin temperature (estimated)	1
Heat dissipation	10
Rectal temperature	10

controllers for regulating the temperature of the water entering the water-cooled suit. Their first automatic controller relied upon the exponential character of the response of oxygen consumption and its direct relation to the metabolic heat being produced in the active muscle. The relatively rapid response of oxygen consumption was sufficiently ahead of the release of heat on the skin surface that a controller could be made to match, in time and magnitude, the need for

heat removal. The controller equation was

$$\tau \dot{T}_{wi} = -T_{wi} + B(M_0 - M) \qquad (5)$$

where τ is the time constant for heat dissipation; $\dot{T}_{wi}$ the rate of change of temperature for water entering the suit; T_{wi} the instantaneous temperature of water entering the suit; B the gain of the system; M_0 a reference (maximal) metabolic rate; and M the instantaneous metabolic rate.

A second type of automatic controller was based on the observation that heat dissipation, which could be continuously measured by watching the change in water temperature traversing the suit, was in fact a physiologic signal from the man. As the amount of heat appearing in the suit increased, so water temperature could be lowered and more heat extracted. If too much cooling occurred, cutaneous vasoconstriction would reduce the amount of heat appearing in the suit and the cooling would accordingly be reduced. However, this alone as a control system was unsatisfactory because of oscillations in the control loop. By adding a skin temperature signal to the input of this controller, smooth and effective control of heat removal was achieved. The controller equation was

$$T_{wi} = T_{wi_0} - \frac{\alpha}{\dot{m}c}(H - H_0) - \beta(T_{cs} - T_{cs_0}) \qquad (6)$$

where the subscript zero indicates initial condition at rest; α and β are proportionality constants; $\dot{m}$ is the mass flow rate of water, and c is its specific heat; H is rate of heat removal by the suit; and T_{cs} the mean skin temperature used for control purposes.

Some authors suggest that cooling capacity with a water-cooled suit is limited so that work should be kept below levels of about 700 W (10 kcal/min). For example, Waligora and Michel [52] reported such limitations, but the Apollo suit used in their studies did not provide for cooling in the head, hands, or feet. The head is particularly important for heat extraction. Blood circulation in the head is high and the blood vessels apparently do not constrict when strong cooling is applied. Studies by Nunneley et al [40] and by Shvartz [45] emphasize the value of head cooling as a major component of total body cooling.

The effectiveness of the water-cooled garment as a means of thermal control in space suits worn by active men has an added significant advantage: it has proved to be an extremely effective measuring tool. Berry [5] reported that the measurement of heat extraction in the water-cooled suit during lunar excursions was subsequently relied upon during the Apollo program. There were three methods for monitoring the work rate of the astronauts: individual heart rates as a function of activity level determined for each astronaut; the decay of pressure in the oxygen supply bottle in the astronaut's portable life-support system; and heat removal measured by the temperature change of water traversing the water-cooled suit. The heart rate data, unfortunately, showed not only the metabolic activity level but also the state of excitement or anxiety of the man. The pressure change in the oxygen bottle was a relatively insensitive measure, which might be greatly in error should there be leakage of gas from the space suit. However, the temperature change of water traversing the suit was continuously available for monitoring and indicated in real time the quantity of heat removed. This method of measuring heat extraction in the water-cooled suit and comparing it against measured heat production has been extensively studied in the laboratory [57–60].

The water-cooled garment makes an excellent direct calorimeter [59]. Complete metabolic heat balances for 24-hour periods have proved quite accurate, and interesting data on circadian rhythms in metabolism, heat storage, and similar topics [57] are coming from such studies. This method of estimating metabolism during prolonged space flight may prove useful, since our direct measurements of metabolic level during space flight are only approximate. It should be possible to carry out not only indirect (respiratory) calorimetry by measuring oxygen consumption, but also the direct heat dissipation from men by using the water-cooled garment.

TOLERANCE FOR EXTREME HEAT AND BODY HEAT STORAGE

Because of the special nature of thermal balance in a spaceship, the major problems in man's energy exchange are related more to

removing excess heat, than to cold exposure and serious body cooling. Investigators in both the Soviet Union and the United States have been interested in high thermal loads and developing means of protection against them. The foundations were laid during the past 40 years while investigators were concerned with the problems of heat exposure in industry; much of this work has been summarized in the US and Soviet literature [12, 22, 24, 37, 38]. Additional interest in heat exposure was generated in the period just prior to the space era, when aerodynamic heating in high-performance aircraft led to the ever-present possibility of exposure to high temperature in the aircraft cabin. Spacecraft that pass at high speed through the atmosphere of Earth, or possibly that of other planets, have a similar potential problem; the temperature stress could be even higher, if briefer, should the mechanisms for heat dissipation and cabin cooling fail.

Human response above the zone of thermal comfort falls into three recognizable zones.

The first zone is where the heat exposure is compensable; that is, vasodilation and sweating permit thermal balance to be achieved, usually at a higher than normal body temperature, and a steady state can exist for some hours. These exposures are fatiguing and time-limited, depending on how much physiologic activity is called for to maintain thermal balance.

In the second zone, the heat exposure is not compensable, and no thermal balance exists. Heat is stored, both metabolic heat and that which may be arriving from the environment, and the limit is set by how much heat storage the body can tolerate.

A third zone exists at even higher temperatures where the thermal influx is so high that surface heating causes severe pain, followed by skin burns if the exposure continues. Experimental determination has been made of the conditions that produce intolerable pain, just as conditions have been defined for limits of body heat storage and for lower but compensable heat exposures.

The zone of compensable heat exposure will not be discussed here, which is presented fully in standard works on physiology. In the age of space flight, more attention has been paid to higher levels of heating, and the two zones of heat storage and surface pain will be considered in greater detail.

Overheating Limited by Body Heat Storage

When the temperature of the air and surrounding walls exceeds 60°C (140°F), the body cannot maintain a heat balance, even through profuse sweating, and it begins to store heat. This is the zone of noncompensable heat exposure and hyperthermia. The higher the temperature, the shorter the time a man can tolerate such exposures, since the quantity of heat stored and the rate of storage increases. However, the more clothing he wears and the greater its insulating value, the longer it takes to reach tolerance. Also, at altitudes where the barometric pressure is low, it takes longer to reach tolerance than under the same high temperature conditions at sea level. The end point of such exposures, the tolerance limit, is reached when physiologic mechanisms begin to break down, but even before this performance has deteriorated. Most investigators relate the tolerance condition to the quantity of heat stored. The same physiological end point is reached whether the added heat is from an external load or from the condition where body heat loss is prevented and metabolic heat is stored.

The temperature range that has been studied is from 60° to 120°C, with the majority of research done at 70° to 80°C; beyond this temperature the instruments in aircraft and spacecraft would begin to fail before the man reached tolerance. Experimental subjects have been exposed unclothed, with light flight coveralls, and wearing heavier clothing up to and including Arctic flight gear and insulated antiexposure suits. Nearly all reports concern subjects in the resting condition.

The tolerance time for exposure to these high temperatures is shown in its simplest form in

Figure 13, which is based on data from major Soviet studies reported by Dorodonitsin et al [19], and that of the major American study summarized by Blockley [8]. In both cases the experiments were conducted at ground level with air and wall temperatures approximately equal and with resting subjects clad only in light clothing. Figure 14 shows similar data from men resting at a low barometric pressure equivalent to 8000 m altitude wearing both light flight clothing (1.2 clo) and medium flight clothing (1.9 clo), based on the study of Dorodonitsin et al [19].

It is possible to combine the many factors necessary to calculate the tolerance time for these high temperatures. The factors include air and wall temperatures, radiant load from the sun and other high temperature surfaces, air density, air velocity, clothing, and activity level. After carrying out many experiments, Blockley et al [9] derived mathematical expressions for each major factor and presented them in graphic form for easy solution when specific conditions are known. The general form of these calculations is that the rate of accumulation of heat in the body, or heat storage, is equal to the sum of

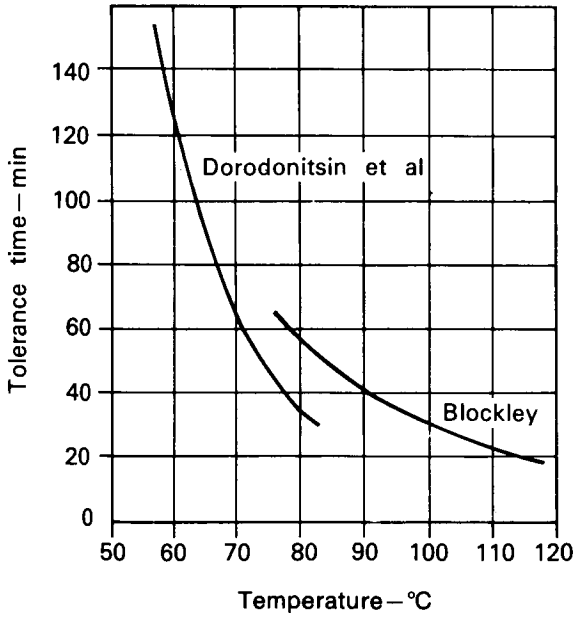

FIGURE 13.—Tolerance times for lightly clothed resting men during noncompensable heat exposures at 1 ata where the limit is determined by body heat storage. (After Blockley [8] and Dorodonitsin et al [19])

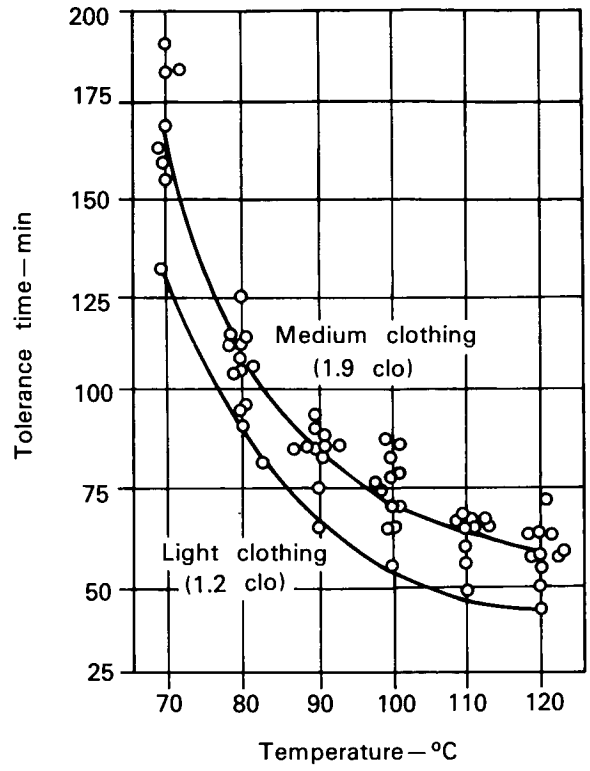

FIGURE 14.—Tolerance times for resting men at an altitude of 8000 m (26 240 ft), or 0.35 ata, during noncompensable heat exposures while wearing light and medium weight clothing. (After Dorodonitsin et al [19])

metabolic heat production and heat transfer to the body by convection, conduction, radiation, and evaporation. It was important to establish empirically the rate of heat storage and total quantity of heat stored that was tolerable, both physiologically and in the performance sense. Figure 15 shows a prediction chart based on the work of Blockley et al [9], where the body storage rate can be determined for a number of conditions over a range of "operative temperatures," the solution being to find the tolerance limit in terms of the heat storage rate in the body. The example on the graph is for a man lightly clothed in underwear at sea level in an operative temperature of 100°C, whose physiologic tolerance limit is predicted to be 27 min.

Body Heat Storage and Thermal Tolerance

The condition of the subject who is approaching the physiologic tolerance limit during a

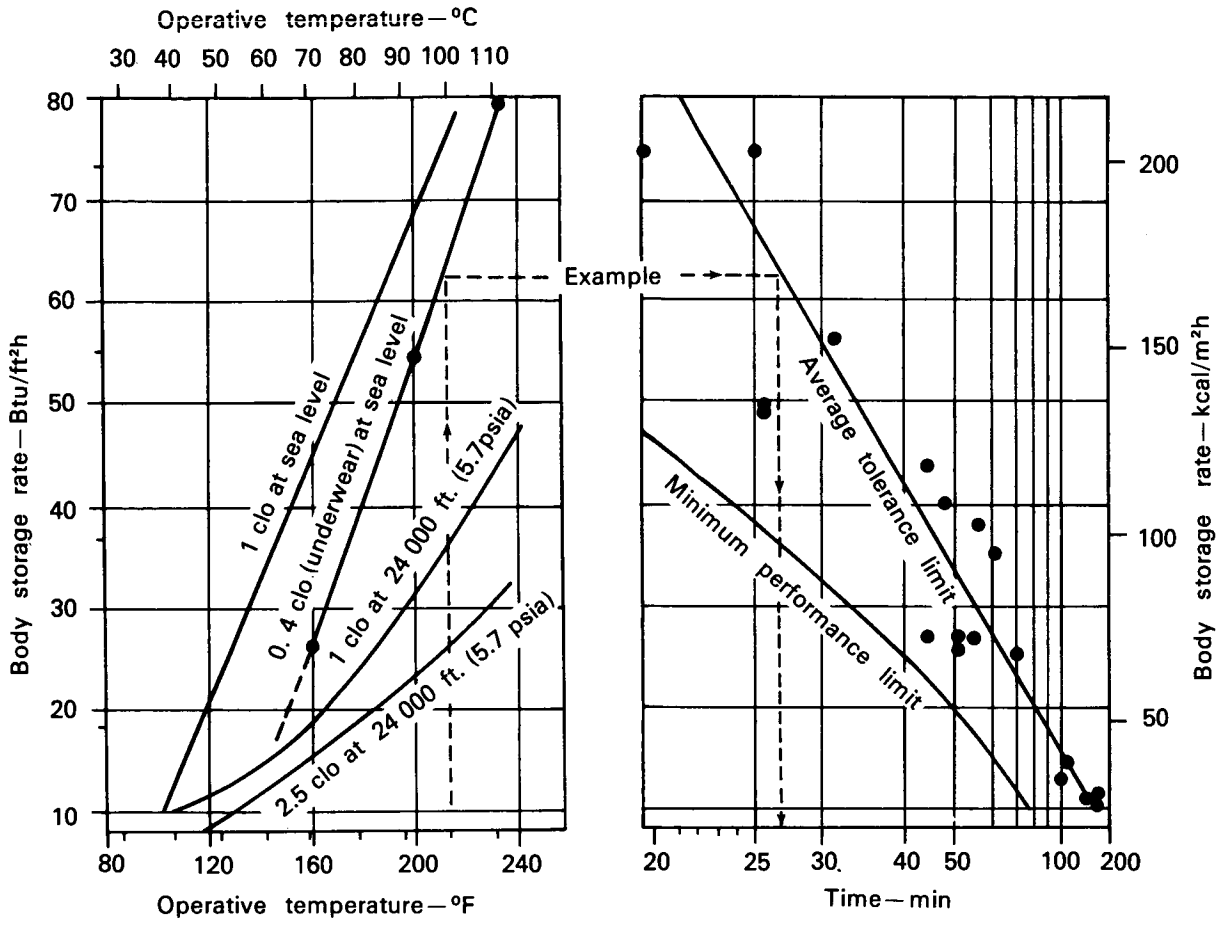

FIGURE 15.—Chart shows rate of storage of body heat for several conditions of clothing and altitude, where seated and untrained men are exposed to noncompensable heat. Entry is by means of the reference operative temperature, defined as the temperatures of air and walls which, in combination with a vapor pressure of 20 mm Hg, has equivalent effects to some other combination of humidity and temperatures. Operative temperature is the weighted mean of air and wall temperatures, where the weighting coefficients are the respective heat transfer coefficients for convection and radiation. (From Blockley et al [9])

noncompensable heat exposure is quite clear to the trained observer. The subject has been subjectively hot and sweating heavily, but quite able to perform tasks, read, and otherwise be occupied. As the tolerance point is reached, the subject becomes anxious, restless, and is unable to keep his attention fixed for very long. His performance has begun to deteriorate and he becomes more difficult to handle. The subject's heart rate has become quite high, usually in the range of 140 to 180 beat/min, depending somewhat on his physical condition. The pulse is full and strong and blood pressure shows a wide distance between systolic, which may be somewhat elevated, and diastolic, which is usually very low; the man's cardiac output is two or three times the resting level. His body temperature is high, rising rapidly, and his skin is hot and somewhat dry; his sweating is reduced. Some observers note a pallor developing around the eyes, which is quite striking since the rest of the face is flushed and red. This condition has been described by Blockley et al [9], Kaufman [33], and Webb [53]; it is also summarized in Soviet literature based on the work of Shepelev [44], Dorodonitsin et al [19, 20], as shown in

TABLE 4.— *Certain Functional Changes Related to the Degree of Overheating of the Body* [1]

Functional change	Degree of Overheating			
	1	2	3	4
Nature of sweating	moderate	profuse	significant decrease	cessation
Temperature increase, °C	to 0.3–0.5	to 1.5–2	to 2.5–3	2.5–3
Heat accumulation, kcal/m²	to 10–15	to 45–55	to 70–90	70–90
Heat production, kcal/m²·min	below 0.2–0.3	above 0.4–0.5	above 0.8	increase stopped; possible decrease
Pulse increase, beats/min	to 15–20	to 55–60	double or more	drop to original and below
Change in maximum arterial pressure, mm Hg	intermediate or no change	increase to 20–30	increase to 40–50	rapid drop to original or below
Change in minimum arterial pressure, mm Hg	"	decrease to 30–40	decrease to 50–60	decrease stopped; possibly increased

[1] From A. N. Azhayev, *Third All Union Conference on Aviation and Space Medicine*, Moscow, 1969.

Table 4. When the subject has reached this state, heat exposure must be terminated or he will lose consciousness. Should heat exposure continue, the subject's life would be threatened, either from circulatory failure or heat stroke.

This physiologic tolerance limit is reached in resting subjects when a certain quantity of heat has been stored. Heat storage is not measureable directly, but most investigators measure internal body temperature, either rectally or orally, and skin temperature. There is a tradition that storage can be found from a change in average body temperature, which can be determined by combining the change in skin and rectal temperatures with weighting coefficients.

$$\Delta \bar{T}_b = \alpha(\Delta T_{re}) + (1-\alpha)(\Delta \bar{T}_s) \qquad (7)$$

where $\bar{T}_b$ is mean body temperature, α is a constant, and T_{re} is rectal temperature. This change in average body temperature is multiplied by the subject's body weight and by the specific body heat, which is 0.83. The original weighting coefficients, dating from the studies of A. R. Burton in the 1930s, were approximately 2/3 times the rectal temperature plus 1/3 times the mean skin temperature. However, it can be argued that in severe heat exposure, the weighting coefficient for the skin should be less, since supposedly it accounts for the usually cool shell temperature compared to the more-or-less constant core temperature. In heat exposure the skin and subcutaneous tissue approach and sometimes exceed the rectal temperature. The tendency, in Soviet literature, is to calculate heat storage on the basis of internal temperature alone, or the internal temperature with a weight of 0.9 and the skin temperature with a weight of 0.1. The difficulty is that heat storage cannot be measured directly, only temperature change; it is extremely difficult to sample enough parts of the body mass to be sure of determining a mean body temperature.

Another difficulty is that accumulation of heat in the body does not produce a linear rise in rectal temperature. For the first 5 to 10 min at least, there is either no rise or a fall in rectal temperature. This observation indicated to Blockley et al [9] a body storage index—the rate of rise of rectal temperature after the initial period. They pointed out that the rate of rise was essentially linear after the first 10 minutes. The only way to be sure of the actual quantity of heat accumulated in storage-limited heat exposures is to do a direct calorimetric study capable of adding heat to the body while at the same time measuring metabolic heat production from oxygen consumption. These experiments have not yet been done.

Although different authors calculate heat storage from core and surface temperatures in different ways, the values given by most investigators for the tolerable amount of heat stored do not vary markedly. When a resting subject has accumulated 120–150 kcal, he reaches the tolerance limit. Or (as it is usually expressed), the rate of storage of heat plotted against the tolerance time gives the type of curve shown in Figures

16 and 17. Dorodonitsin et al [19, 20] point out that when the heat exposure is severe and tolerance time short, a greater quantity of heat can be stored than when the heat exposure is less and the tolerance time longer. This idea, illustrated in Figure 18, shows the total heat stored at tolerance as a function of the heat storage rate.

The origin of the accumulated heat stored in the body is clearly a combination of metabolic heat production and external heatload. Shepelev [44] shows that evaporative heat loss is greater than the external heatload at temperatures up to 70°C, so that the accumulation of heat to that temperature can be thought of as increasing amounts of the metabolic heat production being retained. Evaporative loss equals external load at 70°C at ground level, in a resting man lightly clothed. Beyond 70°C, accumulation from both metabolic heat and the external heatload is not met by evaporative heat loss. Figure 19 shows this analysis graphically. Figure 20 shows that at 8000 m altitude, the evaporative heat loss accounts for the external heatload up to a temperature of 90°C, when the subject is wearing light clothing. In Figure 21, again at 8000 m but with clothing of greater insulation, evaporative heat loss balances the external load up to a temperature of 110°C. This sort of analysis illustrates the improved thermal tolerance for given ambient temperatures when the barometric pressure is lowered, which improves evaporative heat loss, also when the insulating quality of the clothing increases. But it is clear that at any temperature above 60°C, a significant rate of heat storage, i.e. 0.5 kcal/m^2 − min, or 30 kcal/m^2 − h, leads to tolerance after exposures lasting about 2 hours.

Tolerance levels for stored metabolic heat alone have been described in the experimental work of Roth and Blockley [42]. They measured the rate of heat storage and the tolerance limit of men totally insulated—that is, when no heat exchange occurs with the environment by any pathway, and at the same time the men are working at rates comparable to those during extravehicular activity. Interestingly, the tolerable amounts of heat storage were greater in those exercising men who could lose no metabolic heat, than for resting subjects in 70°–110°C heat exposures, but who could lose heat through the evaporative pathway. The total accumulation of this heat of only metabolic origin ranged between 200–250 kcal, compared to an average of 146 kcal shown in earlier work of Blockley et al [9] whose subjects were resting and there was high external heatload.

The intent of these experiments with working men who were "totally insulated" was to simulate the condition of an astronaut during extravehicular activity in case of complete failure in the cooling system of his space suit. In the laboratory simulation, the subjects wore impermeable garments in an environmental chamber where the chamber temperature was kept equal to the rectal temperature, while at the same time the men were breathing saturated air at the same temperature. Thus there was no evaporative water loss either from the respiratory tract or from the skin, and the exchange between the man and the environment was essentially zero. As the men worked on a

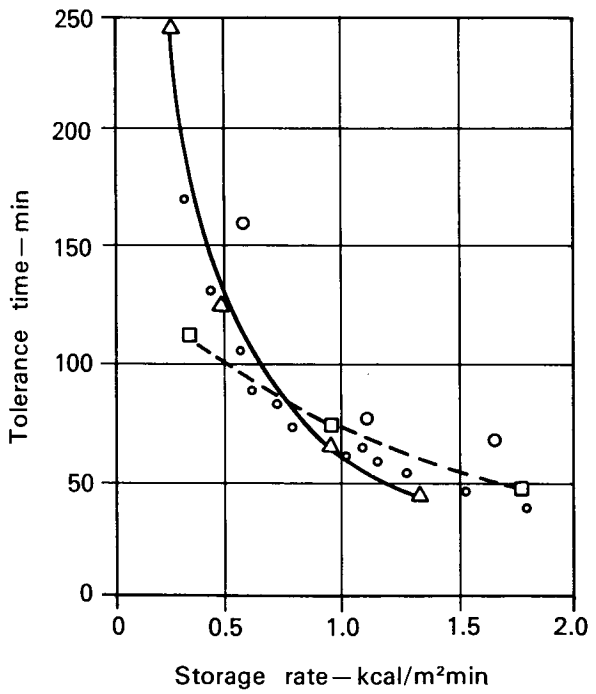

FIGURE 16.—Tolerance times as function of heat storage rates for different types of noncompensable heat exposures. Diamond symbols for resting men in light flying clothing (1.2 clo) at ground level and temperatures 50°–75°C; small circles for men at rest dressed in either 1.2 clo or 1.9 clo uniforms at 8000 m alt and temperatures 70°–120°C; large circles for men working in 1.9 clo uniforms; and three squares for men resting in a heat-insulating suit at 35°C. (Based on Dorodonitsin et al [19])

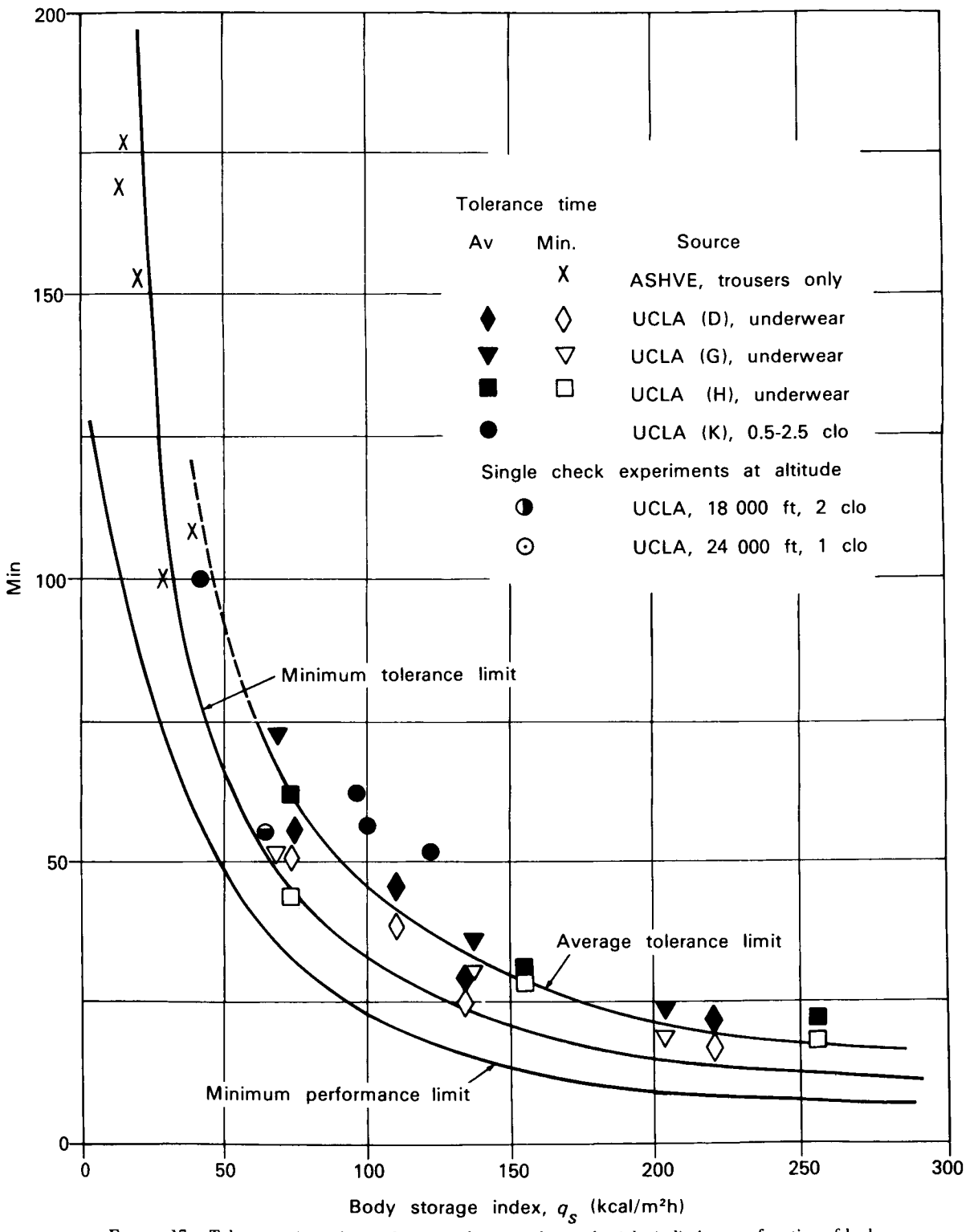

FIGURE 17.—Tolerance times for performance limits and two physiologic limits as a function of body storage index (see text) for resting men in light to heavy clothing at ground level, or at 5472 m (18 000 ft), or 7296 m (24 000 ft). (From Blockley [8])

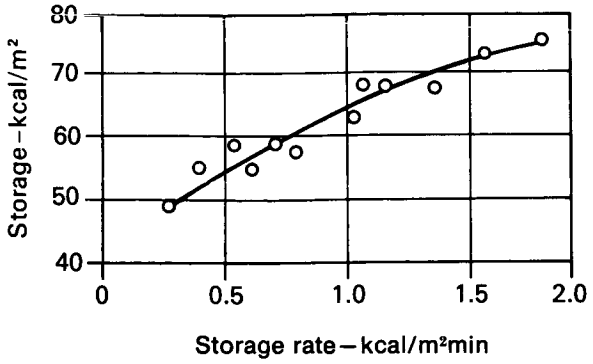

FIGURE 18.—Total heat stored to the physiologic tolerance limit as a function of rate of heat storage. (After Dorodonitsin et al [19, 20])

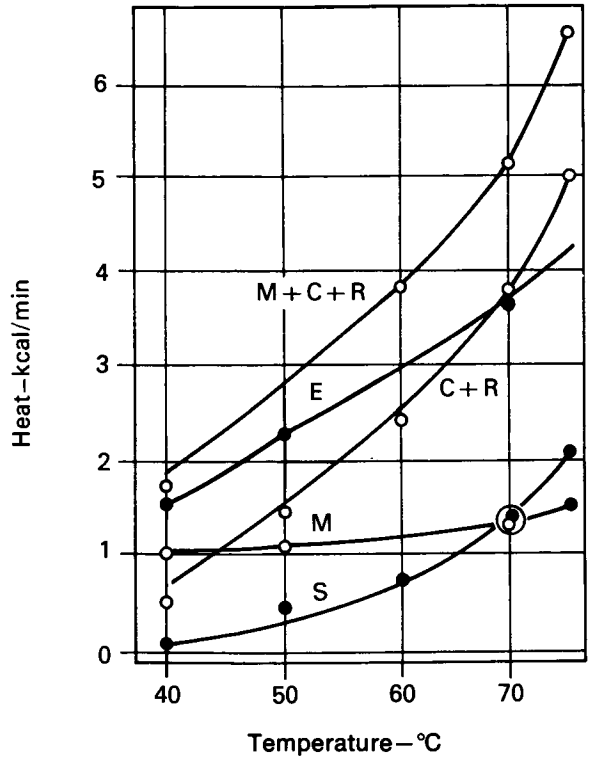

FIGURE 19.—Analysis of heat fluxes during noncompensable heat exposures between 40° and 70°C—for resting men, lightly clothed, at ground level. S is heat storage, M is metabolic heat production, $C+R$ is heat transfer by convection and radiation combined, E is evaporative heat loss, and $M+C+R$ is the sum of convective and radiative heat gain with metabolism. (After Shepelev [44])

treadmill, metabolic heat accumulated as it was generated. They reached a terminal condition characterized by air hunger and respiratory distress, restlessness, dizziness, and extreme fatigue.

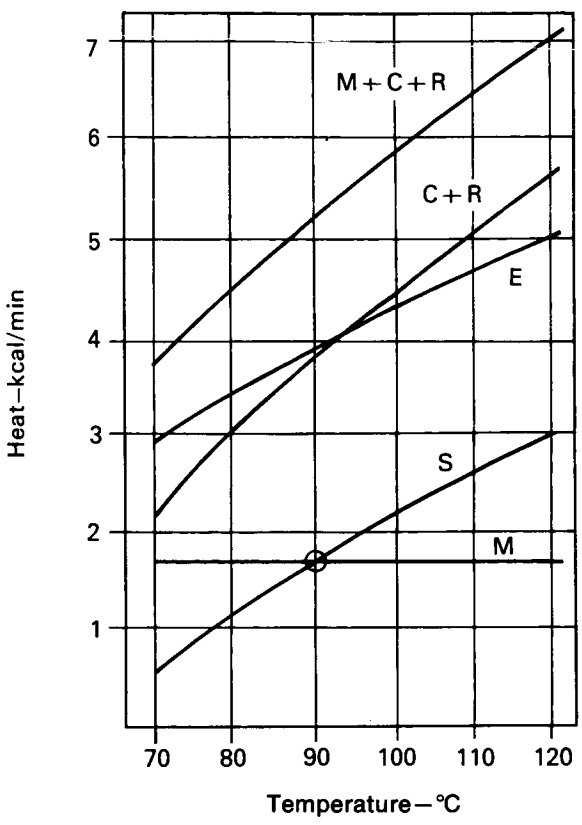

FIGURE 20.—Subjects at 8000 m alt wearing light clothing (1.2 clo); indices are the same as in Figure 19. (After Shepelev [44])

The internal temperature measured in the auditory canal rose as high as 39.7°C, and the heart rate was between 160 and 180 beat/min at termination. Roth and Blockley [42] noted that the temperatures in the auditory canal and rectum did not rise rapidly during the first 10 min but the rise thereafter was linear. The ear canal temperature rose faster and higher than the rectal temperature. There were interesting differences in the 10 subjects studied, some being able to tolerate greater quantities of heat storage than others. The endurance times at each metabolic level were:

> 4.2 kcal/min (293 W)—47 min; 6.3 kcal/min (439 W)—38 min; 8.3 kcal/min (579 W)—30 min; 10.4 kcal/min (725 W)—24.5 min.

These authors calculated the quantity of heat stored as the change in internal temperature measured from the linear portion of the rate of

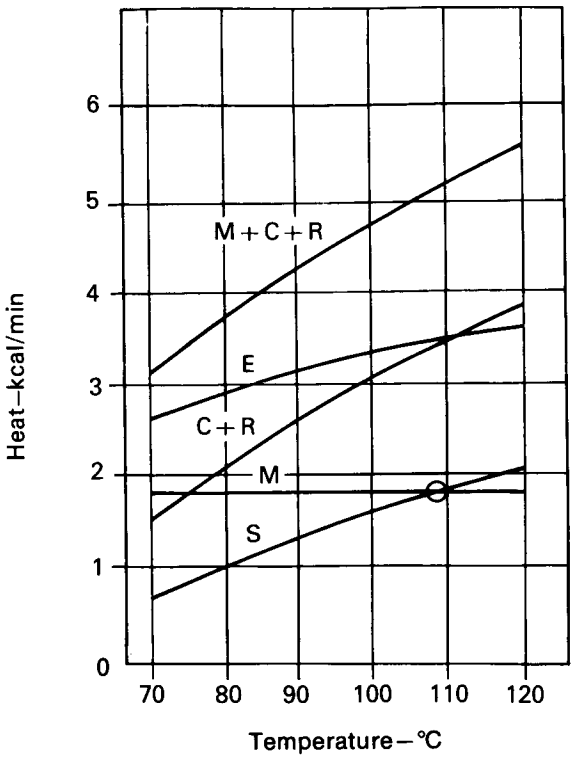

FIGURE 21.—Subjects are at 8000 m wearing heavier clothing (1.9 clo); indices are the same as in Figure 19. (After Shepelev [44])

rise of the temperature in the ear canal multiplied by ⅔ and the change in skin temperature multiplied by ⅓. They noted that the predictability of tolerance as a function of the quantity of heat stored was not as good as the predictability of tolerance time from the rate of rise of the temperature in the auditory canal. However, they felt that their calculation of heat storage based on these temperature data was reasonably accurate since it was nearly equal to the total metabolic heat generated (and retained) in the same period.

Heat Exposures Limited by Pain

When heat exposure is severe enough, as it is when the air and wall temperatures are greater than 120°C, the blood circulating under the skin cannot carry heat away as fast as it arrives, and skin temperature rises quickly. When the skin temperature in a local area reaches 42° to 44°C, subjects report pain. When the skin temperature reaches 45°C, the pain becomes intolerable. If the heat exposure continues and skin temperatures rise above this point, burns result. The experimental work in this zone of heat tolerance has been done using high-intensity radiating sources aimed at small areas of skin [13, 26, 46]; other experiments have been done with exposure of large areas of the body or the entire body [34, 54]. Figure 22 summarizes data from all these studies, showing tolerance time as a function of the irradiance, or the heat energy arriving per unit area of body surface. Exposures at any given irradiance longer than those shown on the figure will cause surface burns.

Because the pain threshold is variable between individuals and because it varies from day to day in a single individual, most recent studies have used as an end point unbearable or intolerable pain. The use of this end point reduces the variability between subjects. This end point has been studied by Webb [54] in exposures of two varieties. In the first type of experiment, the exposure to intense heat was abrupt. A preheated chamber about the size of an aircraft cabin was rolled on tracks to the subject, surrounding him. The heat exposure lasted until the subject requested termination, or pushed the chamber away. When subjects were unprotected by any sort of clothing, the tolerance time for whole body heating ranged from 15 min at 110°C to about 15 s at 260°C. Figure 23 shows data of this kind in a study involving five subjects who reached the end point of intolerable pain at the various temperatures shown. At 110°C for 15 min, the subjects stored a great deal of heat and responded with heavy sweating, high heart rate, and rising rectal temperature. The experiment was terminated because of surface pain.

Lightly clothed subjects showed storage tolerance limits at temperatures of 115°C at about 20 min in studies of Blockley et al [9]. There is, then, a transitional zone between 110° and 120°C and with times to tolerance between 15 and 20 min, when the exposure may be terminated either from pain or from excessive heat storage. This is depicted in Figure 24, which shows the same data as that in Figure 23, plus the data of Blockley et al.

The presence of clothing, of course, makes a great difference in the ability of a man to tolerate

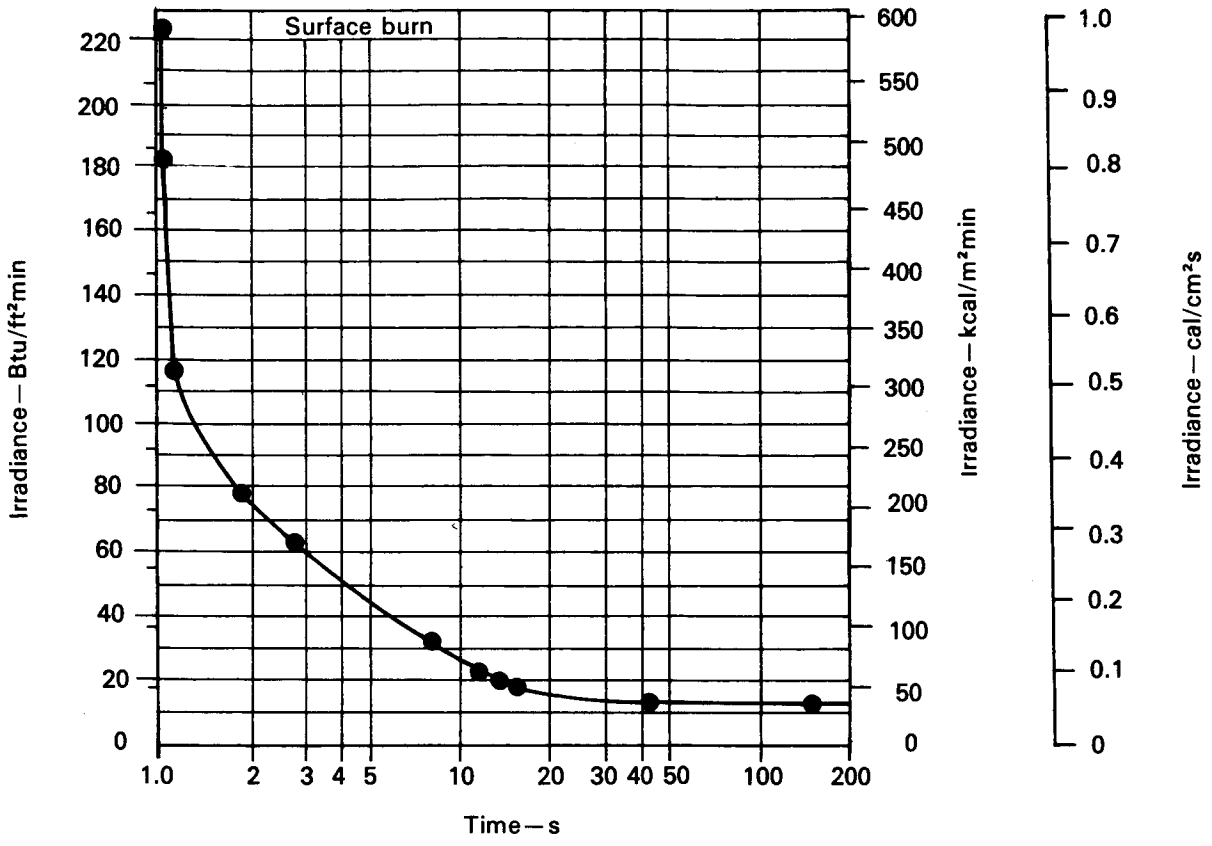

FIGURE 22.—Curve denotes combinations of heating (irradiance) and duration of exposure which produce intolerable skin pain. The highest levels of heating are similar to those from a thermonuclear flash, the lower ones from slow heat pulses related to supersonic flight and reentry of a space vehicle into the atmosphere. (Based on Buettner [13], Hardy [26], Kaufman et al [34], Stoll and Greene [46], and Webb [54])

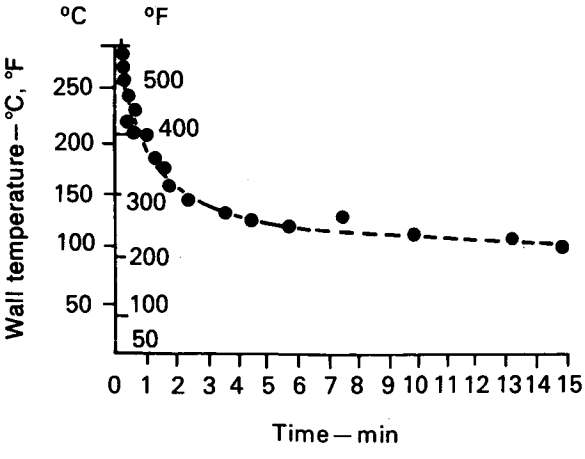

FIGURE 23.—Tolerance times set by intolerable pain for nude subjects abruptly exposed to high wall temperatures. (From Webb [54])

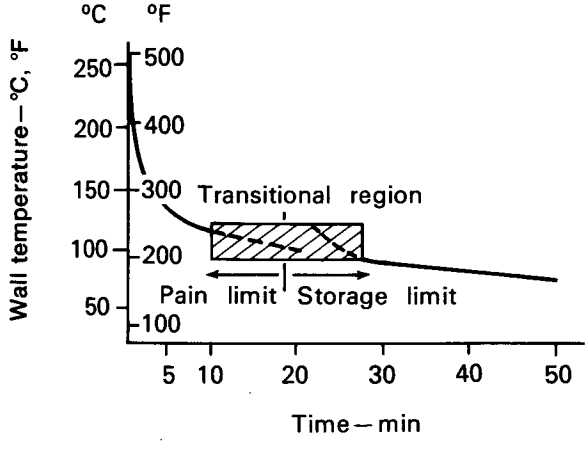

FIGURE 24.—Approximate definition of transitional region between pain-limited abrupt heat exposures of nude subjects (as in Fig. 23), and storage-limited heat exposures reported by Blockley et al [9]. (From Webb [54])

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these extreme heat exposures. In another form of heat exposure, which has been called a slow heat pulse, subjects were exposed (first nude and then clothed more and more heavily) to rising temperatures that rapidly reached levels similar to those that caused unbearable pain during abrupt exposure. A typical slow heat pulse starts with a chamber temperature of 20°C, then the walls are heated to produce a rise in wall temperature at the rate of 55°C/min. Figure 25 shows that in this kind of exposure the nude subject can tolerate a wall temperature of 210°C while light underwear allows him to reach 220°C. More layers of clothing allow him to reach higher temperatures, while heavy clothing with an aluminized layer, or the same clothing ventilated, allows the subject to go for many minutes at 260°C without undue distress. The slow heat pulse type of exposure was intended to simulate what would occur during failure of cooling equipment, either in high-speed aircraft flying supersonically in the atmosphere, or during reentry of a space vehicle. The report of Kaufman [33] has similar data for heating transients related to a theoretical curve for the Mercury vehicle during reentry.

Fortunately, there have been no major failures in cooling equipment to cause exposures of this sort to astronauts or pilots during flight. However, knowledge of means to protect men in these situations may be useful in future design studies.

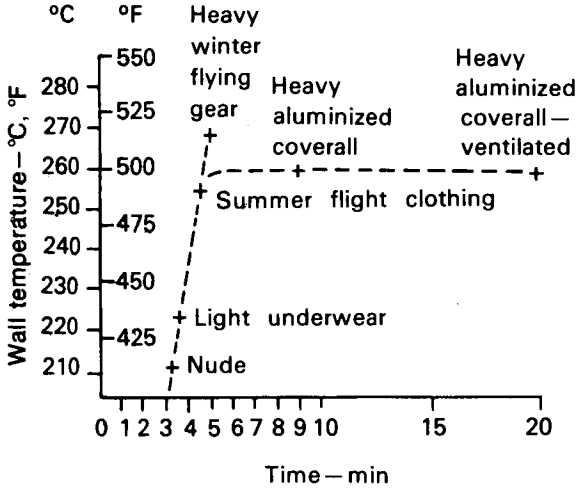

FIGURE 25.—Averaged values for pain-limited tolerances to slow heat pulses with subjects wearing different clothing assemblies. Dotted line traces hotter portion of slow heat pulses which began at 20°C with wall temperature rising at 55°C/min. (From Webb [54])

MODELS OF HUMAN TEMPERATURE REGULATION

It is possible to write equations describing heat exchange between the man's surface and the environment, heat flows within the body, and the temperature changes in the various parts of the body when the man works or is exposed to either heat or cold. Further mathematical descriptions can be made of the physiologic adjustments that help to dissipate excess heat or to conserve heat when necessary. Such systems of equations, or mathematical models, are useful to those who design life-support systems for space vehicles and cooling devices such as the water-cooled suit. Two such models will be described briefly, both having been of use in the US space program.

A general model of human temperature regulation has been described by Stolwijk and Hardy [48], and a revised and more complete version reported by Stolwijk [47]. The man is considered to be made up of a spherical head and single cylinders for the trunk, the two arms, the two hands, the two legs, and the two feet. Each of the six segments has four concentric layers of skin, fat, muscle, and core. All 24 compartments are connected by a central blood compartment, thus making 25 separate nodes. Each of the 25 compartments is represented by a heat-balance equation to account for conductive heat exchange with adjacent compartments, metabolic heat production, convective heat exchange with the central blood compartment, and evaporative heat loss and heat exchange with the environment where appropriate. Further, a controlling system or regulator receives temperature signals from all compartments and, after integration of this input, sends appropriate commands to appropriate compartments to produce changes in metabolic heat production, blood flow, or the rate of sweat secretion.

The model was presented in the form of a documented FORTRAN program. By putting the model on a digital computer, the authors were able to simulate man's response to exposures with abrupt changes in environmental temperature at

rest, and able to simulate 30-min bouts of exercise at 25, 50, and 75% of maximum aerobic capacity at different ambient temperatures. The computer output provided predictions of rectal and skin temperatures, sweat rate, and metabolism, which gave reasonable approximations of experimental data gathered in the laboratory. Thus, the assumed characteristics of the physiologic controller produced regulatory responses and compartment temperatures that appeared similar to those actually measured in the laboratory. This complex and thorough model is quite powerful, and flexible enough to permit combining it with models of a space life-support system, so that reasonable predictions can be made about the interactions between the two systems. During the lunar extravehicular activities of the Apollo program, computer programs containing models of temperature regulation and of the portable life-support system were used effectively, in determining the physiologic state of the astronauts from the relatively small number of telemetered signals available.

A Self-Regulating Model

The complete biothermal model described by Stolwijk is too complex to reproduce here, but a simplified 2-node self-regulatory model from the same laboratory can be presented.[4] The model generates for any exposure time, t, values for: mean skin temperature, core temperature, volumetric flow rate of blood in the skin, evaporative heat loss from the skin and thermoregulatory sweating, body heat storage; and it predicts the important variable skin wettedness for a given set of conditions.

The model begins with a definition of a standard man:

Body mass = 70 kg
Surface area = 1.8 m^2
Skin mass = α70 kg
Core mass = $(1-\alpha)$70 kg

Latent heat of evaporation of sweat = 0.58 W-h/g

Minimal skin conductance = 5.28 W/m^2-°C

Thermal capacity of the body = 0.97 W-h/kg-°C

Thermal capacity of blood = 1.163 W-h/l-°C

Initial conditions at time 0 for physiologic thermal neutrality are:

Metabolic heat production (M) = 58.2 W/m^2-h
Mean skin temperature ($\bar{T}_{sk}$) = 34.0°C
Core temperature measured in the rectum (T_{cr}) = 37.0°C
Skin blood flow ($\dot{V}_{skbf}$) = 6.3 l/m^2-h
Skin/core mass ratio (α) = 0.1
Evaporative heat loss from skin (E_{sk}) = 5 W/m^2
Thermoregulatory sweating. (E_{rsw}) = 0

Heat balance equations for skin and core at any time t are expressed in terms of heat flow from the skin (H_{sk}) and heat flow from the core (H_{cr}) *in* W/m^2:

$$H_{sk} = (5.28 + 1.163\dot{V}_{skbf})(T_{cr} - \bar{T}_{sk}) - E_{sk} - hF_{cl}(\bar{T}_{sk} - T_0) \quad (8)$$

where h is the combined transfer coefficient for convective and radiant heat exchange; F_{cl} is the thermal efficiency factor for clothing when clothing insulation (I_{clo}) is known ($F_{cl} = 1/1 + 1.55hI_{clo}$); and T_0 is the operative temperature, which is the average of mean radiant temperature and air temperature.

$$H_{cr} = M_{net} - (5.28 + 1.163\dot{V}_{skbf})(T_{cr} - \bar{T}_{sk}) \quad (9)$$

where M_{net} is M minus respiratory heat loss and positive work accomplished.

Body storage of heat (S) in W/m^2 is:

$$S = H_{sk} + H_{cr} \quad (10)$$

$$S = M_{net} - E_{sk} - hF_{cl}(\bar{T}_{sk} - T_o) \quad (11)$$

The thermal capacities for skin and core are:

$$J_{sk} = \alpha\ (0.97)\ (70) \quad (12)$$

$$J_{cr} = (1 - \alpha)\ (0.97)\ (70) \quad (13)$$

Changes in skin and core temperature ($\Delta t = 1$ min) are:

$$\Delta\bar{T}_{sk}/\Delta t = 1.8H_{sk}/J_{sk} \quad (14)$$

$$\Delta T_{cr}/\Delta t = 1.8H_{cr}/J_{cr} \quad (15)$$

[4] This model is adapted from the appendix to the article: Gagge, A. Rational temperature indices of man's thermal environment and their use with a 2-node model of his temperature regulation. *Fed. Proc.* 32:1572–1582, 1973.

At the end of each succeeding minute of exposure to given conditions:

$$t = t + \Delta t \tag{16}$$

$$\bar{T}_{sk} = \bar{T}_{sk} + \Delta\bar{T}_{sk} \tag{17}$$

$$T_{cr} = T_{cr} + \Delta T_{cr} \tag{18}$$

The above definitions and equations describe man in a passive state. The model continues now to describe the control system with its various regulations, at any time $t + \Delta t$.

A control signal from the skin is:

$$(\text{Sig})_{sk} = \bar{T}_{sk} - 34 \tag{19}$$

and a warm signal is positive $(\text{Sig})_{sk+}$, while a cold signal is negative $(\text{Sig})_{sk-}$.

Similarly a control signal from the core is:

$$(\text{Sig})_{cr} = T_{cr} - 37 \tag{20}$$

and warm and cold signals have appropriate signs.

The control of blood flow through the skin is by vasoconstriction (Stric) or vasodilation (Dilat).

$$(\text{Stric}) = 0.5\ (\text{Sig})_{sk-} \tag{21}$$

$$(\text{Dilat}) = 150\ (\text{Sig})_{cr+} \tag{22}$$

$$\dot{V}_{skbf} = [6.3 + (\text{Dilat})]/[1 + (\text{Stric})] \tag{23}$$

Sweat production ($\dot{Q}_{sw}$) in g/m²-h is based on the difference between mean body temperature ($\bar{T}_b$) and a threshold mean body temperature of 36.7°C.

$$\bar{T}_b = \alpha\ (T_{sk}) + (1 - \alpha)\ T_{cr} \tag{24}$$

$$\dot{Q}_{sw} = 285\ (\bar{T}_b - 36.7) \tag{25}$$

Evaporative heat loss by thermoregulatory sweating (E_{rsw}), in W/m²-h is:

$$E_{rsw} = 0.68\ \dot{Q}_{sw}^{(\text{Sig})_{sk}/10} \tag{26}$$

For a given environment, the maximum rate of evaporative heat loss ($E_{\max}$) is:

$$E_{\max} = 4.22\ h_c(\bar{T}_{sk} - T_{\text{dew}})\ F_{pcl} \tag{27}$$

where h_c is the convective transfer coefficient; T_{dew} is the dewpoint temperature; and F_{pcl} is the permeation efficiency factor for clothing (defined by $F_{pcl} = 1/1 + 0.143\ h_c I_{clo}$).

The wettedness of the skin from regulatory sweating (W_{rsw}) is:

$$W_{rsw} = E_{rsw}/E_{\max} \tag{28}$$

and total skin wettedness (W) is:

$$W = 0.06 + 0.94\ W_{rsw} \tag{29}$$

Evaporative heat loss from the skin (E_{sk}) is defined by:

$$E_{sk} = W\ E_{\max} \tag{30}$$

The skin/core mass ratio (α) is modified by vasoconstriction, and $\dot{V}_{skbf}$ becomes less than 6.3 l/m²-h.

$$\alpha = 0.1 + 0.25\ (6.3 - \dot{V}_{skbf})/6.3 \tag{31}$$

Shivering is seen in the model as a regulatory response to cold signals, the effect being to increase metabolic heat production.

$$M = 58.2 + 19.4\ (\text{Sig})_{sk-}\ (\text{Sig})_{cr-} \tag{32}$$

Using the model equations, one may simulate the regulation of body temperature by iterative calculation. From the heat balance Equations (8) and (9), at any time t the $\Delta\bar{T}_{sk}$ and ΔT_{cr} are determined from Equations (12) through (15) for each successive interval of 1 min. These new values for $\bar{T}_{sk}$ and T_{cr} are used to calculate new values for $\dot{V}_{skbf}$, $\dot{Q}_{sw}$, E_{rsw}, W_{rsw}, W, E_{sk}, α (if there is vasoconstriction), and a new M if there is shivering, using Equations (16) through (32). These new values are reinserted into Equations (8) and (9) for new heat balances at time $t + \Delta t$. The entire cycle is repeated to derive new values for the other variables.

Successful regulation of body temperature occurs when:

$$S = O = H_{sk} + H_{cr}$$

Model of Man in a Water-Cooled Suit

A different and simpler model [56] has been used to develop automatic controllers for the cooling required from a water-cooled garment worn by a man exercising in the thermally isolated state. The problem involved here was simpler because it was assumed that with proper control, the man would need minimal regulatory responses internally in order to dissipate the varying levels of metabolic heat produced during various levels of work. In this model there were only three anatomical compartments: the skin, the core, and the skeletal muscle. Equations were written for heat production in each compartment and heat flows between compartments and to the water-cooled garment. Predictions could be

made for temperatures in the various compartments and for the course of heat removal required from the water-cooled garment. One useful equation described the transfer function between heat production and the cooling required to maintain the man in comfort—that is, a man who was virtually sweat-free and who could dissipate metabolic heat at minimal physiologic cost.

At equilibrium during rest, compartment temperatures do not change, and heat production equals heat loss:

$$M = M_{re} + M_m + M_s = H + L \qquad (33)$$

where M_{re}, M_m, and M_s are heat productions in the core, muscle, and skin compartments respectively; H is heat removed by the water-cooling garment; and L represents the small losses of heat elsewhere than to the suit.

In about an hour, after the man starts to work, a new equilibrium between heat production and heat loss is reached, with new steady-state values for compartment temperatures:

$$M = \Delta M + M_{re} + M_m + M_s = H + L + W \qquad (34)$$

where ΔM is the added heat production from working and W is external work done.

The instantaneous heat content, Q, of each body compartment may be written as:

$$Q_m = m_m c_m T_m \qquad (35)$$

$$Q_{re} = m_{re} c_{re} T_{re} \qquad (36)$$

$$Q_s = m_s c_s T_s \qquad (37)$$

where m is mass, c is specific heat, and T is absolute temperature.

During the transition from rest to work, and from work to rest, compartment temperatures change according to the general equation for change in heat content:

$$\Delta Q(t) = H(t) = mc \int_{t_1}^{t_2} T(t)dt \qquad (38)$$

Heat flow between any two compartments is defined by:

$$H = h(T_2 - T_1) \qquad (39)$$

where h is a heat transfer coefficient.

An expression may now be written for temperature changes in the muscle compartment:

$$C_m \dot{T}_m = \Delta M + M_m - W - h_{m-re}(T_m - T_{re}) - h_{m-s}(T_m - \bar{T}_s) - L_m \qquad (40)$$

where

$$C_m \dot{T}_m = m_m c_m \int_{T_1}^{T_2} dT,$$

and $\bar{T}_s$ is mean skin temperature.

Similarly, in the rectal compartment:

$$C_{re} \dot{T}_{re} = M_{re} + h_{m-re}(T_m - T_{re}) - h_{re-s}(T_{re} - \bar{T}_s) - L_{re} \qquad (41)$$

And in the skin compartment:

$$C_s \dot{T}_s = M_s + h_{m-s}(T_m - \bar{T}_s) + h_{re-s}(T_{re} - \bar{T}_s) - h_{s-w}(\bar{T}_s - T_{wi}) \qquad (42)$$

where T_{wi} is the temperature of the water entering the water-cooled garment.

No loss term is shown for the skin, since it was assumed that all heat from the skin went into the water-cooled garment. Respiratory heat loss was assigned to L_{re}.

Heat flow from the skin to the water in the cooling garment is determined by a transfer coefficient, h_{s-w}, and the temperature gradient:

$$H_{s-w} = h_{s-w}(\bar{T}_s - T_{wi}) \qquad (43)$$

The water-cooled garment was treated as having no mass and no losses, hence $H_{s-w} = H$, which can be measured experimentally from change in water temperature across the cooling garment multiplied by the mass flow rate and specific heat of the water.

Finally, the model included an equation for generating T_{wi} from M. Inspection of the data had shown that for step increases in M the manually controlled T_{wi} had changed exponentially, with a new level being achieved in about 50 min. Since T_{wi} appeared to be proportional to M, one can write:

$$\Delta T_{wi} = T_{wi}(0) - T_{wi}(t) \qquad (44)$$

where $T_{wi}(0)$ is an initial inlet temperature, and $T_{wi}(t)$ is the inlet temperature at time t.

Using the empirically observed proportionality between M and T_{wi}:

$$(M_0 - M) \approx T_{wi} \qquad (45)$$

or, adding a proportionality constant, B,

$$B(M_0 - M) = T_{wi} \qquad (46)$$

The exponential change in T_{wi} can be written as:

$$T_{wi}(t) = T_{wi}(0)e^{\frac{-t}{\tau}} + B(M_0 - M) \qquad (47)$$

or, rearranging terms:

$$\tau \dot{T}_{wi} = -T_{wi} + B(M_0 - M) \qquad (48)$$

Equation (48) is the equation defining the function of an automatic controller; it was given earlier as Equation (5).

The terms used in the model Equations (40), (41), (42), and (48) were given the numerical values shown in Table 5.

These biothermal models help to summarize what has been useful in the area of human thermal response in the space environment. As more information about human heat production and thermal tolerance is gathered, such models can be further refined and expanded. As new thermal problems arise or as new protective equipment and life-support systems are developed, models of this sort will continue to be helpful both in design of equipment and in monitoring the use of equipment and the state of the astronaut during flight.

TABLE 5.— *Values for Terms in the Model Equations*

B	1.95	°C-min/kcal
C_m	18	kcal/°C
C_{re}	40	kcal/°C
C_s	3.2	kcal/°C
h_{m-re}	5.0	kcal/min-°C
h_{m-s}	0.3	kcal/min-°C
h_{re-s}	0.3–0.6 (generated)	kcal/min-°C
h_{s-w}	0.5	kcal/min-°C
L_m	0.07	kcal/min
L_{re} (at $M=5$)	0.15	kcal/min
(at $M=10$)	0.22	kcal/min
M_0	20	kcal/min
τ (for T_{wi})	10	min

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Part 2

EFFECT OF DYNAMIC FLIGHT FACTORS ON THE ORGANISM

Chapter 4

PRINCIPLES OF GRAVITATIONAL BIOLOGY

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The study of gravity has been of special importance in the development of physical science. Its study in Aristotelian times marked the beginning of physics—and later inquiries into the behavior of gravity by Galileo and Newton in the 17th century provided the foundation of modern physical science [215].

The appreciation of the biological effects of gravitation developed much later. The first recognized overt effect of gravity on organisms was the geotropism of plants. In 1806 [114], Thomas Knight built a small water-driven centrifuge and placed germinating bean seeds about its perimeter. At accelerations of 1, 3.5, and 10 G the plants grew parallel to the field, rather than to gravity. He concluded that the ambient acceleration field was the orienting influence on plants. Somewhat later, Piorry [163] examined the influence of Earth gravity on the circulation of blood. He used the patient's response to supine and upright postures to differentiate between apoplexy and syncope; this was quite important inasmuch as the contemporary treatment for apoplexy was bloodletting.

Experimentation of gravitational effects on animals was instituted by Salathe in 1876. Initially, he investigated the relationship of posture—head up or down—upon cerebral volume, and heart and respiratory frequencies in dogs and infants. He found that rabbits held in a vertical position died after 15 minutes to 2 hours from a progressive failure of circulation and respiration. Subsequently [179], he adapted a device that his teacher, Marey, had used for serial photography of bird wing-beating for the centrifugation of small animals. He developed instrumentation for measuring cardiorespiratory phenomena on the operating centrifuge, and found that the condition of orthostatic hypotension could be induced with centrifugal forces. About the same time Tsiolkovskiy constructed a centrifuge and studied the acceleration tolerance of insects (200 G) and chicks (5 G)—to determine the permissible operational characteristics of rockets for space travel [177].

Definitive scientific study of the physiologic effects of acute acceleration began about 1917 when Garsaux of France studied circulatory changes in centrifuged dogs [3]. Soon "grey-out" and "black-out" were reported by pilots in airplane races during turns about pylons [6, 166]. Interest in centrifugal forces developed rapidly, and within a decade several large-diameter human centrifuges were constructed and used in

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studies of aviation medicine [71]. Animal experimentation also was renewed, after a lapse of 60 years, in order to investigate the physiology and pathology of extreme acceleration conditions [25, 136].

Aviation-oriented interest in acceleration was restricted largely to short-term phenomena, with exposures of no more than a few minutes' duration. Interest in longer term exposure to centrifugation—simulating an increase in gravity—developed later in anticipation of space exploration. In 1951, Haber and Gerathewohl [91] discussed the potential problems of prolonged space flight, and various ways that it might be simulated and studied. In 1953, Matthews [128] reported the results of as much as a year's exposure of rats to fields of 3 G and 6 G. Subsequently, chronic acceleration programs developed in the United States and elsewhere to study the effects of simulated changes in gravity; however, these number fewer than a dozen at present. Exposures of animals to weightlessness in Earth-orbit began in 1957 with the launching of the dog Laika in Sputnik 2 [74].

Thus, gravitational biology has existed as an experimental science only since the 1950s. Obviously, the constancy of gravity, and our inability to alter it for significant periods on Earth were impediments to its earlier study. For physical systems, brief periods of weightlessness obtained in free-fall were sufficient for useful study. However, in biologic systems, much longer exposure periods are required to elicit important physiologic changes. Were gravity as variable as the other common environmental factors, it would be quite well understood.

PHYSICAL PRINCIPLES

Gravitational and Inertial Forces

Newton's laws of motion, derived from the laws of fall, relate force and displacement of unrestrained objects. The second of these laws is particularly important to gravitational biology, since it mutually defines forces (F) and acceleration (a):

$$F \alpha ma \tag{1}$$

The behavior of the acceleration field, gravitation, is described by Newton's law of universal gravitation. This law proposes and quantifies the mutual gravitational attraction existing between all bodies of matter—the force being proportional to the product of masses, (m_1 and m_2) and inversely related to the square of the distance (d) separating them:

$$F \alpha \frac{m_1 m_2}{d^2}; \text{ or } F = G \frac{m_1 m_2}{d^2} \tag{2}$$

The relationship between the mass indicated by Newton's laws of motion (the inertial mass, m, in Equation (1)), and by his universal law of gravitation (the gravitational mass, m, in Equation (2)) was dealt with by Einstein in 1911 as the *principle of equivalence* [172, 233]. He concluded that these masses were equal for a given body and that the effects of accelerative forces were equivalent, irrespective of their physical bases. This principle was tested experimentally by Eötvös in 1922 and found valid to one part in 10^8, and subsequently Dicke [53] confirmed it to one part in 10^{11}. This concept is particularly important to gravitational biology since it justifies comparisons between experimental observations on the effects of fields developed by motion (centrifugation) and those developed by gravitation.

Weight and Mass

Mass is a fundamental property of matter, also defined by Newton's law of motion—as expressed in the absolute system of units:

$$m = F/a \tag{3}$$

Thus mass (m) is recognized behaviorally, by the force (F) required to impart a unit of acceleration (a). Weight, however, is a phenomenon which develops in objects restrained from movement in an acceleration field[2]. The distinction between weight and mass is the fundamental physical principle of gravitational biology. Since these entities frequently are described by the same units (lb, g, etc.), also being essentially numerically equal in Earthly situations, there is little popular recognition of the distinction. Even in scientific situations, weight and mass are only rarely differentiated. For example, "weighing"

[2] By convention, existence in an acceleration field also is frequently referred to as *acceleration*—even though any displacement is prevented.

with a balance is actually a determination of mass. The standards, commonly called "weights," function as mass units since they, and the unknown object, are affected equally by changes in the ambient acceleration field. However, the analogous operation with a spring scale is properly a weight determination since this device is affected by variation in the acceleration field as well as by variation in mass.

The gravitational system (used by engineers) is particularly useful to biologists, and generally is applied in a modified form:

$$W/M = a/g = G \qquad (4)$$

Either ratio can be used to evaluate the dynamic properties of an environment—that aspect which tends to make things move, or, if restrained, exhibit weight. The ratio a/g, called "gravitationally normalized acceleration" (GNA) [55], presents a field (a) as multiples of the Earth's gravitational constant (g). The weight-to-mass ratio, numerically equal to a/g, is the operational principle of accelerometers—devices, resembling a spring balance, commonly used to measure accelerative forces. Either ratio is expressed as the dimensionless coefficient G ("g" being reserved for Earth's gravitational constant).

Weightlessness

A condition of critical importance to gravitational biology is *weightlessness*, where objects with demonstrable mass lack a detectable weight. The acceptance of the term, *weightlessness*, is conditioned by one's concept of weight. Physicists conceive weight as merely another force—abstractly, and without material connotations, since, in their treatment the units of weight and mass are different. Popularly, weight is considered rather specifically as a material descriptor. For example, *body weight* describes a quantity, indicated by the morning encounter with the bathroom scales without reference to the ambient acceleration field. Engineers have an intermediate concept: although fully aware of the physical basis of weight, they consider it through the gravitational system in units as ordinarily equivalent to mass. Biologists, apparently, have not considered the matter and hold more-or-less the popular concept. Scientifically, they use weight as index of relative material magnitude—phenomenologically derived.

From the physicists's point of view ($W = ma$), a body could be weightless only in the absence of accelerative forces, which, by the Law of Universal Gravitation, is theoretically impossible. Free-fall, denoting unrestrained movement under the influence of the ambient forces, has been offered by physicists as an inoffensive alternative to weightlessness for objects in Earth orbit. However, this nomenclature has limitations; it does not include all situations which many biologists wish to describe as weightless.

Weightlessness was first encountered, briefly, in diving aircraft during World War I [67], and for greater duration in World War II aircraft [54]. In 1950, the Habers [90] proposed a flight maneuver (a *Keplerian arc*) which would prolong the period of weightlessness; they used high-performance aircraft achieving as long as 45 seconds [171]. After World War II, experiments initiated with rocket-launched capsules could accommodate small animals [100]. In these experiments, the weightlessness commencing at rocket burnout could be extended for many minutes. This weightlessness was truly the result of a free-fall, which was only partially the situation for the aircraft-produced weightlessness. About the same time, experiments were undertaken on the effects of buoyant immersion [76] which statically produced a condition of weightlessness that could be maintained for many days.

Thus, over the past two decades the biologic effects of several conditions that are interrelated by a weightlessness aspect have come under scientific investigations. With the anticipation of manned space flight, the significance of these biologic effects, and the tempo of the research, have become greatly enhanced. It is obviously conducive to progress to adopt a generic term *weightlessness* to cover these varied conditions without demonstrable weight and their effects. In this usage, *weight* and *weightless* are dealt with phenomenologically, without reference to the component physical factors. Such latitude in definition has been recommended by NASA [2] which provides two criteria for weightlessness:

1. A condition in which no acceleration,

whether of **gravity** or other force, can be detected by an observer within the **system** in question; or

2. A condition in which gravitational and other external forces acting on a body produce no stress, either internal or external, in the body.

Size and Scale Effects

An important consideration in gravitational biology is the magnitude of the organism, since systems (both physical and biological) of different size have many different properties. This was first recognized in 1638 by Galileo [70] and the Galilean concept of *similitude* has been paraphrased by Thompson [216]: "Man can not build a house, nor nature construct an animal beyond a certain size without altering the design or materials."

Strength and load relationship have important similitude considerations. Load (weight) is not an important consideration in small organisms. However, as the body size of an animal enlarges, the load will increase proportional to the cube of some dimension—but the strength of the load-bearing structures will increase only in proportion to its cross-sectional area, the square of some dimension. Thus, if mice were scaled up proportionately to elephant size, the body mass would increase to a much greater extent than the strength of the leg bones, and at some point they would fail and fracture spontaneously. The solution, of course, is the one suggested by Galileo. As animals increase in body size, there is an increase in relative skeletal size [216] (Table 1).

TABLE 1.—*Increases in Body Size and Relative Skeletal Size*

Animal	Body mass	Skeleton, % body mass
Mouse, wren	20–30 g	8
Dog, goose	5 kg	13–14
Man	75 kg	17–18

Thompson recognized that these differences are due to gravitational influence, since marine mammals have lesser skeletal size and approximately the same relative skeletal proportions are found in porpoises and whales. Among terrestrial species, skeletal size increases proportionally to the 1.15 power of body mass [111] and similar kinetics of skeletal growth also apply within species [193].

A very important consideration of size-related biologic phenomena is that a minimum impediment from gravity will obtain below some size limit which was proposed in 1896 by Crookes [49] and later by Thompson [216], J. B. S. Haldane [93], and Went [228].

Scale Limits of Gravitational Effects

Although gravitation is quite a pervasive and constant phenomenon, it provides only a very weak field. For example, the gravitational attraction between two protons is only 10^{-36} as great as the electrostatic repulsion [47]. In conditions compatible with animal life, Earth gravity is so much weaker than thermal energies or intermolecular forces that no influence is considered at the physical level (atoms and molecules) of organization [180]. At the submicroscopic and microscopic levels of organizations, structures remain generally insensitive to forces in the order of Earth-gravity. For example, to selectively move the organelles in animal cells at significant rates requires fields in the order of 1000 G, and to separate large molecules (e.g. proteins) requires fields in the order of 100 000 G [51]. However, even in these very intense fields, particles less than 1μm are significantly affected by diffusion effects—thermal phenomena. Even at 250 000 G, diffusion cannot be considered negligible until particle sizes are 0.05 μm [162].

Some phenomena which appear to result from gravitational effects at the molecular level may have other explanations. For example, Ensanian [60] reported a change in electrochemical potential in batteries during free-fall. In such systems, thermally induced convections may be of substantial importance to the electromotive force produced. Consequently, the physical basis for the observed changes in electrochemical potential in brief weightlessness may be a much greater than molecular scale. Mel has reported a system ("staflo" [131]) in which discreteness of moving columns of solutions is maintained by suitable density gradients. In

this preparation, he has noted a selective movement of enzyme molecules along the field of gravity. Particle-medium interactions in such systems may lead to an *entrainment* of molecules, which would provide units of much larger dimensions that are readily susceptible to gravity. A similar entrainment, resulting in gross movement, has been observed in red blood cell suspensions under the influence of gravity [32]. Pickels [162] concluded that gravity is a directly effective sedimenting force only for objects that are at least as large as erythrocytes.

Pollard [165] examined the theoretical bases for anticipating effects of mechanical forces, in the order of Earth gravity, at the cellular scale. For bacterial cells of 1 μm dimensions, he found that the influence of gravity on the statistical distribution of large molecules was insignificant. For larger cells, with relatively larger and denser organelles, the situation was quite different. In a mammalian tissue cell, 10 μm diameter, the influence of gravity on the distribution of mitochondria was potentially quite significant. However, when he compared the displacing effect of gravity with the convective streaming induced by metabolic activity (local density variation resulting from uptake of adjacent molecules), Pollard concluded that a lack of gravity would not significantly affect the statistical distribution of organelles.

Pollard also considered the effect of hydrostatic stress upon membranes, and the effect on their permeability, of anticipated degrees of distortion. At the tissue cell level, 10 μm, no effect from gravity-induced hydrostatic pressures was anticipated. However, in an organism, the hydrostatic effect of a 1-m column, transmitted to the membrane of the bottom cell would produce enough mechanical stress to theoretically affect its permeability to large molecules.

Others have considered the minimum-size organism which is directly affected by gravity. Thompson [216] divided organisms into three size categories according to their susceptibility to physical forces:

> large animals, such as man, affected primarily by gravity,
>
> smaller organisms, such as insects, more affected by such forces as surface tension,
>
> microorganisms, principally affected by viscosity, Brownian movement, and other intermolecular phenomena.

Haldane [93] considered hazards of gravity, such as those involved in falling, limited to organisms larger than mice.

Went [228] has provided a particularly interesting analysis of the influence of size (scale) on the susceptibility of objects to various categories of forces. He proposes a critical dimension which appears to be in the order of 1 mm. At a lesser scale, forces of molecular origin have a dominant effect; at a greater scale, gravity and mass-related phenomena dominate (Fig. 1). Since macro- and microsystems have different mechanics, Went proposed a formal distinction:

> *Newtonian World* consisting of macrosystems where mass and acceleration phenomena largely determine behavior.
>
> *Gibbsian World* (honoring the American physical chemist, Josiah Gibbs, 1839–1903) consisting of microsystems regulated largely by forces of molecular origin. Systems of

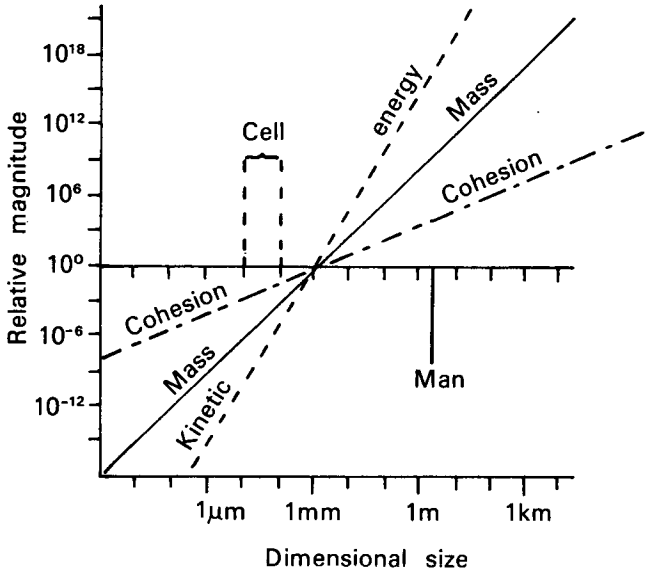

FIGURE 1.—Size and susceptibility to various forces. The relative importance of (1) cohesion between surfaces, (2) mass (weight), and (3) kinetic energy upon the behavior of a system is compared with linear dimension. Both cohesion and kinetic energy values are only approximate, based on average roughness of surface and on average velocities of masses of various sizes [228].

this category would be recognized by greater behavioral modification with changes in temperature.

Important exceptions to Went's rule are, of course, readily apparent. For example, weightlessness exposure has been uniformly observed to induce spindle malfunction in the reproductive cells of *Tradescantia* [73, 208a], indicating an effect of Earth gravity upon the genetic mechanism. Also, the geotropism in woody plants must originate at the level of the cell, and in the growing point soon after cell division. Otherwise, the rigid cellulose walls would prevent the orienting response. However, in higher animals, acceleration fields appear to become effective only at the gross (organ) level. Isolated (cultured) animal cells show little or no response to acceleration, up to fields of 200 G [59, 95], but in intact homoiothermic animals, effects are noted in relatively weak fields (2–7 G) and the severity of effect of the increased acceleration is proportional to body size. Cells are quite similar among such animals, despite a wide variation in body size (Driesch's law of constant cell volume), and diversity—which would account for differential acceleration susceptibility—can be seen first at the organ level. Even weak forces can become effective if their influence is *amplified* through action on a large mass. For example, the Moon's gravitational field at the Earth's surface is approximately 2×10^{-6} G. But when this small force is applied through the volume of the seas, high energetic tides result. Similar situations, on a much smaller scale, may be encountered in animals with moderate changes in the acceleration fields. For example, a field of 1 G acting on the whole organism may produce forces on the antigravity muscles that are 1000-fold its direct effect on those tissues. In this way, the effects of acceleration on a relatively large structure may become focused on a relatively small part, and elicit a specific response—such as the release of a humoral agent or a neural stimulus.

Gravity as a Biogenic Factor

The development of terrestrial organisms, both phylogenically and ontogenically, involves an increasing susceptibility to gravity. Life originated at no greater than cellular dimensions in an aquatic environment; consequently, it may be assumed that gravity had little direct effect on the origin of life. Gravity was of critical importance in the ordering of the physical environment where life originated. Without gravity there would be no seas or atmosphere, nor thermal convection or other separation of materials of different density—phenomena essential to the origin of life.

Certain animals became terrestrial at a relatively small size, after an intermediate step of increased density and *bottom-dwelling*—which induced adjustments necessary for life on a solid substratum [81]. Subsequently, there was a general tendency for these species to develop slowly to larger size (Cope's law). In becoming terrestrial and increasing in size, such animals had to adapt and conform to the greater requirements imposed by gravity-induced loads. It is perhaps significant in this regard, that the largest terrestrial animals became extinct. However, among current terrestrial animals, lifespan does not appear to be regulated by gravitational susceptibility; on the contrary, it tends to be proportional to body size [98]. Those terrestrial animals that returned to an aquatic existence, the marine mammals, were able to continue development without gravitational interference [206]. The largest animals that ever lived—the blue whales—are among them.

GRAVITY ORIENTATION

Gravity is a vector, with direction as well as magnitude, and it is the principal orienting agent in the Earth environment. All but the most primitive organisms are gravity-responsive—either morphogenetically, posturally, or in locomotion. This requires that gravity be perceived.

Statocysts

The prototype organ for gravity perception is the crustacean statocyst. This organ was identified in 1893 by Kreidel [120] as gravity-responsive, with the well-known experiments where iron replaced sand as the granular content of the organ. In this condition, orienting responses were obtained with a magnetic field,

rather than gravity—to which the normally sand-filled organ responded. The gravity stimulus is transduced by sensory hairs which line the statocyst cavity. The structural and functional aspects of this response have been discussed by Schöne [183]. Similar gravity-responsive organs are encountered in many other invertebrates [103, 219, 220]. Insects have somewhat different mechanoreceptors that respond to gravity—neck proprioceptors in dragon flies [135] and hair plates in bees [123]. Gravity perception and orientation in insects have been reviewed recently [127, 227, 231].

Otolithic Organs of Vertebrates

Vertebrates have developed somewhat more elaborate gravity-sensing organs than the invertebrate statocyst—but the functional principles appear quite similar. These are associated with the labyrinthine mechanism of the ear region which also senses motion. The anatomy and physiology of these organs have been summarized by Lowenstein [124]. Among vertebrates, the otolithic organs appear to be much less dominant in determining orientation, being well-integrated with ocular and proprioceptive inputs [83, 84, 85, 104, 153, 167, 170]. The acceleration-response of these organs also may be conditioned by repeated stimulation [88].

Gravity Reception in Plants

Plants exhibit a complex geotropism rather uniformly: stems respond negatively; roots, positively; with root hairs being ageotropic. The early centrifuge experiments by Knight [114] established that this orientation was in response to the ambient acceleration field. However, since plants lack a demonstrable acceleration-responsive organ comparable to the animal statocyst, the mechanism for the geotropism was not obvious. In 1900, Haberlandt [92] and Nemec [141] reported that the sedimentation of cytoplasmic starch granules in a plant's cell was closely related to its geotropism and they proposed that these granules (amyloplasts) were the gravity-susceptible statoliths that initiated the geotropic response. Subsequently, a variety of exceptions was noted with substantial discussion on the *starch statolith problem* that has been reviewed by Larsen [121].

Very little is known regarding the nature of the transduction of the gravity stimulus in plants—i.e. the intermediate processes that may be initiated by statolith sedimentation. Various concepts have been proposed which have been summarized by Audus [4] and by Merkis [133]. However, geotropic response (the appropriate bending of the plant) is necessarily the immediate result of differential growth between the upper and lower halves of the displaced plant tissue. Apparently this is caused by an unequal distribution of plant growth-promoting substances; numerous observations supporting this conclusion have been reviewed by Wilkins [230].

Particularly interesting results have been obtained with mutant tomato plants, which are naturally ageotropic [208, 213, 246]. The factors responsible for this condition are inherited in simple Mendelian ratios. Their geotropism can be restored by several treatments (prolonged darkness, ethylene, supraoptimal auxin concentrations)—indicating the importance of physiologic processes in geotropism [247]. Continued study of these unusual materials should greatly enhance understanding of geotropism.

Interesting variations in the geotropic response are encountered in acceleration fields artificially increased by centrifugation. There appears to be a time-intensity summation in the rate of response and field intensity—the *reciprocity rule* of Rutten-Peckelharing [178]—although this is subject to some limitations [82]. This implicates the transport rate of growth-promoting substances in determining the kinetics of geotropic responses. However, with normal orientation, an increased field strength has little effect on growth rate—and in fields greater than 100 G, growth is diminished [82]. Since transport of growth-promoting substances should be enhanced in stronger acceleration fields, the results of centrifugation studies with plants in normal and abnormal orientations are paradoxical.

Clinostat Studies

Since particulate (statolith) sedimentation would be a time-required process, indicated by Stokes' law, continual reorientation of a plant

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with regard to gravity prevents its completion. At an appropriate rate, such treatment eliminates the orienting influence of gravity.[3] The responses of plants to clinostat scalarization of gravity have been reviewed by Gordon and Shen-Miller [77]. Generally they support the geotropic theory: there is a reduction in auxin transport and a proportional decrease in growth rate. The threshold for a geotropic response (examined by Shen-Miller et al [192]) appears to be 0.005 G, a figure that is substantially less than the 0.012 G threshold required for otolithic stimulation in animals [223].

CHRONIC ACCELERATION

Chronic acceleration describes the exposure of organisms to an increased field for sufficient durations to permit physiologic adaptation. Consequently, animals so treated attain a new steady state, and exhibit rather uniform physiology indefinitely, i.e., "chronically." During the preceding period involving biologic stress and physiologic adaptation, their physiology will be quite labile. These periods are equivalent to those indicated by the terms "sojourners" and "residents" that are applied in high-altitude research. Sojourners have a limited and variable exposure and, physiologically, may be at any state of reaction or adaptation to the environment. Residents, however, have had very long exposure and are assumed completely physiologically adapted to the environment.

[3] In the clinostat literature, the effect is frequently called *gravity compensation* or *gravity nullification*. Ordinarily, *compensation* describes the addition of one agent that acts equally and oppositely to another, offsetting the effect, a counterbalance. Nullification implies the elimination or reduction to zero of gravity, which of course is not the case. So the application of these terms to clinostats does not seem appropriate.

Gravity is a vector quantity, possessing both direction and magnitude. In order to be effective in orienting a biologic system, gravity must act for some minimum time—the *presentation time*. The clinostat merely changes the orientation, with regard to the acceleration field, at a greater rate than the presentation time—functionally removing the orienting (directional) aspect of gravity. Effectively, the clinostat transforms gravity from a vector to a scalar quantity, and the process of transformation is perhaps preferably described as *scalarization*, rather than compensation or nullification.

Animal Centrifuges

For technical reasons, chronic acceleration necessarily involves centrifugation. Linear acceleration can be maintained for only brief periods—a linearly accelerating object developing a 2.5-G field would attain an Earth-orbital velocity in about 8 min. Laboratory centrifuges have been adapted for the prolonged treatment of avian eggs [17, 18], cultured cells [95], and microorganisms [139, 236]. Several animal centrifuges suitable for protracted operation also have been reported [40, 48, 56, 110, 125, 224].

Centrifugation involves turning as well as the development of an acceleration field. Since turning has separate biologic effects, its participation in the results must be determined. A convenient method is to carry rotated controls—animals housed around the axis of rotation of the centrifuge, that share the rotatory stimulus but not the acceleration field of the chronically accelerated animals. Such rotated controls would also serve as vibration controls. Alternatively, chronically accelerated labyrinthectomized animals, insensitive to rotatory stimuli, can be compared with intact animals to determine rotatory-induced effects [242]. The influence of rotation on rather slow processes (growth, feed intake, and the like) has been examined, and no separate effect has been detected. This apparently does not result from habituation to the turning, since chronically accelerated animals retain a labyrinthine sensitivity—even with repeated cupulometric testing [232]. A major factor in the apparent lack of rotatory stimulation in centrifuging animals may be the provision of "one degree of freedom" [55], which permits the centrifuge cage to orient in response to gravity as well as the centrifugal force. With this arrangement, only the resultant force, which is perpendicular to the cage floor, is perceived.

Generally, the operation of animal centrifuges is not continuous, but is interrupted daily for observations and tending the experimental animals. The influence of repeated intermittent centrifugation, varying from 10 min to 23.8 h/d, has been investigated [29, 37]. In many respects, there is a time-intensity summation for the intermittent treatment, so that exposure of animals to a given field 98% of the time would induce

physiologic changes equivalent to continual exposure to a field of 98% of the intensity. Consequently, daily interruptions in acceleration are not considered significant to the results for vegetative phenomena.

Acceleration Stress and Adaptation

Animals readily tolerate exposure to low-intensity acceleration fields (e.g. generally between 1–1.5 G [201]). No biologic changes are obvious from such minimal treatment—since it is accommodated by homeostatic mechanisms. With more intense fields, biologic stress is induced which is recognized as a frank sickness. In the domestic fowl, two well-defined acceleration sickness syndromes were identified [33], one of which was reversible, and the other which became progressively more severe, and was uniformly fatal. Removal from the acceleration field generally resulted in a prompt recovery (< 24 h) indicating that processes capable of rapid change were responsible. Postmortem examinations indicated no limiting organic lesions, either grossly or microscopically, in acceleration sickness. So the pathogenic changes are submicroscopic and perhaps metabolic, as indicated by their ready reversibility. Acceleration stress involves an adrenocortical response that is ameliorated with physiologic adaptation. A convenient measure of this involvement is by the transient lymphopenia (Fig. 2; [31]) which is highly correlated with the animal's degree of physical debilitation [35].

There are limits in the intensity of the acceleration field to which animals can become physiologically adapted; these are inversely related to body size. *Drosophila* larvae can survive several days' exposure to 2000–3000 G [236]. Mature *Diptera* can tolerate fields of 20 G [181]. Larger insects, such as grasshoppers, can survive in fields of 9 G [58]. Among small homoiotherms, the estimated acceleration tolerance is less, but still size-related.

Tolerance limits also are affected by posture, with bipeds surviving in more intense fields than quadrupeds. This appears to result from the visceral vasomotor apparatus—and when this is inhibited, as by reserpine treatment—bipeds become more susceptible to acceleration. The

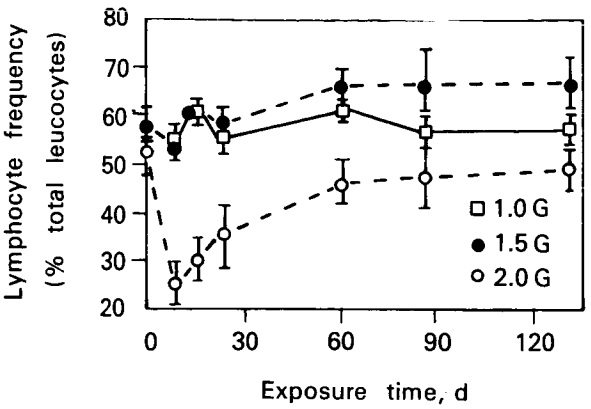

FIGURE 2.—Relative lymphocyte frequencies in adult male chickens exposed to increased acceleration fields. Fields of 2 G intensity induce a cycle of stress and adaptation, whereas a 1.5 G field is compensated homoeostatically. The points on the curves are mean values ± standard errors [31].

TABLE 2.—*Estimated Acceleration Tolerance*

Species	Approximate mass (g)	Estimated chronic acceleration tolerance
Mice	30	7 G [238]
Rats	200	5 G [145]
Chickens	1800	3 G [33]

evolutionary aspects of the development of upright posture in man, and its physiologic bases and consequences relative to gravity, have been reviewed [99, 107, 109].

Acceleration tolerance is affected by age, with young adults (shortly after skeletal maturity) the most capable of physiologic adaptation to intense acceleration fields. Sex is a factor also, with females more tolerant to acceleration as they are generally to other environmental stressors. Selye [188] explains the greater adaptability of females on an endocrine basis ". . . folliculoids tend to enhance and testiculoids repress adrenocortical function . . ." In laying hens, however, the mechanical properties of the functional (hypertrophied) oviduct are poor, and in fields greater than 2 G they are quite susceptible to oviduct prolapsis, which is terminal.

Physiologic adaptation to chronic acceleration is not necessarily permanent. Individuals who have adapted to acceleration may, at later times, develop acceleration sickness and die. This

apparent *exhaustion* is quite similar to Monge's disease [137], which is high altitude sickness in Andean natives of pre-Colombian stock. Such individuals must seek lower elevations or die since they are no longer capable of physiologic adaptation to altitude. The acceleration sickness developing in previously adapted individuals appears quite similar, if not identical to, that developing in susceptible individuals early in the treatment.

An important aspect of physiologic adaptation to chronic acceleration is the quite great heritability for its capacity; this has been reported only for fowl [204], but presumably the principle is general. After five generations of selection (on the basis of survival) for acceleration tolerance, a strain was produced that suffered only 10% as great a mortality as encountered in unselected stock with equivalent treatment. The operating factor in the development of this acceleration-tolerant strain is selection rather than treatment. The mechanism is merely an increase in the frequency of genes that determine processes contributing to physiologic adaptation, rather than mutational development of a new process. No qualitative distinctions became apparent between individuals of the acceleration-selected line and unselected stock. Acceleration-tolerant or susceptible individuals from either source behaved quite similarly, if not identically, on the centrifuge. The obvious advantage is greater survival of the acceleration-selected line, more of whom are available for experimentation after protracted centrifugation.

The *selection progress* (improvement per generation) was quite rapid in development of the acceleration-tolerant line. Because of directness of the sequence—metabolic process-enzyme-gene—geneticists associate a metabolic basis with processes that exhibit great heritability [222]. Thus, tolerance of chronic acceleration appears to have a metabolic basis and is thus similar to susceptibility to acceleration sickness.

Growth and Development

The influence of gravity on development in amphibian eggs has a long history of investigation. In 1883, Pflüger [161] observed that these ova oriented spontaneously so that the axis between animal and vegetal poles remained parallel to the field of gravity. He also noted that the first division was parallel to the field of gravity even in eggs restrained to abnormal orientation. He concluded that gravity was a determining factor in embryogenesis. Roux [173], however, found that such eggs developed normally upon clinostats—which scalarized gravity—and concluded that gravity was unimportant to embryogenesis. This led to a spirited debate (lasting almost two decades) between Roux [173, 174, 175, 176] and Schultze [184, 185, 186, 187] regarding the role of gravity in early development. Later experiments [156, 157, 158, 159] indicated that the participation of gravity in these experiments was indirect—the immediate basis being a turbulent rearrangement of yolk and cytoplasm as a result of their different densities. A similar phenomenon was observed in centrifuging avian eggs [17, 18] with the turbulence dispersing cells of the blastoderm (germinal tissue), inducing a proportional embryo death.

In 1897, Hertwig [101] reported that the development of amphibian embryos is not particularly sensitive to acceleration, proceeding normally up to fields of 4.1 G, but becoming completely suppressed at 9.2 G. This was also examined in 1908 by Konopacka [116] who concluded that acceleration fields interfered with development by limiting the distribution of cytoplasmic materials during cell division. Yolks of avian eggs also have an asymmetric density distribution which causes them to become oriented to acceleration fields greater than 0.05 G [194]. Normally, the ovoid shape of the shell and the yolk orientation result in placement of the blastoderm close to the *air cell*—the air space inside the shell formed initially by contraction of the egg content upon cooling, and later enlarged by evaporation. This arrangement is important to early development of the avian embryo because of the greater exchange rate of gases through the air-filled pores in the shell, and a shorter diffusion distance through the albumen. When this proximity is altered, e.g. by incubating eggs in an inverted (small end up) position, there is a marked reduction in hatchability of the eggs [38]. Consequently, gravity is important to the early development of chicken eggs, but indirectly, by maintaining reasonable diffusion distances.

Other ova are more tolerant of acceleration. Sea urchin eggs [96] and *Ascaris* eggs [7] continue to develop at 5000 G, although there is a substantial stratification of cytoplasmic materials. Grasshopper eggs [21] continue to develop in fields of 20 000 G—although there is decreased respiration above 1000 G. Prenatal development does not appear necessarily susceptible to acceleration fields or gravity.

Posthatching growth has been examined in *Drosophila* [138, 236, 239, 240], a viviparous fly, *Sarcophaga perigrina* [181], and grasshoppers [58]. In all cases, a repression of growth rate is proportional to field strength.

Early postnatal growth also has been examined in homoiotherms: mice [23, 146, 238]; hamsters [24]; rats [145, 146]; and chicks [207]. Ordinarily such growth has geometric kinetics [26]:

$$M = M_0\, e^{kt} \qquad (5)$$

where M is the body mass at time t; M_0 is the birth mass (i.e. M when $t=0$); and, k is the proportionality coefficient.

These kinetics apply to animals born and raised on the centrifuge [146]. However, in most studies, animals have been introduced to chronic acceleration at a later age and the initial change is a marked reduction in body mass. A major factor is a marked but transient decrease in feed intake—which may be the result of an increased secretion of FMS (fat mobilizing substance) [8, 142]. After a period of some days or weeks, feed intake increases, and growth rate resumes. Oyama and Platt [145] analyzed this resumed growth in rats in terms of early growth kinetics (Equation 5), finding a rectilinear reduction in the growth rate (k) with increasing field intensity (G):

$$k \times 100 = 2.45 - 0.086\ G \qquad (6)$$

Later growth kinetics (comprising about two-thirds of the growing period) tend to be hyperbolic, with growth decreasing geometrically towards a mature body mass [26]:

$$M = A - Be^{-kt} \qquad (7)$$

where M is the body mass at time t; A is the mature body mass—an asymptote which M approaches exponentially; B is an arbitrary (integration) constant; and $-k$ is the proportionality coefficient.

Late growth is quite responsive to change in acceleration field strength, and conforms immediately to the kinetics appropriate to the second field (Fig. 3).

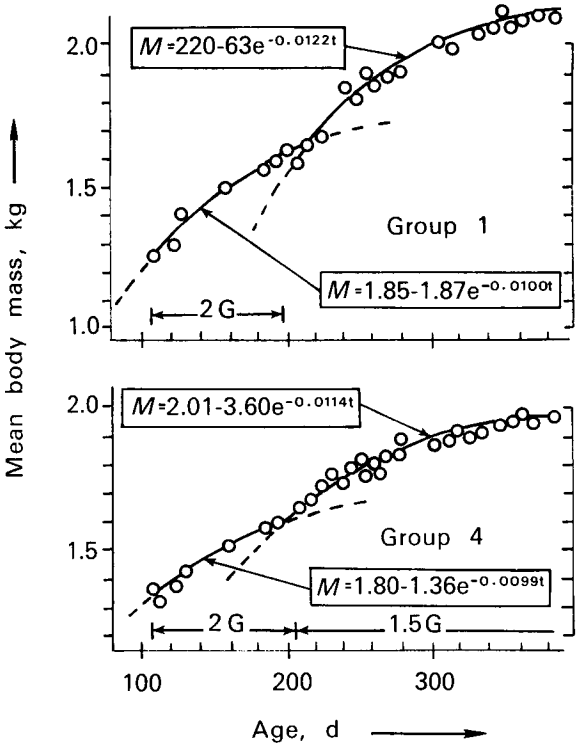

FIGURE 3.—Growth kinetics of chickens with a change in the ambient acceleration field. Mean body masses are indicated, before and after a reduction in the acceleration field—for birds which survived to the end of centrifugation (516 d age). Standard errors for Group 1 vary from 0.05 around 100 d age, to 0.12 around 350 d; and for Group 4, 0.04, and 0.08, respectively [198].

The late growth coefficient ($-k$ in Equation 7, with "t" in days) is affected by acceleration (G), but differently among the species examined:

Chickens [198]: $-k \times 100 = -0.85 - 0.24G$ (8a)

Rats [145, 146]: $-k \times 100 = -3.20 + 0.24G$ (8b)

Mature body mass (A, Equation 7) is decreased rectilinearly with increasing acceleration:

$$A = A_0 - bG \qquad (9)$$

where A is the body mass on a field of G intensity and is A_0 where G=0; and, $-b$ is the proportionality coefficient.

TABLE 3.—*Acceleration Fields and Mature Body Mass*

A_0 is the potential mature size indicated in Equation (9), and $-b$ is the decrement induced by a 1 G field. $I = [(-b/A_0) \times 100]$ is the "inhibitory effect" (% size reduction) of Earth gravity

Species	A_0	$-b$	$I = [(-b/A_0) \times 100]$	References
♀ Mice	38.5 g	−0.33	−0.9%	[146]
♂ Mice	40.5 g	−0.33	−0.8%	[146]
♀ Rats	307. g	−17.	−5.5%	[145]
♂ Polish rabbits	1.76 kg	−0.33	−18.6%	
♂ NZ rabbits	4.70 kg	−0.66	−14.0%	
♂ Coturnix quail	128. g	−6.1	−4.8%	
♂ Leghorn chicken	2.29 kg	−0.23	−11.5%	[168]
♂ Leghorn chicken	2.13 kg	−0.17	−8.0%	[202]
♂ Arbor acre chicken	5.50 kg	−0.77	−14.0%	

The degree of this acceleration-repression of mature body mass is proportional to body size (Table 3). From this summary, it appears that 1 G change in acceleration field—and perhaps Earth gravity—would have no particular effect in animals of less than 20 g body mass. Consequently, in orbital experiments to determine the influence of weightlessness upon the vegetative functions of animals, it would be advisable to utilize some large species (perhaps 1 kg or more of body mass). However, for orbital experiments with other objectives (e.g. biorhythmicity) which might be complicated by changes in nutritional/metabolic function, it would appear that small animals (less than 20 g body mass) would be more useful.

It also is important that this lesser body mass of chronically accelerated animals is regulated. Male chickens subjected to a 3-day fast while exposed to 1.5–2.0 G may lose 200 to 300 g body mass; however, upon realimentation, they recover the lost body substance as quickly as the gravity controls [198]. This indicates clearly that the acceleration-repression of body mass is not the result of any limitation in synthetic capacity, nor from restriction in feed intake. Instead, it is a physiologic phenomenon which is closely regulated. This is interpreted as indicating that the greater acceleration field merely resets the end point which is effective in the feedback regulation of mature body size, with the specific processes functioning unchanged.

Visceral Growth

The growth of organs, as a function of body size, generally conforms to exponential kinetics [26]

$$y = ax^b \tag{10}$$

where y is the size of an organ or part; x is the size of the entire organism; b is the proportionality coefficient; and, a is the positioning constant, the value of y when $x = 1$.

The calculations to fit data to this equation generally involve a linear regression of the logarithmic transforms, although this procedure is subject to some technical error [206]. Within a species, the relationships for differential growth of organs may be quite diverse, as indicated in Table 4. Since acceleration systematically affects body size, estimation of its effect on organ growth by comparison to body size (e.g. as percent body mass) is suitable only for organs that are isogonic with body mass (such as blood volume) where the proportionality constant b is characteristically unity. Application of this simplified procedure to other organs may lead to spurious conclusions. Miller and Weil [134] have provided a good discussion of the absurdities obtained when exponential relationships are treated arithmetically. However, in analyzing such data, a variety of procedures may be used to avoid these difficulties.

Oyama and Platt [145] evaluated the influence of chronic acceleration on organ growth by comparisons between experimental animals and

TABLE 4.—*Differential Growth of Organs in Several Species*

The relationships between organ mass (y, kg) and body mass (M, kg) are generally parabolic [26]: $y = aM^b$. Marked differences are evident between the differential growth constants (a, b) among the organs in a particular species, but for a given organ these constants have rather uniform values, even between species of markedly different size.

Organ	Rats	Chickens	Dogs	Horses
Blood	$0.070\ M^{0.98}$	$0.038\ M^{0.99}$	$0.072\ M^{0.95}$	—
Brain	$0.734\ M^{0.17}$	$0.0034\ M^{0.39}$	$0.044\ M^{0.25}$	$0.141\ M^{0.24}$
Heart	$0.0029\ M^{0.80}$	$0.0048\ M^{0.87}$	$0.010\ M^{0.93}$	$0.013\ M^{0.91}$
Kidney	$0.0065\ M^{0.82}$	$0.0045\ M^{0.85}$	$0.0115\ M^{0.70}$	$0.0243\ M^{0.66}$
Liver	$0.280\ M^{0.68}$	$0.0024\ M^{0.67}$	$0.064\ M^{0.71}$	$0.137\ M^{0.61}$
Lung	$0.0038\ M^{0.72}$	$0.0049\ M^{0.87}$	$0.0138\ M^{0.82}$	$0.133\ M^{0.58}$

size controls (younger animals of equivalent body mass). A similar procedure [205] involved controls fed in order to maintain the same body mass as the accelerated animals. Another way to avoid errors induced by scale effects is to compare organ sizes within the same animal, which involves selecting a *standard organ* that matures early, and is consequently less affected by environmental influences imposed later. Brain and eye have been considered appropriate organs for such comparisons [152]; organ-size data for centrifuged and irradiated rats have been presented as ratios to brain mass [41]. However, the most satisfactory procedure in rationalizing size differences would be to carry numerous controls, sacrificing them, and measuring organ sizes over an appropriate range of body sizes. With regressions, the somatic relationship ($y = ax^b$) can be established.

Studies of organ growth have been reported for hamsters [24], rats [145], and chickens [205]. In general, there is little systematic effect of chronic acceleration upon visceral size except for an enlargement of the liver, which, it appears, results from the general mobilization of fats.

Skeletal growth

The skeleton, the principal load-bearing system of terrestrial animals, might be anticipated as quite susceptible to weight-to-mass changes in chronic acceleration. The responsiveness of bone structure to mechanical forces is one of the classics of biomechanics; it was described in 1892—Wolff's law [234]—later discussed by Ham [94] and by Thompson [216]. Changes in functional demand (load) also lead to gross changes in bone structure and increasing bone density [132].

More than a century ago, Sedillot (cited by Thompson [216]) found that removal of a tibial segment (a principal load-bearing bone) from the leg of a puppy, led to a fivefold to sixfold overgrowth of the paired fibula, which attained the usual tibial diameter. The stimulating influence of moderate mechanical load on growing bone at Earth gravity has been demonstrated in sheep by Tulloh and Romberg [217] and in dogs by Denilova and Sviridov [52]. Tulloh and Romberg [217] maintained weanling lambs on two levels of nutrition (high and low), and loaded low-level lambs with *rugs* that carried lead weights, deriving three groups:

HP: optimum nutrition, maximum growth rate;
LP: restricted intake, with growth rate about half that of HP group;
LPW: similar to LP group, but mechanically loaded to 30–40% of their body mass.

By this procedure, there was little difference in body-growth rates between LP and LPW groups, but the leg-loading of the LPW group was about 80% of the HP group. Bone growth (metacarpal) was greatly altered by these treatments. Bone growth (mass) on the high plane of nutrition (HP) was greater, almost double that of the low plane (LP). However, mechanical loading also increased growth (mass)—at a rate midway between the HP and LP groups. Bone conformation also was affected, mechanical loading (LPW) and maximum growth (HP) inhibiting bone elongation—but enhancing epiphyseal width, leading to "stubby" bones.

The removal or decrease of mechanical forces on the skeleton, by immobilization or by counterweighting, leads to a reverse effect—a decrease in bone mass (disuse atrophy)—largely through greater porosity [94].

In vitro studies with embryonic bone indicate that bone and bone-forming tissues also respond to mechanical stresses. Glucksman [75] observed that the application of mechanical forces to periosteum and perichondrium led to the disappearance of collagen, and enhanced the formation of cartilage. Differentiated cartilage, however, responded to tension or compression with disintegration of haline matrix and its replacement with fibrillar tissue, enhancing ossification.

Growth of bones has been examined in several terrestrial species during chronic acceleration. Female mice at 4 G had a relative, but not absolute, increase in femur growth [241]. Bone shape also changed, the diaphyseal cross section tending to become circular in centrifuged animals. However, no change in femur mass was observed in female hamsters exposed to 4 and 5 G for 4 weeks [24], although length was both relatively (significantly) and absolutely larger than in gravity controls. No significant change in diaphyseal cross section was observed. In female rats exposed to fields of 2.5, 3.5, or 4.7 G for up to one year, femur size was increased 10 to 18% after 4.5 months—but not related systematically to field strength [145]. After 1 year, the effect was much less—a field of 3.5 G reducing femur size about 6%, and 4.7 G increasing it 8%. This indicates that the maximum acceleration effect is obtained early in the treatment, which is reasonable in view of the more rapid skeletal maturation, compared to soft tissue.

Changes in skeletal development were studied in growing chickens exposed to a field of 1.5–3 G for 75 days [205]. It appeared that the nonload-bearing humerus in growing chickens was as responsive to acceleration as the load-bearing femur—generally the bones tend to become stubbier, the width increasing more than the length. Other observations on birds skeletally mature at onset of chronic acceleration did not reveal any skeletal differences with a year or more of treatment. Acceleration is effective in altering bone morphology principally during skeletal development. No consistent or significant influence of chronic acceleration was found on the composition of rat bone (Ash, Ca, P, Mg, and N [147]). However, in chronically accelerated mice there was an increased bone density in females, but not in males [69].

The influence of 4- and 5-G fields on embryonic chick bone growth has been examined [168]. This treatment leads to more rapid dimensional growth (length and width) for the first 17 days of development, but later is markedly depressed so that at hatch the accelerated embryos have smaller bones. This effect is quite uniformly evident among several bones of the appendicular skeleton (Fig. 4). The proportionality of the degree of response to field strength indicates that the changes are acceleration-induced. In the period of enhanced bone growth, the effect is more pronounced on length than on width, so that the result is the opposite of the stubbier bones encountered with postnatal acceleration. These effects are consistent, however, because in the embryonic environment, the soft tissues tend to be bouyant and exert a tension, rather than a compression on the bones. Galileo [70] was the first to note this reversal on the loading of bones in terrestrial and aquatic animals.

Several explanations have been offered to account for the acceleration-induced skeletal changes. Wunder et al [241] and Briney and Wunder [24] have considered these effects in terms of Wolff's law—the greater load leading to a compensatory bone growth. However, in bipeds, equivalent response of the nonload-bearing humerus, as compared to the load-bearing femur (a situation not shared by quadrupeds) indicates that it is not a simple local response, but represents a *whole animal* regulation.

Muscle Growth

Muscle is specifically involved, in terrestrial organisms, in postural maintenance and the performance of mechanical work. Since these functions are largely antigravity in nature, muscular growth, like skeletal growth, may be expected to be especially responsive to changes in the ambient acceleration field. After the attainment of mature body size, muscle readily

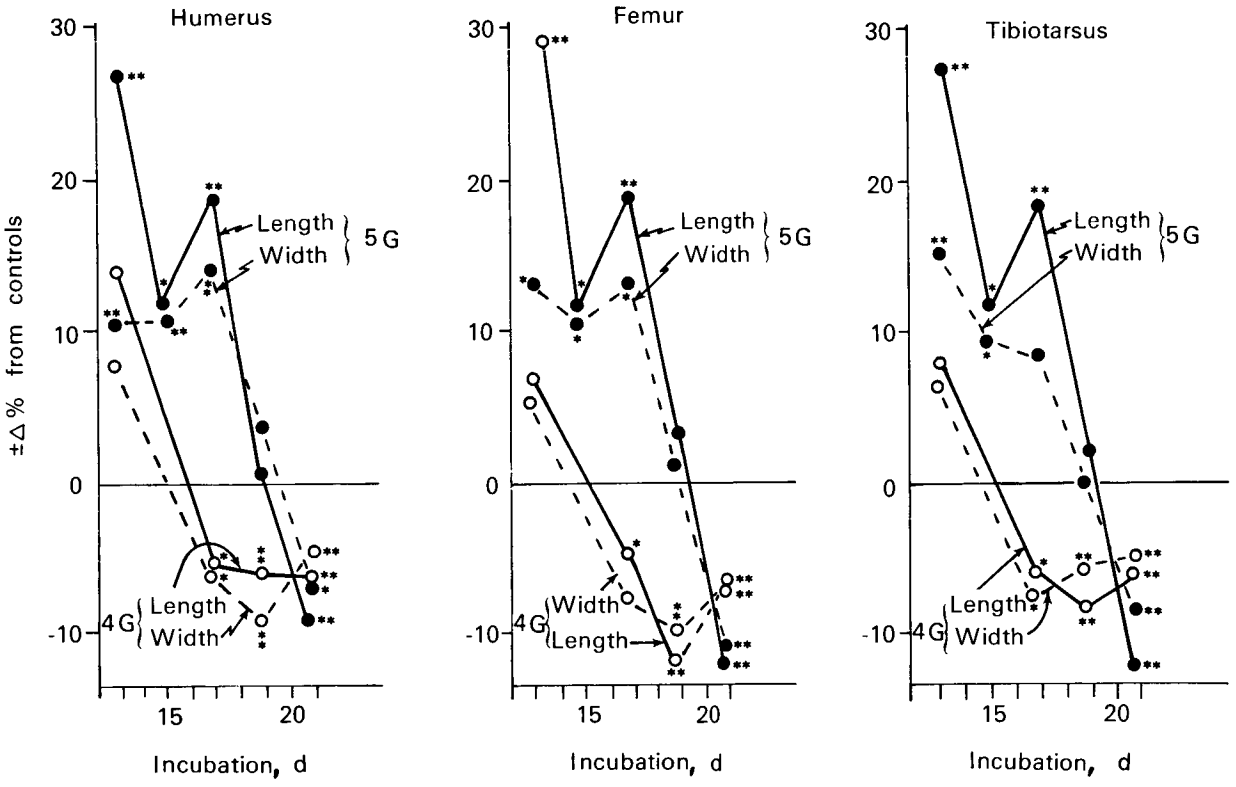

FIGURE 4.—Influence of chronic acceleration upon chick embryo bone growth. The characteristics of bones of centrifuged embryos are compared with those of static controls [168]; random probability: * < 0.05; ** < 0.01.

responds to an increased functional load with hypertrophy—a form of compensatory growth. A similar selective growth of extensor muscles in early postembryonic life has been described in chicks [200] and in young humans in relation to development of an erect posture [189, 190, 214, 218].

The first chronic acceleration experiments [128] were undertaken to determine the effect of loading on muscle function. Small animals (rats) were selected to minimize circulation effects (increased hydrostatic pressure) and to emphasize muscular response. After a year at 3 G, the centrifuged animals exhibited marked decerebrate extensor tonus.

Briney and Wunder [24] found significant increases in relative sizes of heart, diaphragm, and gastrocnemius in female hamsters exposed to fields of 4 and 5 G for 4 weeks. However, Bird, et al [19] did not report significant relative size changes of these muscles in mice exposed to fields of 4 G for a period of 8 weeks. Canonica [40] also observed a relative increase in gastrocnemius muscle mass in hamsters after 4 weeks at 4 G. Oyama and Zeitman [147] found increases in relative gastrocnemius size in rats after 3 months, and a year's exposure to fields of 3 to 4.7 G—but these were not statistically significant.

Burton et al [30] examined the effects of chronic acceleration on antagonistic skeletal muscles (Fig. 5), which eliminates scale effects. A hip flexor (sartorius) and hip extensor (adductor) were selected (because normally of comparable size), and the latter is a principal postural muscle. The muscles responded differentially, greatly increasing the extensor-flexor ratio, as a result of increased extensor size and decreased flexor size. It appears that paired muscles tend to establish a specific mass ratio that is gravity-dependent—but responsiveness is slow.

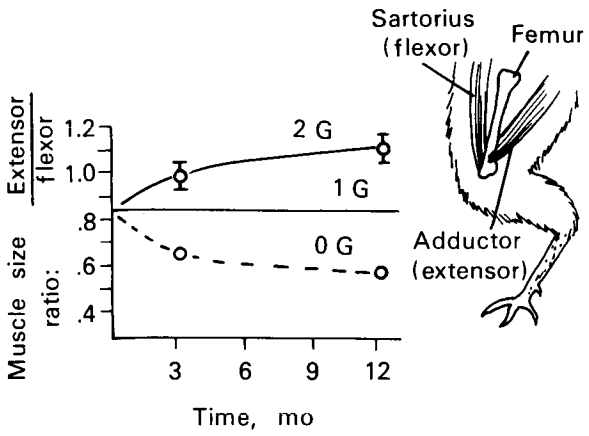

FIGURE 5.—Effect of duration of acceleration on extensor: flexor muscle ratios. Rates of change (with t in months) in the mass-ratios of adductor (E) and sartorius (F) muscles have the kinetics:

$$\overline{E}:\overline{F}_{(2G)} = 1.17 - 0.33e^{-0.16t}$$

$$\overline{E}:\overline{F}_{(0G)} = 0.62 + 0.22e^{-0.49t}$$

Data for 0G represents intercept values from observations at several fields at the exposure times indicated [30].

Canonica [40] studied the contractile properties in situ at Earth gravity, of hamsters' gastrocnemius mucles that had been exposed to a 4-G field for 4 weeks. He found transient increase in strength of tetanic contraction—+21.6% at 1 week, +36.6% at 4 weeks treatment, and equivalent to controls later. The fatigue resistance to tetanizing stimuli was greater at all times for previously centrifuged animals.

Hematology

Susceptibility of vascular columns to acceleration depends on their length and orientation with regard to the field. Hemodynamic properties of the circulation are monitored by a variety of baroreceptors and regulated by reflex mechanisms. The cellular phase of the blood is an important, though disputed, determinant of flow-resistance, which also affects the hemodynamic properties of circulation. The cellular content of blood is regulated by various humoral agents. The fluid phase of the blood, plasma, is important to the distribution of body water—largely the result of plasma protein concentrations and hemodynamic pressures, which determine the partition of extracellular water. Consequently, various hematologic changes may be anticipated with chronic exposure to an altered acceleration field.

Erythrocytes

In rats exposed to fields of 2.5, 3.5, or 4.7 G for 5 months [145] there is a reduction in numbers of erythrocytes (RBC) approximately linear to field strength (G):

$$\text{RBCs/mm}^3 \text{ blood} = (8.4 - 0.227\ G) \times 10^6 \quad (11)$$

Similar reductions in numbers of circulating red cells were reported in mature male rats exposed to 3.2 G for 4 weeks [56], and to 4.5 or 6.5 G for 11 days [221]. The latter report includes data from rats at 1 G on a restricted feed intake, equivalent to that of the 6.5-G animals. Since the hematology of these animals was the same as ad lib feed controls, inanition was eliminated as a factor. The erythropoietic marrow was also examined, which showed decreased rates of cell proliferation and cell maturation. The mitotic index (MI) of the hematopoietic marrow was closely correlated ($p < 0.01$) to the ambient acceleration field (G):

$$MI = 3.36 - 0.27\ G \quad (12)$$

Chickens, much larger than rats, respond to 3-G fields with an increase in erythrocyte frequency [36]. This polycythemia (RBC, cells per mm^3) is hyperbolically related to field strength (G):

$$RBC = 4.08\left(1 - e^{-2.09(G-0.08)}\right) \times 10^6 \quad (13)$$

This erythropoietic response in larger animals is difficult to rationalize in terms of current concepts—that the fundamental stimulus for erythropoiesis is hypoxia [78]. It is possible that interference with pulmonary circulation may limit the animal's oxygen exchange capacity, or that interference with cerebral circulation (or other locality) may lead to a focal hypoxia that triggers the erythropoietic stimulus. However, in this event, different kinetics would be anticipated. The curve described by Equation (13) is sharply inflected—the principal change occurring between 1 and 2 G and with little change between 2 and 3 G. Circulation impairment between 2 and 3 G would be at least as

great as between 1 and 2 G. Also, the increases in cell numbers by centrifugation (+15%) are quite small compared to the hypoxic response of +38% in chickens at 12 500 ft elevation [196].

It was considered possible that hydrostatic pressure in the kidney region might influence erythropoiesis [36]. Humoral agents produced in the kidney appear to be necessary stimulators of erythropoiesis [20, 182]; however, the mechanisms regulating the formation or release of erythropoietin are not completely known. The kidney, however, does respond to hemodynamic pressures with the release of other humoral agents (e.g. renin), and it is possible that a similar mechanism may apply to the release of erythropoietin. In this regard, it is significant that hypoxic situations also induce a hemodynamic response. For reasons of posture and body size, very little hydrostatic pressure would be produced by centrifugation in the renal region of rats—but a significant effect would occur in chickens, which could account for the differential polycythemic response of rats and chickens to chronic acceleration.

Korzhuyev [117] has suggested that erythropoietic function is a primary factor in gravity toleration—the quantity of hemopoietic bone marrow being closely related to the degree of terrestrial adaptation, indicated by body size and activity. He also found a lesser quantity of erythropoietic marrow in marine mammals, equivalent to about 2% of the body mass in Black Sea dolphins and in Caspian seals [118, 119].

Plasma Volume

In rats, after 1 week at 3.2 G, there is a sharp drop in absolute plasma volume (−13%), which is partially recovered (−4.5%) after 4 weeks' exposure [56]. However, because of the decreased body size this constitutes an increase in relative plasma volume (cc/100 g body mass): +5% at 1 week, and +18% at 4 weeks.

Plasma volumes have been measured also in chickens during chronic acceleration in fields of 1 to 3 G [36]. Relative plasma volume (ml PV/100 g body mass) was found to be exponentially related to acceleration field intensity (G):

$$PV = 2.94\, e^{0.169\,G} \qquad (14)$$

In the chronically accelerated animal there is a tendency for the blood volume to be displaced toward the lower portions of the body. As a consequence, atrial filling also is limited, inhibiting the Henry-Gauer reflex [72] which ordinarily blocks the secretion of antidiuretic hormone (ADH). As a result, fluid retention continues, and plasma volume increases until a new steady state is attained. With increased plasma volume, the normal activity of blood volume regulating mechanisms is reestablished.

Water immersion is a particular efficient stimulator of the Henry-Gauer reflex, causing marked diureses [79, 80], corresponding reduction in plasma volume and severe tissue dehydration [105, 160]. The recent report on the lack of ADH in the blood of marine mammals [169] is particularly interesting.

Plasma Proteins

At 3.5 and 4.7 G, rats respond with decreases in plasma protein concentration [147]. After 1 year at 4.7 G, the reduction is 10%, and statistically significant ($p < 0.01$) from gravity controls.

However, chronically accelerated chickens have elevated plasma protein levels [36], and the plasma protein concentration (PP, g %) is consistently and rectilinearly related to the acceleration intensity (G):

$$PP = 4.0 + 0.61\,G \qquad (15)$$

The increase in plasma protein concentration with chronic acceleration is an appropriate compensation to increased hydrostatic pressures in maintaining capillary water exchange—the Starling hypothesis. The arithmetic nature of Equation (15) indicates that plasma protein concentrations are regulated proportionately to increased hydrostatic pressures. No mechanism for regulation of plasma protein level is readily apparent in the literature. However, if intravascular pressures are involved, the regulatory mechanism would perhaps be located on the venous side of the circulation, since increased plasma proteins are not characteristic with hypertension.

Chronic acceleration also differentially affects the serum proteins reducing the A/G ratio −47%, $p < 0.01$, at 3 G [36]. The gamma globulin con-

tent was closely related to the individual status with respect to stress or adaptation, indicated by its correlation with relative lymphocyte frequency.

Body Composition

The chemical composition of organs or organisms can be quite informative in evaluating physiologic status or in interpreting the metabolic influence of various environmental conditions. A variety of methods, both direct and indirect, has been employed in estimating body composition [28], and recent reviews summarize the influence of various biologic and environmental conditions on body composition [27, 140]. The nature of hormonal involvements in acceleration stress affect body composition. For example, blood lipids and other metabolites are significantly increased by a short period of acceleration [89, 136].

Lipid

The most frequently observed change in body composition of chronically accelerated animals is a visually obvious decrease in depot fat, reported in mice [108, 238]; rats [41, 66, 145, 164, 211]; hamsters [23, 40]; and chickens [33, 61, 205]. Consistent with these observations is an increase in body fat in humans subjected to 9 days of bed rest [16], which greatly reduces gravity-imposed energetic requirements. Although caloric intake was reduced 29%, chronically recumbent individuals accumulated about 100 g/d fat.

Accleration-induced changes in the proximate composition of the dressed carcass of chickens, the edible portion, have been measured [195, 205]. The influence of acceleration upon carcass relative fat content (F_G, the fat content ratio: experimental/control) is exponentially related to acceleration field strength (G) (Fig. 6):

$$F_G = 2.24\, e^{-0.79G} [r = -0.992;\ p < 0.01] \quad (16)$$

Similar reduction of fat content, (as percent body mass) in the chicken, less feathers, has been reported [62, 63] as arithmetically related to field intensity (G):

$$F_{\%} = 31.5 - 8.5\ G\ [r = -0.83;\ p < 0.05] \quad (17)$$

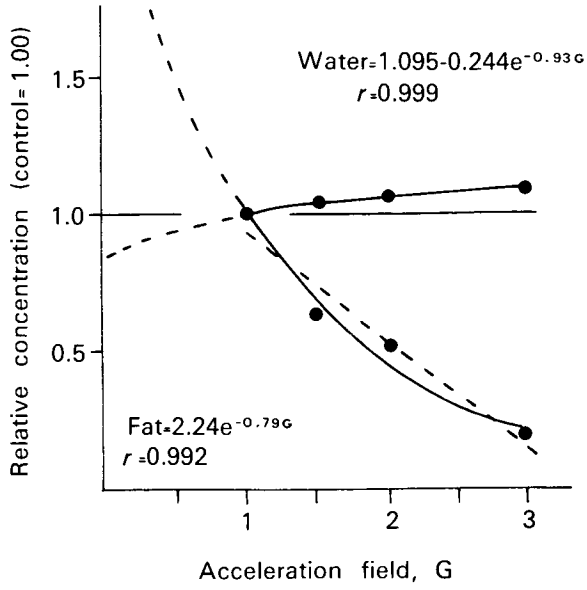

FIGURE 6.—Influence of chronic acceleration on the relative fat and water contents of the dressed chicken carcass. The dotted line in the lower-right quadrant indicates the fat content treated as having zero-order kinetics.

Most observations on acceleration-induced changes in body composition reveal virtual absence of discrete fat deposits in animals exposed to intense fields. The prominent abdominal fat pad which is amenable to quantitative dissection is particularly affected. Generally, the size of the abdominal fat pad (AFP; g) is closely related to the body fat content (F_c; % body mass)—for example, in chickens:

$$AFP = 0.036\ F_c^{2.1} \quad (18)$$

The relationship between AFP and body fat is not greatly affected by chronic acceleration—so the effect is proportional upon all body fat. However, the relative size of this depot decreases exponentially with increasing field strength (G) in chickens:

$$AFP_{(\%\ carcass)} = 11.5\ e^{-1.73\ G} \quad (19a)$$

A similar acceleration-induced reduction of the abdominal fat pad occurs in rats [147]:

$$AFP_{(\%\ body)} = 10.2\ e^{-0.924\ G} \quad (19b)$$

The greater exponential coefficient for loss of depot fat in chickens (about double that for rats) is consistent with the size relationship generally

encountered for acceleration effects—larger animals being more severely affected. However, at the limit of chronic acceleration tolerance (3 G for chickens, 5 G for rats) the loss of body fat is approximately equal for the two species.

This selective effect of acceleration in the reduction of depot fat is similar to findings in a human syndrome, lipodystrophy [43, 191]. Patients with this disorder uniformly show: an enhanced musculature, enlarged liver, and virtual absence of depot fat—changes generally characteristic of chronically accelerated animals. The etiology of lipodystrophy involves an oversecretion of a hormone, FMS. Release of FMS in small mammals also accompanies fasting, low carbohydrate intake, or low temperature exposure [8, 9, 10, 11, 44, 45, 212, 226]. This substance appears to be a polypeptide (molecular weight, about 5000) which is produced in the pituitary of mammals, and in the hypothalamus of birds [142]. When administered to normal animals it increases circulating free fatty acids (FFA) and plasma glucose, and decreases circulating triglycerides and nonsaponifiable lipids. One FMS fraction depresses feed intake, and another enhances circulating FFA.

Evans found FMS activity in aqueous extracts of excreta from chronically accelerated chickens, but not in the excreta of gravity-controls [195]. On the basis of chemical behavior (extraction and inactivation) the acceleration-induced FMS activity has a basis similar to that found in lipodystrophic or fasting humans. Thus, the mechanism of fat loss accompanying chronic acceleration may result from stimulus to the pituitary or hypothalamic region of the brain, resulting in overproduction of FMS. Since reduction in body fat is proportional to field strength, it appears that increments of acceleration produce approximately equal increments of FMS production. And since any mechanical effect on this region of the brain would be proportional to field strength, it appears that the acceleration-related stimulus for FMS production may be mechanical and direct.

Water

Based on the classical Starling hypothesis for regulation of tissue water (balance between hydrostatic and osmotic pressures), increases in tissue hydration might be anticipated as a result of increases in the ambient acceleration field. There are few measurements of water content of tissues and organisms exposed to chronic acceleration. Generally, an increased hydration is indicated—however, the observations are not entirely consistent.

In chickens, carcass relative water content (water content ratio: experimental/control) increases hyperbolically with increasing acceleration field strength (G) Fig. 6:

$$W_G = 1.095 - 0.244\, e^{-0.98G} \qquad (20)$$

Inverse changes in hydration and fat content are anticipated even at normal gravity because of the lesser water content of adipose tissue [115, 151]. Comparisons of carcass fat and water content among individuals receiving similar treatments indicated a rectilinear relationship between these components:

$$\text{water} = a - b\ (\text{fat})$$

where: a represents the hydration (% water) of lean tissue—the Pace constant; and, $a\,(100 - b)$ is the approximate water content of the adipose component. For various acceleration fields, such analyses indicate that tissues of chronically accelerated individuals have greater hydration which is unrelated to changes in fat content. Increase in tissue hydration is consistent with the greater relative plasma volumes.

Metabolism

Chronic acceleration increases the weight-to-mass ratio so that an exposed animal of 1-kg body mass may weigh 2 or 3 kg. Since weight, rather than mass, is the determinant of mechanical work, chronically accelerated animals expend more energy for equivalent tonus, locomotion, and the like, which increases their metabolic requirements.

Feed Intake Maintenance Requirement

The immediate response to acceleration is a marked decrease in feed intake and growth. Later increased ad libitum feed intake rates have been reported for rats [42, 144, 145, 210, 211]

and for chickens [202, 205]. Growth rates of pair-fed mice at normal gravity were greater than for those in increased acceleration fields, up to 5 G—indicating an increased metabolism in the latter [237].

Maintenance feed requirements[4] at several acceleration field intensities have been reported for chickens [202]. These indicate that metabolic requirements increase with field strength to a maximum between 2–2.5 G, then decline toward limit of acceleration tolerance (3 G) (Fig. 7). In the extreme fields, metabolic requirements may become less through decreased mobility, lesser mechanical work, and lower body fat, since fat synthesis requires about 20% more energy than synthesis of lean body substance [26].

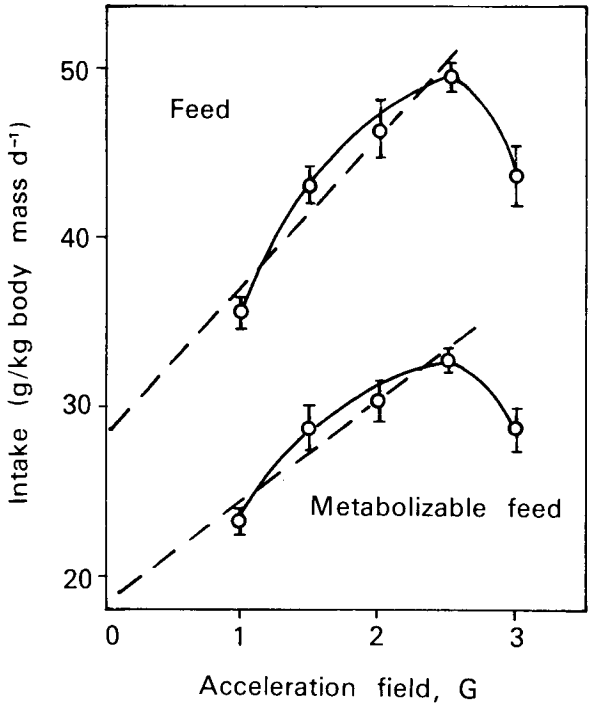

FIGURE 7.—Influence of the ambient acceleration field upon the maintenance requirements of chickens [202].

[4] The feed energy required to maintain a constant body mass (with a fixed composition) approximates the energy metabolism [26, 112]. The procedure can be refined by measuring metabolizable feed intake (feed less excreta), which is simplified in birds due to their single phase excreta.

Up to 2.5 G, the maintenance requirements may be related rectilinearly to field strength:

$$F_G = F_M + kG \qquad (21a)$$

where: F_G is the maintenance feed intake rate (g feed/kg body mass · day^{-1}) in an acceleration field of G strength; F_M is the feed intake rate which is mass determined (where G=0); and, k is the proportionality constant. Regressions of the maintenance feed requirements [Equation 21a] on field strengths indicate:

$$\text{maintenance feed: } F_G = 26.6 + 9.6\,G \qquad (21b)$$

$$\text{maintenance metabolizable feed: } F_G = 17.3 + 6.5\,G \qquad (21c)$$

Thus, about 27% of the maintenance requirement of chickens is determined by Earth gravity: 16 kcal/kg mass · G^{-1} · day^{-1}. As a physically determined requirement, this should apply generally, irrespective of body size, and in animals of 75-kg mass, gravity would require 1200 kcal/d. Since the metabolic rates of 75-kg animals are 2500–3000 kcal/d, the gravity-determined component constitutes 40–50% of the metabolic energy. This is in good agreement with the energetic requirement for normal ambulation of young men at normal gravity [16]. Kleiber [113], utilizing preliminarily reported results with chickens [199], estimated the influence of gravity on the energetic requirements of larger animals on the basis of isokinetic behavior. He concluded that 40% of the energy metabolism of 70-kg animals would be gravity-determined under natural conditions.

Intermediate Metabolism

Changes in the metabolic pattern also have been reported at the intermediate level. Feller et al [65, 66] studied the metabolism of labeled acetate by liver slices, in vitro, of rats previously exposed for a year to acceleration fields up to 4.7 G. Liver lipid concentrations decreased (−18%) at 4.7 G, but not at 3.6 G, and the incorporation of acetate into nonsaponifiable lipid increased (Fig. 8). This differential incorporation of the tracer also is proportional to changes in concentrations of saponifiable and nonsaponi-

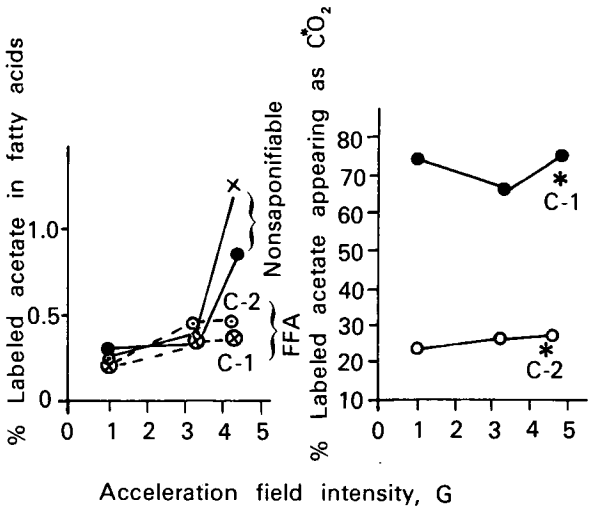

FIGURE 8.—Fatty acid content and metabolism of acetate by liver tissue from rats previously accelerated for approximately 1 year. Acetate labeled in the C–1 or C–2 position was used in separate experiments to determine their utilization or distribution [65, 66].

fiable lipids in tissue. Acceleration differentially affected the fate of the two acetate-carbon atoms. At normal gravity, C–1 and C–2 were equally incorporated into fat, but at 4.7 G, 42% more of the C–2 followed this pathway. Acceleration had less effect on the appearance of acetate-carbon atoms in free fatty acids, or in CO_2.

The activities of enzymes involved in lipid and carbohydrate metabolism were examined by Evans et al [63, 64] in muscle and liver tissue—with changes encountered only in the liver. Glucose-6-phosphatase, a key enzyme of gluconeogenesis, is approximately doubled in activity (+90%) at low fields (1.75 G) but this decreased as field strength increased (to +42% at 2.5 G). Malic and citrate cleavage enzymes, important to lipid synthesis, behaved similarly to glucose-6-phosphatase, increasing at low field strength, and then decreasing, until at 3 G their activity was less than in the gravity controls.

Changes in enzyme activities observed under various acceleration fields apparently correspond with changes observed in energy metabolism. It remains to be determined if the changes are specific to acceleration, or regulated by the animal's metabolic status.

Alpha-glycerol phosphate dehydrogenase undergoes changes unlike the other enzymes examined. In birds, that tolerate 3 G asymptomatically, its activity increases greatly—to more the control level—but returns to normal values after a cycle of stress and adaptation. Since the fatty acid-forming enzymes (malic and citrate cleavage) have low activity in asymptomatic birds, it was considered unlikely that its function was toward triglyceride synthesis. It may serve to recover glycerol for gluconeogenesis, enhancing energy utilization.

Evans concluded that during chronic acceleration, fat becomes mobilized, and less of it is synthesized; this becomes most pronounced in individuals who become physiologically stressed. With physiologic adaptation, changes appear to permit the bird to return to a normal lipid utilization and synthesis, but with an increased carbohydrate utilization. However, even after adaptation, the body fat pool is not restored.

The influence of previous exposure to fields of 2.76 or 4.15 G, for as much as 3 months, on the carbohydrate metabolism of the isolated rat diaphragm at Earth gravity has been reported [50]. Diaphragm tissue incubated with uniformly labeled glucose indicated that chronic acceleration increased glucose uptake by 31%, and glucose oxidation by 101%. No influence of the treatment on glycogen deposition was observed. Chronic acceleration also increased the sensitivity of diaphragm to insulin, its influence on glucose uptake in the centrifuged animals being double that of their controls.

Thermoregulation

Rats exhibited a depression of deep body temperature on exposure to acceleration, and proportional in degree to field strength [148, 150]. The duration of this hypothermia (3–4 days) closely paralleled the acceleration-induced anorexia. With a repeated exposure, lesser hypothermia was elicited—and acceleration-adapted animals maintained their body temperature. With larger homoiotherms (rabbits and dogs), no influence of chronic acceleration on deep body temperature was found [149]. Whether this represents a species difference in thermoregulatory

function, or whether it should be considered merely a similitude-related differential cooling is not clear at this time.

Systemic Responses

The most fruitful investigations of chronic acceleration effects will, perhaps, be those dealing with functional properties of organ systems. Since these are subject to regulating mechanisms which generally have rapid response times, examining them will require observations on operating centrifuges. However, remoteness factors become quite important to such observations, and advanced instrumentation procedures, similar to those required for physiologic research in orbiting satellites, must be employed. For these reasons, most of the currently active chronic acceleration research programs have been oriented toward less rapidly responsive phenomena which can be studied adequately with observations before and after treatment. Such procedures are quite suitable to evaluations of pathology, anatomic change, growth, and feed intake. Physiologic measurements have been made on chronically accelerated animals after their return to normal gravity, which, however, are difficult to rationalize in terms of the centrifuging animal.

Circulation

Duling [56, 57] examined aspects of circulatory function at Earth-gravity, in anaesthetized rats previously subjected to a 3.2-G field for 4 weeks. Femoral venous pressure decreased by about 10% and femoral arterial pressure increased by 15%—only the latter was statistically significant. Pressure-flow relationships in the posterior portions of the rats were measured by cannulating the abdominal aorta below the renal artery, which indicated a 20% decrease in basal resistance (result of vascular geometry and blood viscosity), but the myogenic resistance was doubled.

Measurements of resistance at various blood pressures (obtained by administering acetylcholine and epinephrine) indicated a twofold or threefold increase in the functional properties of baroreflexes. Hemodynamic responses to brief hypoxia indicated repression of chemoreflexes.

Renal Function

Bengele [13, 14] and Bengele and Wunder [15] observed that in rats, a transient (3-day) decrease in water intake followed by increased water intake and excretion, were quantitatively similar at 1.7 and 3 G. In the period of polyuria, plasma ADH decreased, but no change was observed in daily solute excretion.

A more complex influence of chronic acceleration on urinary excretion in mice was reported by Wunder et al [243]. No effect was noted during 3–24 days at 2 G—but at 4 G there was marked polyuria.

RESPONSE OF ANIMALS TO A DECREASED ACCELERATION FIELD

Observations of previously centrifuged animals upon return to Earth gravity have been a rather routine part of chronic acceleration research. From these, it appears that responses to a reduction in the ambient acceleration field are not mirror images of those accompanying a quantitatively equivalent increase in the field. There have been, to our knowledge, neither research data nor reports of a condition of physiologic stress accompanying a decreased acceleration. On the contrary, animals suffering from chronic acceleration sickness, which may have been slowly induced, recover rapidly at Earth gravity [33]. Also, there appear to be no residual physiologic effects in animals at normal gravity from previous adaptation to chronic acceleration. For example, rats adapted to 3 G had the same radiosensitivity as controls, when simultaneously returned to Earth gravity and subjected to whole-body x-irradiation [42] although there was strong interaction between simultaneous irradiation and centrifugation.

Postural Changes

After chronic centrifugation, animals exhibit modification of posture upon return to normal gravity. Deaccelerated chickens generally as-

sume a forward tilting of the body into a duck-like stance [203]. In some animals, deacceleration was accompanied by transient disorientation, which included ataxia, opisthotonus, and somersaulting [33, 203]. The incidence of these post-centrifugation responses varied considerably among the strains observed, and breeding experiments indicated that it was highly heritable. That this abnormal behavior is induced by the reduction of the acceleration field rather than by tangential deceleration, is indicated by its ready reversal upon recentrifugation. Otherwise, such postural difficulties persist for perhaps 12 hours at Earth gravity. Lack of labyrinthine involvement in these debilities is indicated by the evident absence of nystagmus, nor could one be elicited by rotatory stimulation [232]. The characteristically inverted head position in birds with postural difficulties suggested that an abnormal otolithic response, with a sensation of inversion, might be responsible A similar phenomenon, an *inversion illusion*, has been reported in humans during brief weightlessness with a similar explanation offered [86].

Work Capacity

The functional significance of mass ratios of paired antagonistic muscles was examined to determine if muscle groups, adjusted to a particular acceleration field, could perform well or efficiently when transferred to a different field. These studies were prompted by the considerable difficulty encountered with the performance of extravehicular activity in the USA Gemini series. It was considered possible that the influence of the ambient field on extensor-flexor muscle mass ratio [30] might be a factor in the problem.

Animals adapted to 1.75 or 2.5 G were exercised to exhaustion at weekly intervals, on a treadmill at normal gravity [34], being returned to the centrifuge after each exercise test. Learning or adjustments appear necessary to exercise in a reduced-gravity environment. However, with some experience, animals from hyperdynamic environments greatly outperformed Earth gravity controls (Fig. 9). It appears that extensor (anti-gravity) muscle size, which generally is proportional to the acceleration field of residence, is the ultimate determinant of exercise capacity.

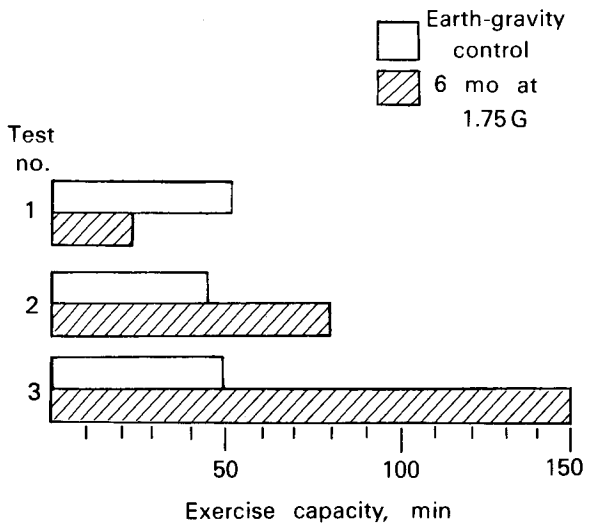

FIGURE 9.—Exercise capacity of chronically accelerated animals at Earth gravity. Running time to exhaustion on a level treadmill operating at 130 ft/min (39 m/min) is shown. Tests were taken at weekly intervals, with accelerated animals remaining on the centrifuge between tests [34].

Growth

The growth repression that usually accompanies chronic acceleration is rapidly reversed with reduction in the acceleration field strength, and growth deficits tend to be restored. Superficially, this resembles retention of the growth potential during periods of malnutrition, first recognized as the *equifinality of growth* by Osborne and Mendel in 1915 [143]. It appears that the greater acceleration field "resets" the standard towards which growth proceeds—and with its removal, the normal growth standard is restored, without apparent effect from the previous treatment. It is indicated in Figure 3 that the growth kinetics appropriate to the ambient field are assumed within a week after change in acceleration intensity. Even after a stable mature size has been reached in chronically accelerated animals, appropriate growth is resumed when returned to Earth gravity. For chickens (animals of 2-kg body mass) about 60 days are required for the change in body size when the acceleration field is lowered from 2 to 1 G (about 30 days, from 1.5 to 1 G). In all likelihood, scale effects apply to readjustments in body mass and composition (perhaps to physio-

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logic phenomena generally) following reduction in the ambient acceleration field.

Information necessary to evaluate scale effects upon such postacceleration changes is not currently available. However, size relationships have been found in the rates at which excesses or deficits of body constituents are resolved (e.g. following fasting or forced feeding) among rats, rabbits, dogs, and man [1]. Generally, the rate at which an imbalance is restored is proportional to the natural variability of that constituent—and the latter is generally inversely related to body size. Consequently, large animals tend to be "less plastic" than small ones and generally undergo physiologic change at a slower rate. Thus, equivalent processes that require 2 months for completion in a 2-kg animal (e.g. chicken) may require 6 months or longer in a 75-kg animal (e.g. man).

Physiologic Deadaptation

Deacceleration studies indicate that decreasing the ambient acceleration field changes both anatomic and physiologic properties of animals—but only to a level appropriate to the new field intensity. The transition will be slow for some factors and include changes comparable to those involved in physiologic adaptation to a hyperdynamic environment. However, processes subject to precise physiologic regulation will change rapidly and the gravitational influences can be studied during brief periods of unloading. Matthews [129, 130] was able to utilize a free-fall of 4 ft (120 cm) (producing 500 ms weightlessness) to determine the effect of gravity-loading on stretch reflexes. He found that the ankle-jerk reflex disappeared after 140 ms weightlessness. Longer periods of weightlessness have been obtained with parabolic flight in jet aircraft [39, 97], during which the effect of removing gravity-load has been examined in:

hemodynamic parameters [171]
maximal torque that can be exerted [229]
sensitivity of otolithic stimulation [245]
cupulometric function [106]
precision in motor skills [46]
circulation time [225]
respiratory dynamics [68]
orientation of blind goldfish [5].

The general reversibility of environmentally induced changes [22] indicates that as the animal becomes adjusted to the new field, it will lose the previously acquired physiologic adaptation to the more intense field. This concept is of particular importance to bioastronautics, since it implies that, with protracted weightlessness, astronauts will lose tolerance of Earth gravity, and must be reconditioned before return to Earth. Evidence of such gravity deadaptation was found in the Cosmos 110 dogs [122, 154].

Observations on the retention of acceleration-adaptation in centrifuged animals returned to Earth gravity [29, 197] indicate that, although hyperdynamic adaptation is lost, it is lost very slowly. For example, if chickens adapted to a 2-G field are returned to Earth gravity, then abruptly reexposed periodically to 2G for 24 hours, some index of retained adaptation can be estimated from their lymphocytic response (in comparison with similarly treated, but previously unadapted controls). On this basis, it was estimated that previously 2-G adapted chickens retained about 70% of their physiologic adaptation after 6 months of Earth gravity.

Pharmacologic maintenance of the gravity-adapted state during space flight has been considered. The nature of anticipated changes with physiologic deadaptation and the potential usefulness of counteracting drugs have been reviewed recently [155].

PHYSIOLOGY OF HYPER- AND HYPODYNAMIC FIELDS

The biologic consequences of weight can be appreciated in several ways, from which the response to alteration of gravity can be predicted. Such scientific speculations have a long history. Galileo in 1638 [70] and Spencer in 1863 [209] considered the influence of buoyant immersion of aquatic animals in terms of weightlessness, and its effects on form and function. In 1827, Sir Charles Bell also dwelt on the influence of gravity on man. Sir William Crookes, a spiritualist as well as physicist, considered the influence of gravity and its alterations on human form and

function [49]. Thompson [216] compared the variations in form and function among animals of different sizes, noting systematic scale relationships which were interpreted in terms of gravity. Thompson also speculated on the biologic responses to a change in gravity.

More recently the effect of gravity has been approached experimentally—loading and unloading individuals and treating the induced changes as resulting from an alteration of gravity [102, 126, 217, 235]. Similar effects (symmetrical loading) can be obtained with the technique of chronic acceleration which simulates a change in gravity. Resolution of results of chronic acceleration experiments, involving several fields, can lead to a mathematical prediction of the effects of weightlessness (e.g. Equations 11–17). Yuganov [244] proposed that changes encountered during brief weightlessness (provided by the parabolic maneuver) can be interpreted to predict the effects of chronic weightlessness. Although the nature of the environmental change is the same, the difference in duration would require assumptions on the nature of the response with continued exposure. This is in contrast with chronic acceleration, where the duration of treatment may be similar to that for chronic weightlessness (permitting physiologic adaptation), but the nature of the environmental change is different.

Any indirect estimate of the biologic effects of weightlessness must be considered speculative—and applied with caution. Although we may prefer to heed Crookes' admonishment [49] ". . . the prudent man shrinks from dogmatizing upon the egg until he has seen the chicken"—the importance of avoiding surprises in bioastronautics may not permit that luxury.

Continuity of Acceleration Phenomena

In the analysis of multifield chronic acceleration data, the hypothesis is inherent that, there is a continuous (or linear in the mathematical sense) biologic effect of acceleration fields from weightlessness (where $G=0$) to the tolerance limit. This concept is, of course, uncertain and will be resolved only by comparable (very long-term) orbital experimentation. However, several factors at present tend to support the likelihood of the principle of continuity of biological effects of acceleration.

(1) Continuity of the physical phenomenon, and the dependent nature of biologic responses:

All investigations indicate that the independent variable in acceleration experiments is the acceleration field, and the biological changes induced are purely dependent upon it. Earth gravity is not a critical point (its value is not zero), and there is continuity of the physical phenomenon from zero to the limit of biologic tolerance. Consequently, it is most logical to assume that there is similar continuity of the dependent biologic phenomena over the tolerable range of acceleration fields.

(2) Continuity of biologic phenomena in short-term weightlessness:

There is relationship between the effects of short- and long-term exposure to chronic acceleration, the former inducing biologic stress to which the latter provides physiologic adaptation. The only experiments performed so far involving both weightlessness and hyperdynamic environments (to 3 G) were carried out by Roman et al [171], using the parabolic maneuver in high-performance aircraft and in greater fields with human centrifuges. He examined hemodynamic parameters in humans during a 45-second test period and found no discontinuity between weightless and supragravity conditions. This continuity of short-term effects tends to support the likelihood of similar continuity between chronic acceleration and weightlessness effects.

(3) General nature of biologic regulation, which tends to be continuous:

If there is no continuity of biologic response between subgravity and supragravity conditions, this would be contrary to the general pattern of biologic regulatory mechanism. It would mean that there are different and discontinuous regulatory mechanisms for fields greater and lesser

than Earth gravity, which would be biologically unique.

Qualifications must be made to the concept of continuity of acceleration effects. Some processes may become saturated by very low fields (< 1 G), so that they would appear to be acceleration-insensitive in hyperdynamic environments. Other mechanisms (dependent on asymmetric density distribution) may require a minimum field—a threshold—for orientation, and in lesser fields their acceleration responses would be completely unpredictable. For example, a field of 0.05 G is required to orient hens' egg yolks [194], about the same order as the threshold stimulus for the gravity-sensing otolith. The geotropic response of plants requires a field of 0.001 G [77]. Consequently, in lesser fields, these systems would not appear to be acceleration-responsive.

Centrifuges and Satellites

Biologic responses to chronic acceleration are of obvious importance (and economy) in identifying phenomena which should be examined in orbital experiments—i.e. those factors that are acceleration-responsive. How far centrifuge results can predict the results of satellite experiments depends on the continuity of acceleration phenomena, which has already been discussed. If the biologies of the two gravity states are unrelated, then chronic acceleration studies will be of only limited usefulness with regard to the biologic effects of weightlessness. However, if there is general continuity of biologic effects in fields above and below Earth gravity, then chronic acceleration will provide a background of information, and perhaps principles, for interpretation of satellite experiments. But, in either case, both kinds of information will be necessary to develop a rational science. If all the information of gravitational biology is limited to two points—weightlessness and Earth gravity—no generalization will be possible. Satellite experiments are equally important; without them, gravitational biology will have no foundation. There is also a practical link between centrifuges and satellites. Since both techniques deal with artificial weight conditions, and impose remoteness factors on the experimenter, chronic acceleration research could provide an excellent intermediate training function for space investigators.

The complemental nature of studies on chronic exposure to weightlessness or to increased acceleration fields, with regard to understanding the biologic effect of Earth gravity, has been discussed also by Gazenko and Gurjian [73].

Human Chronic Acceleration

Although chronic acceleration studies with small homoiotherms can contribute to the development of gravitational biology, there will be limitations in their application to man. Satisfactory progress contributing to gravitational medicine will require chronic acceleration studies with humans. For such experimentation, it would be desirable to develop fields of approximately 1.5–2G, while limiting the rotation rates to 20°–30°/s, which can be tolerated even on a planar basis [87]. To meet these requirements, a centrifuge would have a diameter of 300–600 ft and could be provided by self-propelled cars operating on a circular tract. By switching cars on and off the track, and transferring subjects between them, hyperdynamic exposure for a year would be quite feasible.

A particularly important aspect of such research would be determining the adaptational capacity rate of humans to chronic acceleration. This could be estimated from a series of experiments in which subjects become exposed to a particular accelerative force, each at a different rate (Fig. 10). As long as the accelerative force is low,

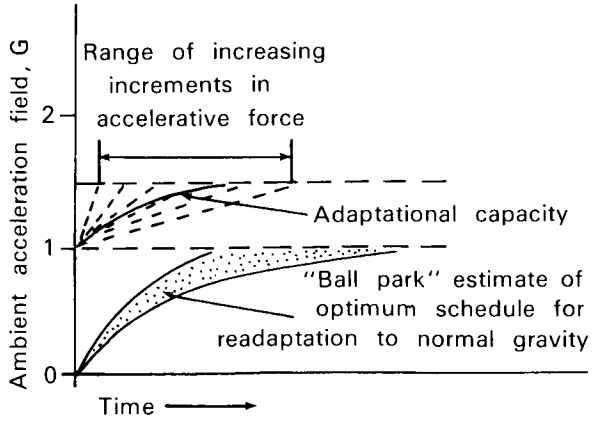

FIGURE 10.—Adaptational capacity to accelerative force.

there probably would be little difference in response between the acceleration schedules. However, with greater forces, untoward changes would probably be evident with the greater rates of change. Consequently, a curve could be drawn for human adaptational capacity, as exemplified in Figure 10. This description may be oversimplified, since the onset of symptoms may be substantially later than the exposure which produced them. However, with interpretation, the data would permit a statement of adaptational capacity to hyperdynamic environments which otherwise would be lacking. Such information would become applied in readapting gravity-deconditioned astronauts to Earth gravity, necessarily involving an orbiting centrifuge, and exposing the astronauts to an increasing acceleration field. Adaptational capacity rate between 1 and 1.5 G should bear some relationship to that between weightlessness and normal gravity. The latter should not occur in lesser time, nor at a lesser rate, which would allow a "ball-park" estimate of the optimum schedule for readapting deconditioned astronauts to Earth gravity. The observations and symptoms where the adaptational capacity had been exceeded would be of particular importance; these would furnish valuable check points for monitoring astronauts during any readaptation process.

The rate at which individuals lose physiologic adaptation to an acceleration field would be important also. When related to Earth gravity this rate would permit an estimate of the maximum duration of weightless exposure compatible with a direct return to Earth. This could be studied with human subjects that had become adapted to an environment of 1.5 or 2.0 G, perhaps after exposure for many months or a year. Upon return to Earth gravity, their loss of tolerance to the hyperdynamic field could be estimated serially. In all likelihood, such loss of physiologic adaptation would bear some relationship to loss of tolerance to Earth gravity during protracted weightlessness—it should not occur in a shorter time, nor at a lesser rate (Fig. 11). This information would permit a "ball-park" estimate of the rate of deadaptation to normal gravity, during weightlessness. From determination of the degree of loss of adaptation that would make the subjects toxic upon return to the higher field, it should also be possible to make an estimate of the duration of space probes compatible with a direct Earth return.

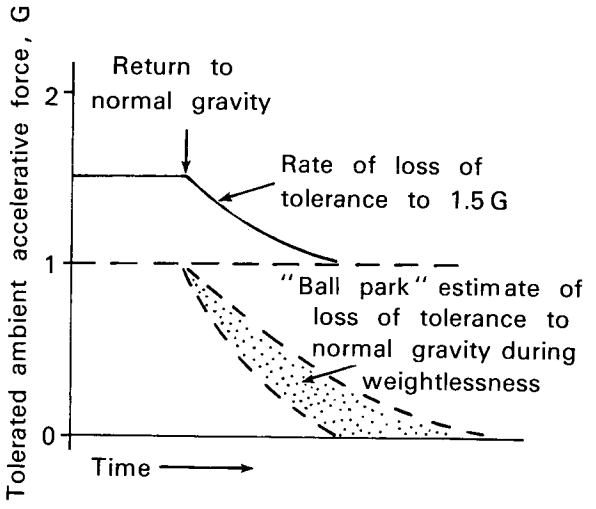

FIGURE 11.—Loss of tolerance to accelerative force.

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Chapter 5

PROLONGED LINEAR AND RADIAL ACCELERATIONS[1]

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Aviation and space medicine specialists have centered their attention for many years on the influence of accelerations on the human body. A vast number of investigations has been made into the nature and degree of manifested reactions by body systems to various acceleration parameters, establishment of tolerance thresholds, determination of basic mechanisms of disorders caused by acceleration, and determination of means and methods to increase body stability to acceleration. A great deal of accumulated material on these problems is found in textbooks [8, 94, 189] and summarized in monographs [73, 94, 175, 195]. The effects of acceleration sometimes reach the limits of physiologic tolerance, and may cause not only significant disruptions in man's work capacity, but also certain pathologic changes.

Increased interest in recent years in the effects of acceleration on the human body resulted from the need to solve pressing problems related to spacecraft flight support. These flights are characterized by specific peculiarities, which are analyzed in this chapter.

The medical problems of acceleration, related to the introduction of new aviation equipment, could form the subject of a special analysis. These problems are touched upon in this chapter only as necessary. Limited space prevents as complete a discussion as might be desirable on all problems concerning the effects of accelerations on the body. Problems relating to long-term (weeks, months, or years) effects of increased gravitation, causing not only physiologic but also pronounced morphologic changes in the body, are not discussed. Results of these important investigations were touched upon in the preceding chapter, *Principles of Gravitational Biology* (Volume II, Part 2, Chapter 4). Finally, data on the effects of alternating accelerations, or combined effects with other flight factors, are not studied. A great deal of material is presented briefly in the form of individual statements without analysis or corresponding references to the literature. However, within the space allotted, as much information as possible is presented, of possible use for specialists involved in space-flight support.

CLASSIFICATION AND TERMINOLOGY

Acceleration occurs when the velocity or direction of motion of a body changes. The magnitude of acceleration, measured in m/s^2 or as a multiple of the ratio of the velocity of a body

[1] Translation of, Vliyaniye na Organizm Dlitel'nykh Lineynykh i Radial'nykh Uskoreniy, Volume 2, Part 2, Chapter 2 of, *Osnovy Kosmicheskiy Biologii i Meditsiny (Foundations of Space Biology and Medicine)*. Moscow, Academy of Sciences USSR, 1973.

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falling freely in airless space (9.81 m/s²), is determined to a great extent by the force acting upon the body and its mass. This is represented by the letter g (the first letter in the Latin word *gravitas*—i.e., gravity). An acceleration of 35 m/s², for example, can be rounded off and expressed as 3.5 g.

This chapter is concerned only with linear and radial accelerations. Linear accelerations occur when the rate of motion of a body is increased or decreased without a change in its direction. Radial or centripetal accelerations occur when the direction of motion of a body is changed—one of the clearest examples is the acceleration noted in a centrifuge or when an aircraft executes a turn during a dive. Linear and radial accelerations, depending on the time of application, are arbitrarily divided into impact acceleration (up to tenths of a second) and long-term acceleration, which is further classified [72, 73, 178].

The direction of the inertial force is always opposite to the direction of acceleration. The term G-load (inertial force) is frequently used in medicine and biology. The G-loads have no dimensions and are expressed in relative units, which essentially show the number of times the weight of a body has been increased by a given acceleration in comparison to ordinary terrestrial gravitation, i.e., it is the ratio of its dynamic weight to its static weight at rest or during linear motion [95].

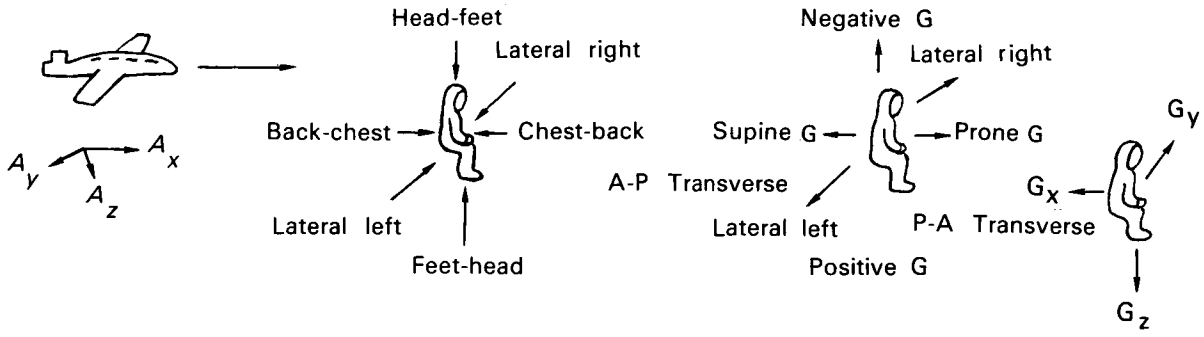
A distinction is made between longitudinal and transverse G-loads, depending on the direction of action of G-loads in relation to the vertical axis of the body. If the G-load vector is directed from head to feet, it is called a positive G-load; if it is from feet to head, it is called a negative G-load. Furthermore, a distinction is made between transverse (back-chest and chest-back) and lateral (side-side) G-loads. The direction of the G-load vector is significant for determining the nature of the body's response reactions. Unfortunately, there is still no unified terminology and classification of accelerations, which frequently leads to erroneous interpretations of identical facts and causes difficulties in understanding certain material in the literature.

The table of terminological equivalents accepted by representatives of a number of countries with membership in the Aerospace Committee on Problems of Acceleration [162] is worthy of attention. Although it does not cover all aspects of this important problem, the table can still be useful in the practical activity of researchers.

Only the relevant portion of a more complete table is presented in Table 1, data which relate directly to the problems under discussion here. Following recommendations of the Aerospace Committee, all terminology is divided into two main groups: columns A and B. Column A, which presents two varieties of terminology on accelerations most frequently used in astronautics, is based on the direction of acceleration of a mass. In column B, the terms are based on the inertia of organs, tissues, and fluids in an undamaged body. In the system of coordinates used, the z-axis passes through the body's center of gravity parallel to the spine. The action of an inertial force along the z-axis in the direction downward, from head to pelvis, is represented by the symbol $+G_z$ (physiologically positive acceleration or positive G-load); the action of these forces in the opposite direction is represented by $-G_z$ (physiologically negative acceleration or negative G-load); the symbol $+G_x$ indicates that the force of gravity is directed transversely from chest to back (chest-back G-load), while the symbol $-G_x$ represents a G-load in the back-chest direction. Lateral transverse accelerations are represented as $+G_y$ (right to left) and $-G_y$ (left to right).

The center of gravity of a flight vehicle and the direction of axes in the system of coordinates do not coincide with the center of gravity and the direction of the corresponding axes of the pilot's body, relative to which vectors of inertial effects on the body are calculated. Thus, in evaluating technical acceleration graphs of a flight vehicle from the standpoint of man's ability to tolerate acceleration, the peculiarities of the physiologic terminology as concerns inertial effects on the body must be kept in mind. However, in this table a number of important factors related to the effects of acceleration on the body are not considered (time of action, rise gradient, and so forth), which require further refinement of terminology and classification [178].

TABLE 1.—*Acceleration Terminology* [77]



Linear motion	A Direction of acceleration		B Inertial resultant g-load on body		
	Aviation symbols (System I)	Descriptive terms of acceleration (System II)	Physiological terms (System III)[1]	Physiological symbols (System IV)	Local descriptive terminology
Forward	$+a_x$	Back-chest acceleration	Transverse A-P, G	$+G_x$	Eyeballs in
Backward	$-a_x$	Chest-back acceleration	Transverse P-A, G	$-G_x$	Eyeballs out
Upward	$-a_z$	Foot-head acceleration	Pronel, back-chest Positive G	$+G_z$	Eyeballs down
Downward	$+a_z$	Head-foot acceleration	Negative G	$-G_z$	Eyeballs up
Right	$+a_y$	Acceleration to right	Lateral left G	$+G_y$	Eyeballs left
Left	$-a_y$	Acceleration to left	Lateral right G	$-G_y$	Eyeballs right

[1]In system III, the letter G is used as a unit to express the inertial resultant acceleration of the entire body, a multiple of the value of acceleration resulting from the force of gravity $g_0 = 980.665$ cm/s². A-P = anterior-posterior; P-A = posterior-anterior.

OVERALL EFFECTS ON THE BODY

Man's reaction to acceleration is determined by a number of important factors, such as the amount of acceleration, time of its action, rise rate and direction of the G-load vector in relationship to the trunk, as well as the body's initial functional state, which depends on many external and internal medium conditions [72, 228].

Body changes may result from barely detectable functional shifts to extremely severe states, and be accompanied by acute disorders in the respiratory, cardiovascular, nervous, and other systems. These disruptions may result not only in loss of consciousness, but sometimes also in pronounced morphologic changes. An individual subjected to accelerations experiences a feeling of heaviness in the entire body, pains in chest or stomach, initial difficulty in moving (and subsequent complete inability to move), particularly the extremities. The soft tissues and a number of internal organs are displaced in the direction of the inertial force's application. Depending on the density (specific gravity) of the internal organs, their location, and elasticity of their connections with the surrounding tissues, the nature of the disruptions may differ. Since the most mobile tissues in the body are blood and tissue fluids, hemodynamic disruptions have a leading position in the genesis of physiologic shifts under G-loads.

Displacement of internal organs and their deformation are also significant, which result not only in functional changes in these organs, but also in unusual afferentation to the central nervous system (CNS), frequently disrupting its regulating and corrective functions.

Under great accelerations, disorders of vision are observed. The nature and degree of manifestation of these disorders are determined not only by the amount of acceleration, but also by the direction of its application in relationship to the body's main vessels. With further increases in the magnitude or time of applying acceleration, loss of consciousness, convulsions, and death may occur; but if acceleration is interrupted, there is gradual normalization of all functions.

MAN'S RESISTANCE TO ACCELERATIONS AND EVALUATION OF CRITERIA

Body resistance to acceleration effects depends on the nature of the tolerance criterion selected. Therefore, the boundaries of survivability and limits of physiologic resistance are distinguished and evaluated on the basis of initial signs of disruptions in activity of various functional systems. Boundaries of survivability are determined only in animal experiments. As applicable to man, subjective and objective symptoms are used to estimate limits of resistance. The upper threshold of subjective resistance is the limit of the subject's ability to withstand the physical and emotional discomfort associated with acceleration effects. Vision disruption, pain, fatigue, and severe difficulty in breathing are most frequently encountered. Investigation of the limit of resistance is quite difficult, however, when the criterion of tolerance used must be subjective sensations.

To determine tolerance to $+G_z$ acceleratory stress, estimations should be based on grayout or blackout, reliable precursors of fainting. Headache and lacrimation are equivalent precursors for $-G_z$ stress. The redout visual disorders observed by certain pilots during flights also serve as precursors with $-G_z$ stress. However, neither Soviet nor US researchers have succeeded in observing redout symptoms during many years of centrifuge studies.

The limiting symptoms for transverse accelerations may be visual disorders, dyspnea, discomfort, and pain, which practically cannot be given a standard evaluation. Even a significant criterion such as grayout is variable both for different people and for the same person on different days. Multiple petechial hemorrhages resulting from increased permeability of various etiologic vessels may interrupt acceleration studies. Cessation of acceleration application would be required by such important indicators as disorders of cardiac activity and respiration, disruption of the subject's ability to control, and presyncopal signs.

Critical states of the body (loss of consciousness, collapse, sudden changes in cardiac activity, hemorrhaging in organs, pulmonary atelectasis, and so forth) may arise in certain situations during acceleration and, in this sense, characterize man's survival ability. Objective criteria of man's acceleration tolerance most frequently used are the indicators related to visual disorders: nonreaction to light signals [39, 90, 91, 125, 126, 211], disrupted oculomotor mobility preceding blackout, loss of ability to follow a given object [28], and others.

Criteria of acceleration tolerance should be differentiated according to basic (or leading), supplementary, and prognostic. For example, under $+G_z$ stress, the basic or leading resistance tolerance criteria are visual disorders in the form of grayout or blackout, and nonreaction to light signals, which indicate almost total loss of work capacity and consciousness. A reduction in systolic pressure in the vessels of the concha auriculae to 40–50 mm Hg and disappearance or sharp reduction in oscillations of the ear pulse precede loss of vision in a great majority. Thus, these indicators can be included among prognostic criteria [210].

For $+G_x$ acceleratory stress, when the gravitoinertial component along the head-pelvis axis is equal to 40% or more of the total stress, visual disorders are also basic criteria for evaluation of resistance. If the $+G_z$ inertial component is slight (10–20%), the basic and most reliable criterion of the tolerance limit of $+G_x$ stress is cardiac activity disorder in the form of relative bradycardia, combined with other

cardiac-rhythm disorders, loss of vision, and dyspnea [113].

The criteria or symptom complex of signs, on the basis of which resistance to accelerations is estimated, may be formally identical for a given position, but at the same time may have different significance for the body. For example, under $+G_x$ stress with the test subject in a position where the angle of inclination of his seat back is 25° and 10° from the horizontal, manifest visual disorders may appear, up to complete loss of vision. In the first case, visual disorders precede loss of consciousness, while in the second case, the subject can tolerate 50% more $+G_x$ stress, while continuing to perform certain operations with information input through the auditory channel [16]. Consequently, the same symptom visual disorders, in the first case indicates danger to life, while in the second case, only work capacity is threatened. Therefore, in studies of man's resistance to transverse acceleration effects, evaluating the vital functions state, rather than work capacity, is important. This criterion can be basic and dominant in some cases, while in others it may be supplementary or prognostic, and vice versa.

Man's resistance to acceleration effects is determined by a number of physical and physiological factors. Among the significant physical factors are the magnitude of acceleration, duration of application, direction of the acceleration's resultant vector in relation to the longitudinal axis of the body, acceleration rise gradient, mode of application ("plateau" or "peak"), use of protective systems and body restraints, position of the body and extremities, and environmental conditions (temperature, ambient pressure, and others). The most important physiologic factor is individual resistance, which is dependent on health, age, training, psychologic preparation, and motivation.

Permissible values and acceleration application time are determined on the basis of physiologic tolerability and the influence of acceleration on man's ability to control his flight vehicle. The physiologic limits of endurance and limits of work capacity may be interrelated, but not necessarily equal. As a rule, work capacity deteriorates before resistance limits are reached. Extensive studies have allowed precise determination of man's resistance limits to acceleration effects in various directions, depending on magnitude of acceleration and duration of application (Fig. 1).

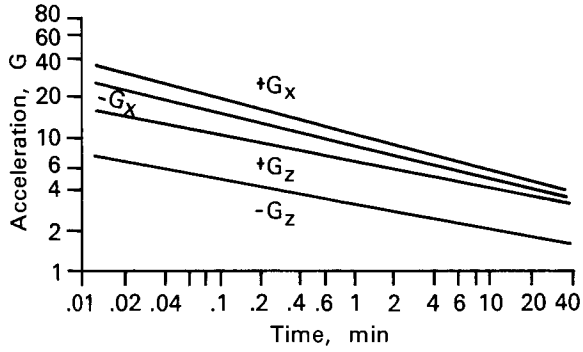


FIGURE 1.—Man's resistance to the effects of acceleration in various directions [45]. Mean data on $+G_z$ (head to pelvis), $-G_z$ (pelvis to head), $+G_x$ (chest to back), $-G_x$ (back to chest) (direction of inertial forces).

Man is least resistant to the effects of $-G_z$ stress where inertial forces are directed along the axis from pelvis to head, and most resistant to $+G_x$ stress where inertial forces are directed from chest to back.

The physiologic tolerance of accelerations is limited primarily by body reactions: redistribution of blood, mechanical hindrance of respiration, and displacement and deformation of internal organs. The more closely the direction of acceleration components coincides with the direction of the body's main blood vessels passing along the spine, the stronger the disruptions of general hemodynamics. Thus, when accelerations are applied along the body's longitudinal axis, the redistribution of blood leads rather quickly to signs of disruption in cerebral circulation, which limits the duration of application.

General hemodynamic changes are significantly less with transverse accelerations. This factor essentially determines the position of the astronaut when subjected to accelerations during spacecraft launch and descent. It has been established from studies that the $+G_x$ direction, when inertial forces act from chest to back, must be considered optimal for acceleration tolerance.

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Endurance Limits

The endurance limit is low for a strictly transverse acceleration direction. Chest pains and dyspnea have prevented reaching high values of acceleration. When $+G_x$ stress is applied while resting flat on the back, the limit of resistance, determined by pain and dyspnea, is at the level of $+8$ G_x [13]. Elevation of the head and thorax yields a positive effect—resistance increases, and pain and dyspnea decrease. However, placing the head and trunk at an angle results in application of the inertial force in the direction of the longitudinal axis of the body and the appearance of related symptoms of loss of vision and consciousness. Consequently, an optimal body position had to be found to provide an intelligent compromise between man's physical capabilities and technically efficient acceleration modes.

In the search for the optimal position for space flight, there was diligent study of man's resistance, in various body positions, to the effects of transverse accelerations [13, 31]. Resistance to $+G_x$ stress proved best with the seat back inclined at an angle of 65°–70° to the acceleration vector (or 20°–25° to the horizontal), and with knees at eye level and legs held in a supporting chair [31]. With the extremities straight, resistance was limited by severe knee pain. However, in this position the primary disruptions in the body's physiologic systems, which limit man's resistance to acceleration, were quite similar to disorders accompanying longitudinal accelerations ($+G_z$ stress), due to the high value of the longitudinal component along the $+G_z$ axis. The limits of endurance in this case generally were not over $+12$ G_x.

In order to decrease the influence of the component along the head-pelvis axis, seats were tested with slight back elevation angles of 2°–12° [17, 48, 55, 117]. Under these conditions, it was possible to reach high values of acceleration with rapid rise rates. Accelerations of 20.0 g could be reached while spinning in a seat with flat supporting surfaces, and 25.0 g accelerations in a form-fitting seat (acceleration rise rate 1.0–1.2 g/s) [48, 50]. Consequently, positioning the body more horizontally in the seat increased resistance limits. This position is now considered optimal by most researchers [17, 91, 92, 117, 228].

When considering the effects of G-loads in the $+G_x$ direction, it is convenient to use the concept of the effective physiologic angle (Fig. 2). This angle is the sum of three angles: the seat angle (SA), angle between the vertical line through the spacecraft and the resulting forces of the accelerated apparatus (ϵ), and aorta-retina angle (ARA). The sum of the first two angles forms the angle of the seat back inclination to the acceleration vector. The retina-aorta angle is determined by lateral roentgenography of the thorax and is enclosed between the lines from the center of the heart to the retina and the longitudinal anatomical axis of the body ($+G_z$ axis).

This angle averages 15°, fluctuating from 13° to 18°. The aorta-retina angle is highly significant, since it changes the direction and magnitude of the acceleration component resulting in visual disorders (the so-called effective retina-aorta component of $+G_z$). For this reason, the value of

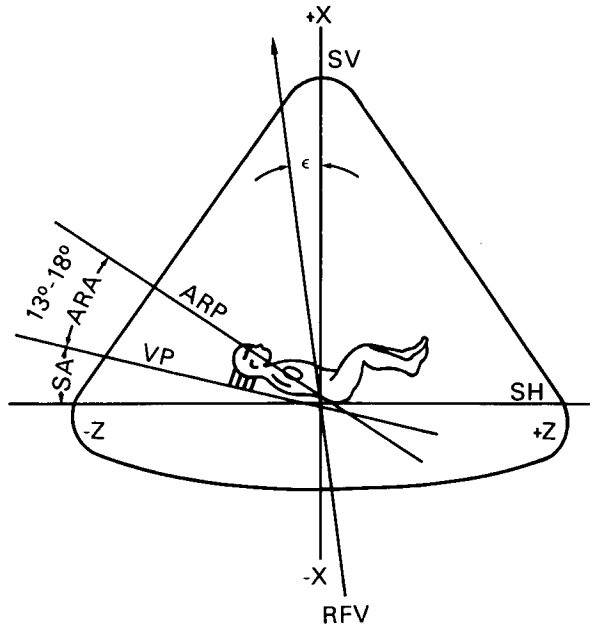

FIGURE 2.—Position of astronaut and terminology suggested by NASA Manned Spaceflight Center [5]. ARA: aortal-retinal-angle; ARP: aortal-retinal plane; ϵ: angle between resulting acceleration vector and vertical line of spacecraft; RFV: resultant vector of acceleration; SH: ship's horizontal; SV: ship's vertical; VP: plane of spinal column; SA: seat back angle; EPA: effective physiologic angle.

the effective physiologic angle allows predicting the resistance limit determined by visual disorders as a function of the inclination angle of the seat back (Fig. 3). The effective retina-aorta component of $+G_z$ varies little during change in a seat back angle of 60°–90° from horizontal. With a 0° angle for the seat back, visual disorders may arise because of an effective $+G_z$ retina-aorta component. Thus, data indicate that the best compromise for tolerance of $+G_x$ stress is a horizontal seat position with angle $SA+\epsilon=8°–12°$, with the astronaut's hips bent so that knees are elevated to eye level. In the Apollo spacecraft, the angle of the seat back ($SA=2°$ and $\epsilon=6.5°$) is 8.5°.

Man's resistance to $+G_x$ stress as a function of acceleration value and position is presented in Figure 4. Tolerance to peak accelerations, as applicable to actual flight conditions, has been fully studied. The profiles of maximum tolerable $+G_x$ stresses of various modes are presented in Figures 5 and 6. The dashed line in Figure 5 encloses the set of possible acceleration profiles related to space flight, all of which, according to experimental studies, are tolerable [28, 46, 50, 51, 55, 133]. The acceleration rise rate is highly significant. With regard to the effects of longitudinal $+G_z$ stresses, it has been established that body tolerance for accelerations generally decreases with increasing rise rate [25]. A nomogram, based on experimental material of Stoll [206], shows the expected time grayout appears for a given $+G_z$ accelerator stress plateau and rise rate (Fig. 7).

Under transverse $+G_x$ stresses, on the other hand, slow rise rates decrease the value and time of body resistance [31]. Opposite effects of acceleration rise rate in these two directions ($+G_z$ and $+G_x$) can probably be explained by the significance of changes in general hemodynamics due to head-pelvis inertial force. In the first case ($+G_z$), it is primary, and in the latter case ($+G_x$), it is secondary. A slow increase in accelerations allows the body to develop and utilize its compensatory reactions more completely. Thus, when $+G_z$ stresses are applied, this slow increase helps to prevent or postpone critical situations, primarily related to disruption of cerebral circulation. When $+G_x$ stresses are applied, the threat that such situations might develop is significantly less, while the increase in rise rate of accelerations allows a gain in value and application time without danger of loss of consciousness.

The effectiveness of using different $+G_x$ rise rates with the optimal position in a contoured seat is shown in Figure 8: an increase in the rise rate of accelerations allows attainment of higher values—at 0.1 g/s, +12.0 G_x; at 0.2 g/s, +14.0 G_x; and at 1.0 g/s, +26 G_x. The total duration of

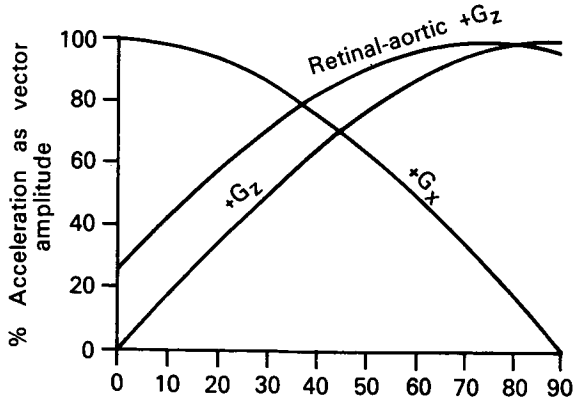

FIGURE 3.—Values of $+G_z$ and $+G_x$ acceleration vectors in percent for any value of seat back angle [91]. Abscissa shows angle of seat back in degrees from horizontal.

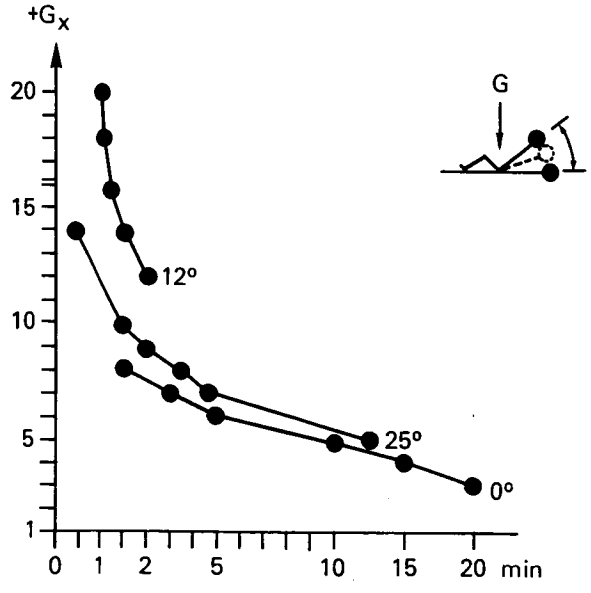

FIGURE 4.—Tolerance time of man to transverse $+G_x$ acceleration as a function of seat back angle [17, 113, 117].

application of transverse accelerations is not less important than their value. The maximum tolerable value of accelerations increase with increasing acceleration rise rate from 0.1 to 1.0. g/s because of reduction in application time of high-value accelerations and absolute decrease in application time of accelerations in general.

Man's resistance to the effects of $-G_x$ stresses, where inertial forces are directed from back to chest, has been studied less; published data on this problem are limited [31, 49, 50, 73]. The most difficult problem when accelerations are applied in this direction is providing body restraint and optimal conditions for interaction with support. The body position and restraint system determine primarily man's resistance to these accelerations (Fig. 9).

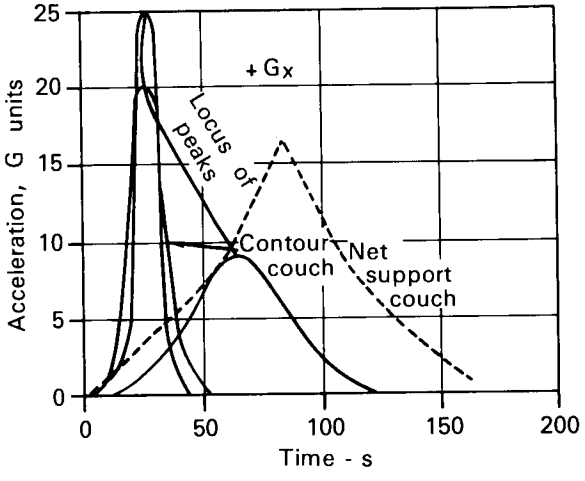

FIGURE 5.—Maximum tolerable acceleration profiles [46].

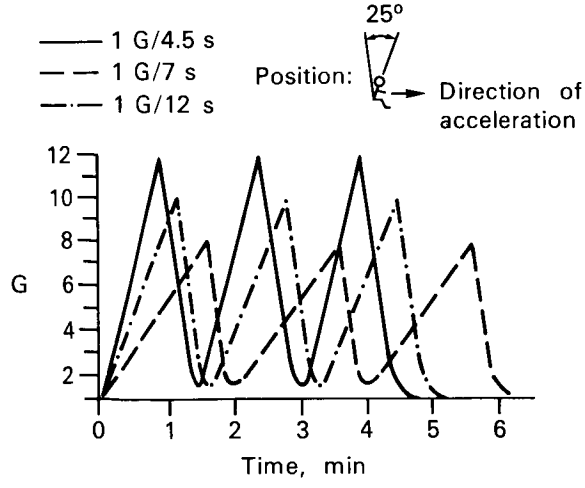

FIGURE 6.—Profiles of accelerations tolerable by man for a three-stage rocket, sufficient to achieve orbital velocity [168].

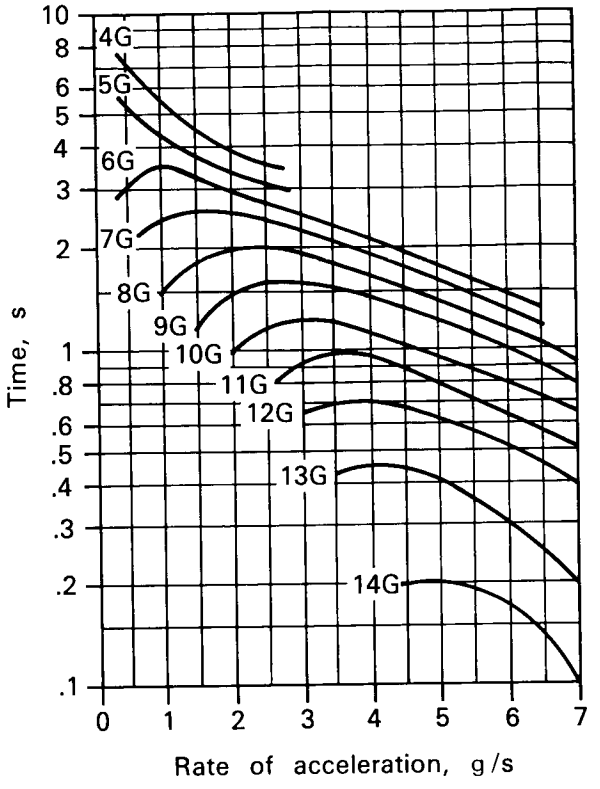

FIGURE 7.—Nomogram of dependence between acceleration rise rate and time of grayout appearance [206].

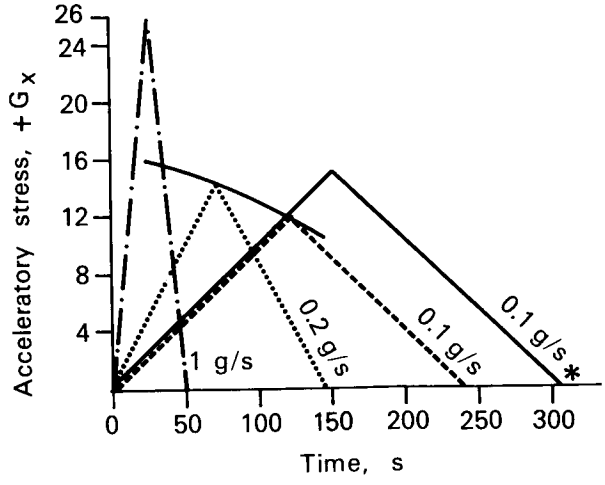

FIGURE 8.—Man's resistance to effects of transverse $+G_x$ peak-type acceleratory stress with various rise rates [17, 113]. Transverse line corresponds to values of acceleration at which visual disorder arises; *—after centrifuge training.

Acceleration Tolerances

Respiratory difficulties encountered with $-G_x$ acceleratory stresses are less than with $+G_x$. However, since pressure is directed forward onto the restraint system, pain and discomfort arise with accelerations producing -8 G_x. The position of the head has bearing on $-G_x$ stresses; if the head is tilted forward, the hydrostatic effect influences brain activity, causing tolerance to $-G_x$ to be still less. Another significant peculiarity of these accelerations is vision disruption (fogging, loss of visual acuity), probably resulting from abundant lacrimation. Extensive data in the literature indicate distinct individual variations in the level of man's resistance to acceleration.

The individual resistance to acceleration is determined by the initial functional state, age, health, degree and nature of the muscular system's development, and state of training for G-loads. When $+G_z$ stresses are applied, the lowest resistance but highest lability of physiologic reactions is observed in test subjects 20–24 years of age (5.6 ± 0.3 G_z), while tolerance to $+G_z$ stress increases 0.5 G by age 30–39 (6.1 ± 0.1 G_z), then decreases again (by 0.4 G) between 40 and 49 years of age (5.7 ± 0.1 G_z). Acceleration tolerance becomes more stable with increasing age, with a smaller range of variation. Apparently, lower acceleration resistance at 20–24 years of age compared with other age groups can be explained by the well-known lability of the nervous-humoral mechanisms of regulation observed at this age. On the other hand, reduction in acceleration resistance at 40–49 years of age (in Suvorov's opinion) results to some extent from the body's aging and accompanying variations inherent at this age. For the effects of $+G_x$ acceleratory stress, dependence on age of toleration to $+G_x$ has not been clarified.

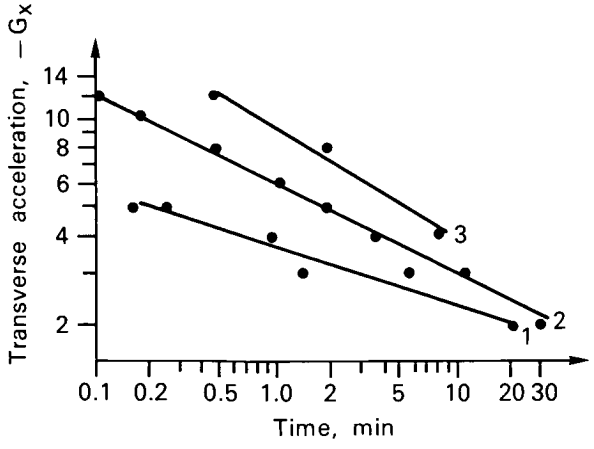

FIGURE 9.—Man's resistance to transverse $-G_x$ acceleratory stresses [73]. 1: "curled" position with fixation of body and head; 2: "curled" position in suit with body, head, and extremities restrained; 3: "supine" position on net support.

The effectiveness of development of the body's adaptive reactions to acceleration effects is also determined by the degree of training. Acceleration tolerance for $+G_z$ averages 0.5 G higher for pilots than for other professionals. Variations in the general state of health are also significant. The least tolerance to $+G_z$ stress was detected where there were indications of vascular-autonomic dystonia [210, 212]. The primary reason for such reduced tolerance is disruption of vascular tonus regulation. In contrast, with first-stage hypertension, there is higher resistance to $+G_z$ stress shown than with vascular-autonomic instability. This results from the corresponding increase in vascular tonus, which provides favorable conditions for maintaining arterial pressure at a high level.

The muscular system is relevant to development of the body's compensatory reactions [11, 189]. When muscular tension is utilized, the threshold of blackout in pilots under longitudinal acceleration is increased by 1.0–2.0 G_z [237]. Tension of abdominal muscles, lower extremities, and shoulder girdle increases body resistance to accelerations by an average of 1.5–1.8 G_z. This effect is apparently related not only to the more favorable type of circulating blood redistribution during the acceleration period, but also reflects influences on cardiovascular system activity [34, 35, 165, 186, 189, 210].

Composition of the ambient gas medium can change man's acceleration resistance. Hypoxia and an elevated oxygen content influence man's endurance under longitudinal acceleration [39, 72, 73, 85, 144]. Degrees of hypoxia which can be compensated by the organism (up to 3–4 km altitude) have no significant influence on the tolerance level for accelerations [63, 73]. Greater

hypoxia reduces acceleration resistance [25, 123]. A deterioration in tolerance to $+G_x$ stress was shown in a study of the summary effects of hypoxia and acceleration [18].

CO_2 content in the gas medium, in the breathing air inhaled, is also significant. An increase in tolerance to longitudinal accelerations of 0.5 G_z was shown when air breathed contained 4–6% CO_2 [147, 177]. Increased resistance to $+G_x$ stress was noted following 10 min respiration of air with 3% CO_2, while prolonged 4-h breathing of this mixture caused deterioration in acceleration tolerance [223]. The sparse data available on the gas medium's influence on man's tolerance to acceleration requires further development, which is important, since gas medium composition in sealed spacecraft cabins might change during emergencies.

The temperature factor has only been studied relative to effects of $+G_z$ stress. Exposure of man to high ambient temperatures (+55°–70° C) reduced tolerance to $+G_z$ by an average of 0.5–1.0 G [40, 87, 146]. Simultaneous exposure to higher temperatures (40° C) and acceleratory stress (+3 G_z for 1 min) led to deterioration in human psychomotor activity [173], which was evaluated on the basis of reaction time to light signals, and numbers of errors. The severe water loss and blood redistribution resulting from surface vessel expansion obviously may influence the circulating blood volume and thus deteriorate the state of the body's cardiovascular system [171].

A special study was made of the influence of dehydration (up to 3.6% body weight loss) on man's tolerance to $+G_z$ stress [87]. It was established that hypohydration led to a 15–20% reduction in the tolerance time to $+G_z$. However, no correlation was noted between the percent loss of body weight, total blood volume, plasma volume, and time of acceleration tolerance.

The influence of reduced temperature on human acceleration tolerance has been studied [146]. With blood temperature of 25° C in the area of the foot, a slight, unreliable increase in resistance to acceleration of +0.4 G_z was noted in comparison to comfortable conditions.

Under spaceflight conditions, accelerations may act on the human body in combination with other flight factors – changes in gas environment, temperature, radiation, and so forth. The influence of these factors may be brief or constant throughout the flight, the end result depending on time and force relationships.

Weightlessness occupies a special position among spaceflight factors. The astronauts' tolerance for accelerations, upon spacecraft reentry into the Earth's atmosphere following long periods of weightlessness, is particularly important in planning long space flights. On the one hand, body asthenia is possible by the end of the flight, while on the other hand, accelerations which might be great are generated upon reentry into the atmosphere's dense layers (Fig. 10). The success of the entire expedition depends on the astronaut's tolerance for accelerations during the flight's final stage.

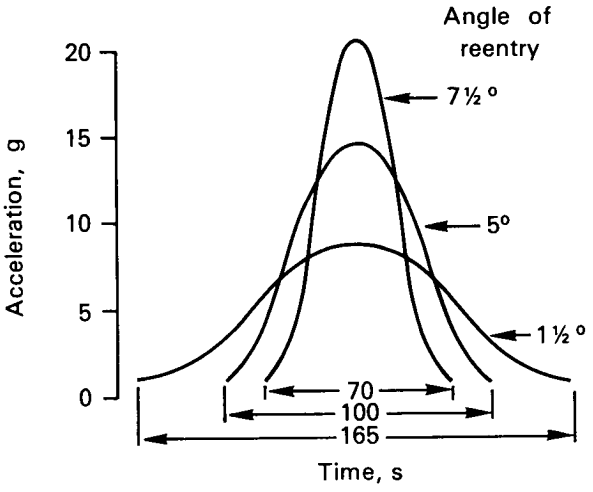

FIGURE 10. – Values of acceleration as a function of spacecraft reentry angle into dense layers of the atmosphere during descent [48].

A reduction in gravitational influence (extended time spent in the horizontal position) and mobility limitations reduce man's resistance to orthostatic effects, up to the development of precollaptoid and collaptoid states. Studies concerned with acceleration effects after weightlessness are limited. Deterioration in man's resistance to effects of $+G_z$ stress was noted after many hours in water [23, 28, 83, 84]; reduction in resistance was 0.50–0.62 $+G_z$. In studies of $+G_x$ accelera-

tory stresses of peak type with a maximum of 8.0 G, reduction in acceleration tolerance was also noted (unreliable), which was evaluated by a compensatory tracking test [23]. Acceleration tolerance in the position used in the Gemini spacecraft was investigated [23]: following 28 d strict bed rest, 22 test subjects were subjected to $+G_x$ stresses reaching a peak of 10.6 G_x, according to the planned reentry schedule of Gemini spacecraft. No reliable difference in the level of individual resistance was found, which was evaluated on the basis of disruptions in central vision. However, an increase in stress on the physiologic systems was observed, resulting from acceleration as compared to initial data (pulse rate increased by 35 ± 20 beats/min).

Acceleration tolerance was practically unchanged following 3 d of hypokinesia (simulating weightlessness) [113, 116]. Increasing the hypokinesia time caused reduction in resistance to $+G_x$ stress. Visual disruptions occurred at lower values of acceleration than usual in these tests (at $+11.6 \pm 0.45$ G_x and 13.6 ± 0.35 G_x respectively) and became primary [113].

Aftereffects

Subjectively, acceleration effects following weightlessness simulation were directly more severe in all test subjects. Muscular weakness with static stress was noted, also more difficult respiration, and earlier development of visual disorders, including total loss of vision. Following hypokinesia, attaining equivalent acceleration values was accompanied by higher functional stress on the physiologic body systems than in initial tests. Cardiovascular system reactions were: an increase in tachycardia and subsequently, earlier development of bradycardia. Progressive reduction of cardiac activity began, following hypokinesia, at 2.8 G_x lower than during usual living conditions (at $+11.2 \pm 1.05$ G_x, respectively).

An extended, multiphase process of arterial pressure normalization was the predominant characteristic during aftereffect: there were periods of reduced pulse pressure, primarily due to increased diastolic pressure. Some test subjects experienced pain around the heart during aftereffect and required medical aid [113] and spasmolytic preparations. Disruption of vascular tonus regulation under such conditions could be decisive. The practical significance should be emphasized of data obtained from prediction of astronauts' states after landing, and determination of the amount of medical aid necessary.

Prolongation of space flights makes it extremely important to determine the dependence between changes in man's resistance to acceleration and the duration of weightlessness. No definite correlation between degree of resistance reduction to $+G_x$ stress and duration of simulated weightlessness has been observed [113, 114]. Following 7–20 d of hypokinesia, tolerance to $+G_x$ was reduced by an average of 2.2 G_x. An increase in the time of simulated weightlessness to 100 d caused no further reduction in resistance limit to acceleration (Fig. 11, Table 2) which was also confirmed by an analysis of human physiologic reactions. During bed rest, adaptation to hypokinetic conditions and the degree of body asthenia, as evaluated by tolerance to $+G_x$ stress, does not progress with prolonged bed rest. Two phases of change in the body's reactivity to accelerations must be distinguished. In the first stage, there is a reduction in resistance to accelerations. The second phase is that of relative stabilization, when tolerance to accelerations, although low compared to its initial level, does not progress as the time of hypokinesia increases, but remains at the level corresponding to 7–20 d of hypokinesia.

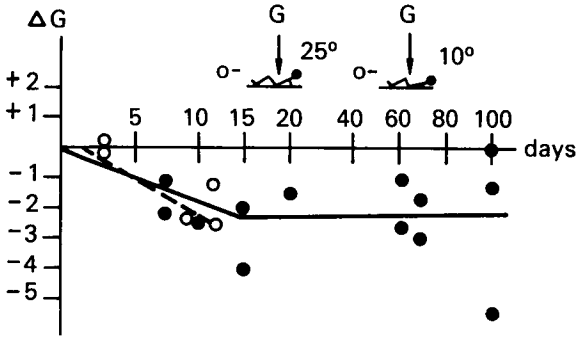

FIGURE 11.—Man's tolerance to transverse $+G_x$ acceleration following simulated weightlessness of various durations [113]. Solid line: seat back angle 10°; dashed line: 25° from horizontal.

Adverse aftereffects under simulated weightlessness can be reduced by physical training and use of pharmacologic agents, which increase subsequent tolerance to $+G_x$ stress. A combination of these protective measures proved the most effective, rather than using one measure alone (Table 3).

Man's tolerance limit to accelerations, following simulated weightlessness, using these protective measures remains the same as in control studies. However, this tolerance for G-loads was achieved at the cost of great stress on the body's physiologic systems. The greatest changes did not involve the cardiovascular system, indicating that preventive measures did not completely eliminate deconditioning.

As changes develop in man's tolerance to transverse $+G_x$ forces following weightlessness, the hypodynamic and hydrostatic factors are of primary importance. Decrease in muscle mass, strength, and endurance; cardiovascular system deconditioning; adjustment of neurohumoral regulation of the physiologic functions; and other changes must, in the final analysis, be considered causes of distinct reduction in resistance to transverse acceleration effects.

In actual space flight, vestibular-autonomic disorders, diseases, fatigue, and other unforeseen situations and factors may arise, which may also influence man's resistance to accelerations during the final stage of return to Earth.

TABLE 2.—*Change in Man's Resistance to Effects of Transverse $+G_x$ Accelerations Following Simulated Weightlessness of Various Durations* [113]

Time of weightlessness, d	Maximum value of $+G_x$ acceleration (M + m)		Mean difference ΔG	Extreme value of $+G_x$ following weightlessness	Overall estimate of change in resistance
	Before	After			
7–20	13.8 + 0.40	11.6 + 0.45	−2.2 ± 0.4[2]	9.8 − 12.9	Reduction
60–70	12.6 ± 0.45	10.5 ± 0.65[1]	−2.1 ± 0.4[2]	9.3 − 14.6	Reduction
100	15.2 ± 0.60	13.0 ± 1.1	−2.2 ± 1.6	10.9 − 14.2	Reduction
Average	13.8 ± 0.40	11.6 ± 0.45[2]	−2.2 ± 0.4[2]	—	Reduction

Peak acceleration with rise gradient, 0.2 g/s. Position: angle of seat back, 10° from horizontal.
[1] $P < 0.05$ [2] $P < 0.01$

TABLE 3.—*Change in Resistance of Humans to Effects of Transverse $\pm G_x$ Acceleration Following Simulated Weightlessness of 60–100 Days, Using Various Preventive Measures* [113]

Time of weightlessness, d	Preventive methods	Maximum acceleration, G_x, M ± m		Mean difference, ΔG	Overall estimate of change in resistance
		Before	After		
60–70	Physical training	12.6 ± 0.55	12.5 ± 0.55	−0.1 ± 0.6	Reduction
70	Pharmaceuticals	11.5 ± 0.8	11.8 ± 0.4	+0.3 ± 0.4	Reduction
100	Physical training plus pharmaceuticals	13.4 ± 1.3	13.1 ± 1.45	−0.3 ± 0.2	Reduction
60–100	Average	12.6 ± 0.5	12.5 ± 0.45	−0.1 ± 0.3	Reduction

Shifts in acceleration tolerance before and after weightlessness and between groups are unreliable. Pharmaceuticals: securinine, caffeine, Phenamine.

Data from actual US and Soviet flights have not revealed any serious disruptions in work capacity or tolerance to accelerations such as those observed in model experiments. However, the possibility cannot be excluded that on longer flights, the deconditioning influence of weightlessness will appear still more sharply, if no preventive measures are found.

Shifts in the physiologic indicators of nervous and emotional origin are apparent during weightlessness, even before spacecraft descent. Toward the end of the flight, astronauts show an increase in pulse and respiration rates, which, apparently, result from anticipation of the descent—the most important, conclusive stage of the flight. Physiologic reactions during descent, as the spacecraft decelerates in the atmosphere's dense layers, are generally more clearly expressed than during ascent into orbit. According to most astronauts, accelerations during descent were subjectively much more severe than similar ones experienced in the centrifuge [115, 225]. Pulse and respiration rates were higher than with the same acceleration in the centrifuge. Some Soviet and US astronauts had pulse rates of 168–190 beats/min. During first flight descent, many astronauts experienced brief vision disruptions, which did not appear under the same accelerations in the centrifuge. Grayout in astronauts during descent might have resulted from orbital flight deconditioning on the cardiovascular system. These data should stimulate broader studies of man's resistance to acceleration effects after prior exposure to weightlessness.

PHYSIOLOGIC SYSTEMS OF THE BODY

Cardiovascular System

Circulatory system disruptions during exposure to acceleration are more significant than other body changes, and have a leading position in physiologic reactions. These disruptions result from redistribution of the blood's circulating mass capable of displacement. The degree of blood redistribution and the resultant general shifts in hemodynamics are determined primarily by the direction of the acceleration action. The greatest changes in general hemodynamics are under longitudinal acceleration ($\pm G_z$ stress), and the least, with transverse acceleration ($\pm G_x$ stress). These changes are explained by the position of the main blood vessels along the longitudinal axis of the body. When inertial forces act from head to feet ($+G_z$), the blood mass is displaced from vessels in the body's upper portion into vessels in the abdominal cavity and lower extremities. Redistribution of the blood changes blood pressure: in vessels located below the heart level, it increases; while in those above, it decreases. Under these conditions, blood flow through veins to the heart will be hindered, and the quantity of blood pumped by the heart is reduced, causing anemia of brain and sense organs, accompanied by vision disorders and possible loss of consciousness. When inertial forces act from the feet to the head ($-G_z$), blood displacement is in the opposite direction, causing blood to accumulate in the upper portion of the trunk with blood pressure above heart level increasing sharply.

Changes in general hemodynamics under transverse accelerations are significantly less than with longitudinal acceleration. However, a strictly transverse position in relation to the acceleration vector is rarely used in practice; in the majority of cases, the subject is in a position with the seat back inclined somewhat, which creates a longitudinal component. Therefore, when transverse accelerations are applied, the longitudinal component determines the value of general hemodynamic changes. Many of the body's organs and tissues have a highly developed network of vessels with approximately even distribution in all directions. Therefore, there will be blood displacement within limits of a given organ regardless of the direction of the inertial forces, which may cause regional circulatory disorders. The transverse component ($+G_x$) causes blood redistribution in pulmonary vessels from front to back.

By spinning animals in a centrifuge at accelerations of +2.5 g, pressure in the carotid artery decreased to 25% of its initial level, whereas it doubled in the femoral artery [100]. The role of the sinocarotid and aortal reflex zones in circulatory compensatory reactions during acceleration was determined in this experiment.

Dependence between the acceleration value and the degree of pressure reduction in the carotid artery has also been determined [9, 170]. These data were later confirmed [139], and it was established that with accelerations increasing at a rate of 1.0–2.0 g/s to a value causing loss of vision, there was an immediate drop in arterial pressure at head level with increased heart rate, reduction in blood content of ear vessels, and decrease in arterial pulse amplitude [129]. The arterial pressure at heart level, however, remained nearly at normal level or increased in connection with the compensatory spasm of the vessels [129].

Under the influence of $+G_z$ stress, animals showed signs of brain anemia. Color motion pictures showed that at an acceleration of $+8$ G_z, the cerebral cortex was pale, capillaries of the pia mater were quite empty, and blood in the large vessels took on a distinctly dark shade [98]. In man, during exposure to $+G_z$, distinct paleness of face and significant expansion of leg veins can be clearly seen. After acceleration has stopped, face paleness is replaced by hyperemia. Insufficient blood flow to the head and increased blood flow in the veins cause rapid emptying of the vascular bed of the head and neck. Simultaneously, reinforced influx of arterial blood to the abdomen and lower extremities is observed, and difficulty in venous drainage from these areas causes pooling of blood. An increase was noted in venous blood [38] and a leg plethysmograph used, to determine an increase in leg volume up to 350 cm^3. Deterioration in venous blood flow may result in a decrease of blood volume per beat and per minute [90, 244].

Blood Pressure

There is a direct dependence between the $+G_z$ forces and arterial pressure decrease. Comparison of curves of blood pressure changes in the carotid artery and increase in acceleration shows a certain lag in the organism's reactions (Fig. 12), and blood pressure changes begin to develop only after a certain time, not immediately after the acceleration application. As a result, at one stage, blood pressure may continue to drop while acceleration remains constant. As acceleration decreases, blood pressure does not return immediately to its initial value, but only after several seconds. These interrelationships indicate why visual disruptions and loss of consciousness arise suddenly sometimes during decreasing acceleration. This lag in blood pressure changes is explained by delay in cardiovascular compensatory reactions to acceleration, which, in turn, results from blood inertia, vessel tonus, and other causes.

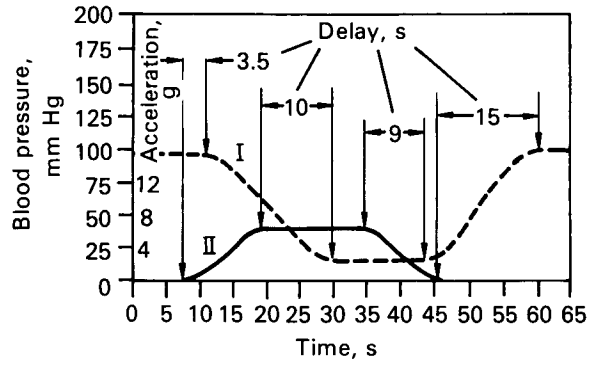

FIGURE 12.—Time relationships of dynamics of change in blood pressure and value of $+G_z$ acceleration [8].

X-ray studies have shown that heart and large vessel images become gradually paler, indicating blood decrease in heart cavities. After rotation stops, there is acute, brief expansion of the heart caused by sharply increased blood influx. Simultaneously, $+G_z$ forces lightened upper portions of the lungs and increased the darkening of lower portions. $+G_x$ forces caused lightening of anterior lung portions with darkening of posterior parts [47, 92, 138, 151].

Direct determinations were made of venous pressure in the jugular vein and arterial pressure at head level during exposure to $+G_z$ [89]. It was shown that with a significant decrease in arterial pressure in the upper half of the trunk, brain circulation was maintained by a pressure drop in the jugular vein of 30–50 mm Hg below 0. The difference between arterial and venous pressure maintained blood circulation even when arterial pressure dropped in the area of the head to 0, caused by the so-called siphon effect. Therefore, it is indicated that the develop-

ment of compensatory reactions retain the vital functions of the body under critical situations.

Investigations of the ear pulse volume showed that under $+G_z$ stress there is a decrease in blood and a reduction in pulse oscillation amplitude. When longitudinal accelerations were applied, a clear correlation was established between the arterial pressure level in the ear's vessels, the state of visual perception, and subsequent syncope. Reduction in blood pressure in vessels located above the heart acts through the sinocarotid zone and other angioreceptors to engage the mechanisms for compensation of hemodynamic disorders. An increase in heart rate and blood vessel constriction in a number of areas results. Under transverse accelerations, hemodynamic changes are primarily regional; therefore, there is no correlation. When consciousness is retained, full vision loss may still occur, while blood pressure at head level may be maintained at a rather high level. Vision disruptions in these cases result from disorders in regional circulation of the eye's vessels.

Complex restructurings in the hemodynamic system involving compensation mechanisms lead to an increase in pulse frequency. There is a rather clear dependence between acceleration and heart rate (Fig. 13). In man, depending on acceleration applied, the heart rate reaches 130–180 beats/min, rarely 190–200 beats/min or more. At transverse accelerations and optimal position, change in cardiac activity usually follows a definite sequence: (1) increase in heart rate; (2) stabilization; (3) decrease in frequency; and (4) restoration of cardiac activity or aftereffect.

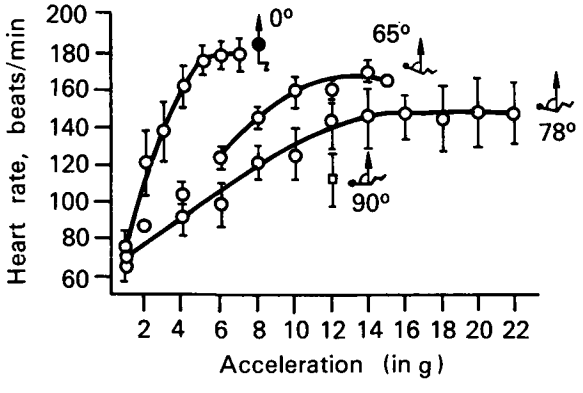

FIGURE 13.—Change in heart rate with accelerations in various directions [214].

No correlation has been found between increase in cardiac rhythm and tolerance to $+G_x$ forces. Disruption of compensation—progressive bradycardia—may occur at various heart rates. Therefore, absolute heart rate level cannot be a reliable criterion for prediction of bradycardia, and, consequently, a criterion for acceleration tolerance.

Special studies on the genesis of bradycardia in man, with preliminary injection of atropine, showed that temporary blockage of nervus vagus eliminated bradycardia not only at accelerations at which it is ordinarily recorded, but even at higher G of 14–16 G_x [113]. Therefore, vagus nerve tonus is important in development of bradycardia under the influence of $+G_x$ forces. Bradycardia developed in apes in spite of atropine injection, although significantly later than in controls [138]. During acceleration, as with many other effects, regulation of cardiac activity and manifestation of its adaptive reactions do not involve only extracardial nervous mechanisms. The heart has a wide range of autonomous adaptive mechanisms, adjusting its function to needs of the organism. Extracardial nervous regulatory influences duplicate largely effects of intracardial regulatory mechanisms [110]. Under transverse $+G_x$ stress, bradycardia may develop by restructure of extracardial influences (predominance of vagus nerve tonus) and by intracardial regulation.

Cardiac Disorders

The pathogenesis of compensatory mechanism failure to regulate cardiac activity is doubtless complex and includes many different changes in the total chain of body reactions to acceleration.

Important factors in overstressing the organism's compensatory capabilities with subsequent cardiac disorders are: functional change of the autonomic centers regulating the cardiovascular system; reflex influences resulting from general and regional circulatory disruptions; displacement of organ positions; myocardial hypoxia; and exhaustion of heart energy resources. The specific significance of each of these links in the patho-

genesis of compensation failure may differ, depending on the acceleration's mode and nature and the body's functional state.

Another disruption in cardiac rhythm under the influence of transverse $+G_x$ stress, encountered no less frequently, consists of various types of extrasystoles (Fig. 14). Ventricle and atrioventricle extrasystoles are encountered most frequently, the auricular type less frequently. Atrioventricular extrasystoles are more unfavorable than ventricular extrasystoles clinically, since auricle and ventricle contractions are simultaneous. Thus, blood from the auricle is not pumped into the ventricle, but back into the veins, hindering emptying of the veins and decreasing systolic volume and volume per minute. The total of extrasystoles arising with a reduction in heart rate is almost 4.5 times greater than those before bradycardia develops. Extrasystoles developing during $+G_x$ stress might be caused by various respiratory maneuvers, hyperventilation, blood oxygenation reduction, possible pulmonary atelectases, as well as fear and alarm, or simply back position, which sometimes facilitates arrhythmia [216]. Most researchers consider extracardial influences dominant, which act on the heart through vagus and sympathetic nerves. Extrasystoles are more frequent with $+G_x$ than with longitudinal $+G_z$ forces.

Attacks of paroxysmal tachycardia have been recorded very rarely [50, 113, 210]. Clinicians believe extrasystoles might be precursors of paroxysmal tachycardia. One instance of paroxysmal tachycardia under $+G_x$ forces was recorded, which was preceded by extrasystoles and relative bradycardia (Fig. 15).

Electrocardiographic studies have shown instances of sinus tachycardia, shortening of the P–Q, Q–T, and R–R intervals, increase in the P-wave, thickening of the T-wave, increase in the systolic index, and various disruptions of cardiac rhythm. Changes in the heart's bioelectric activity might be due to a combination of factors: heart position displacement, changes in tonus of autonomic nervous system and humoral elements, change in blood content of heart cavities, and myocardial hypoxia.

Under $+G_x$ stress, there are significant changes in the hemodynamics of pulmonary circulation – blood redistribution in the pulmonary artery system [104]. Pulmonary circulation disruptions lead primarily to disorders in oxygen delivery from alveolar air to blood. Changes in the normal hemodynamics of pulmonary circulation and reduction of blood oxygen indicate that the heart may undergo hypoxia. $+G_x$ stress might cause myocardial ischemia [199], which in turn might lead to angina pectoris [151]. Changes in electrocardiograms (ECG) have been related to myocardial hypoxia in dogs during $+G_x$ [121]. O_2 in arterial blood and in coronary sinus blood has been shown to be dependent on the value and duration of application of transverse $\pm G_x$ [232], where the demand for oxygen by the heart is indicated by O_2 reduction in coronary sinus blood with simultaneous increase in blood flow from the sinus. Maintenance of a sufficiently high level of coronary blood flow is obviously a primary factor compensating for increasing oxygen demands of the myocardium. Slight ECG changes disappear rapidly after rotation when an increased flow rate from the coronary sinus is observed. In experiments where decreased blood flow was observed at this point, ECG changes were sharper and lasted longer.

Blood Volume

Systolic blood volume, under forces up to $+5$ G_x for brief periods, either remains unchanged or increases slightly. An increase in acceleration duration to 10 min causes a drop in systolic volume [140]. Blood volume per minute, under forces up to $+5G_z$, also remains unchanged or increases. Consequently, reduction in volume per minute depends primarily on pulse frequency. Increases in the blood pressure of aorta and right auricle have been clearly observed [140, 244].

As $+G_x$ forces increased, aorta arterial pressure increased and pulse frequency decreased significantly [202] (Table 4). Cardiac output did not change with forces of $+5$ G_x, but decreased progressively at accelerations of $+10$ G_x and $+15$ G_x, due to increase in peripheral resistance, particularly in the vascular lumen of abdomen and muscles. However, resistance of

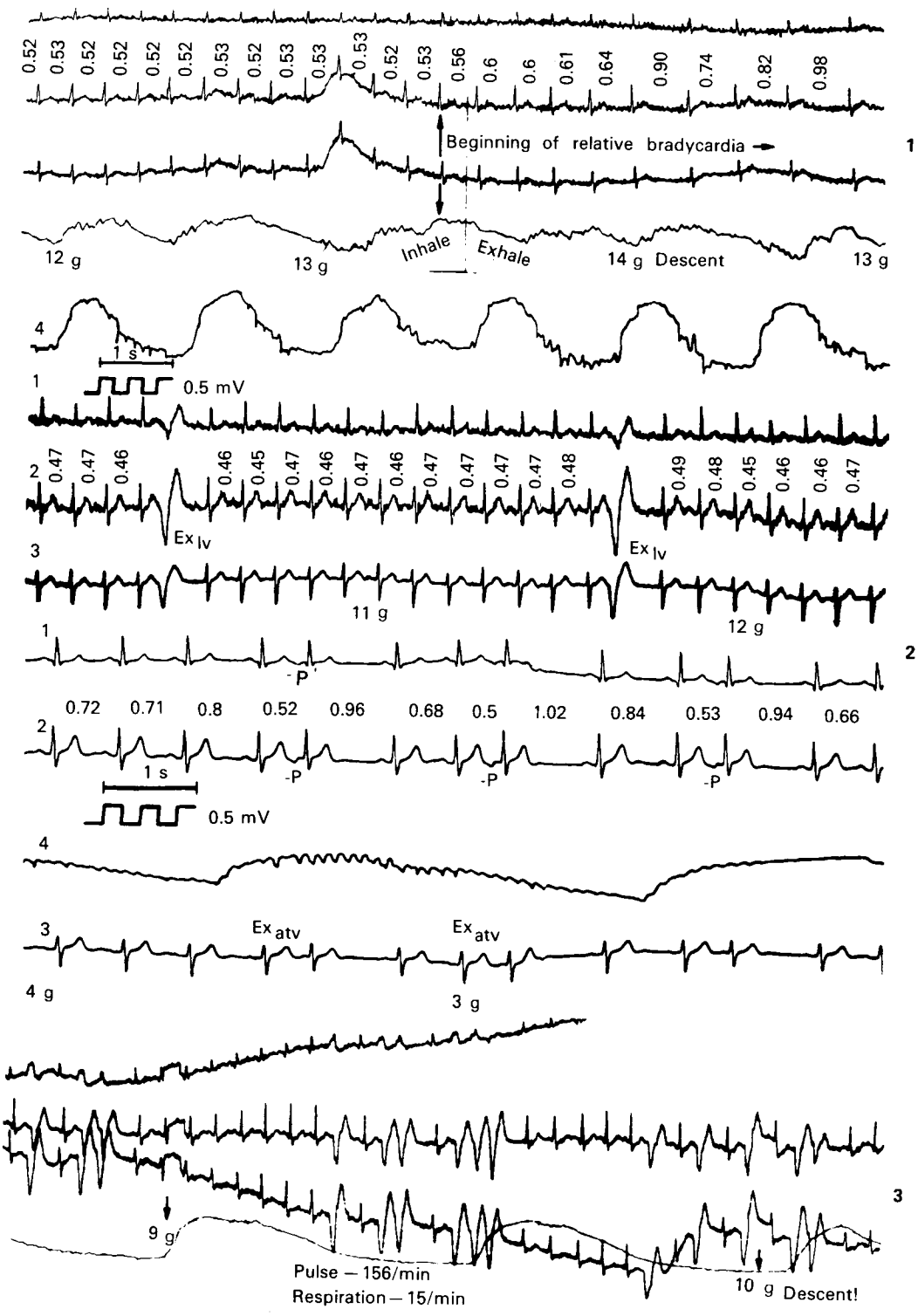

FIGURE 14.—Disruptions in man's cardiac rhythm under transverse $+G_x$ acceleratory stress [113]. 1: Development of bradycardia; 2: individual extrasystoles (Ex_{lv}, left ventricular extrasystoles) (Ex_{atv}, atrioventricular extrasystoles); 3: group extrasystoles.

important vascular formations, such as the left coronary and common carotid arteries, changed only slightly.

Morphologic studies of animal hearts subjected to transverse acceleration indicated oligemia, and in many cases hemorrhaging, edema, and dystrophy of cardiac muscle [162]. There is a definite dependence between cardiac activity

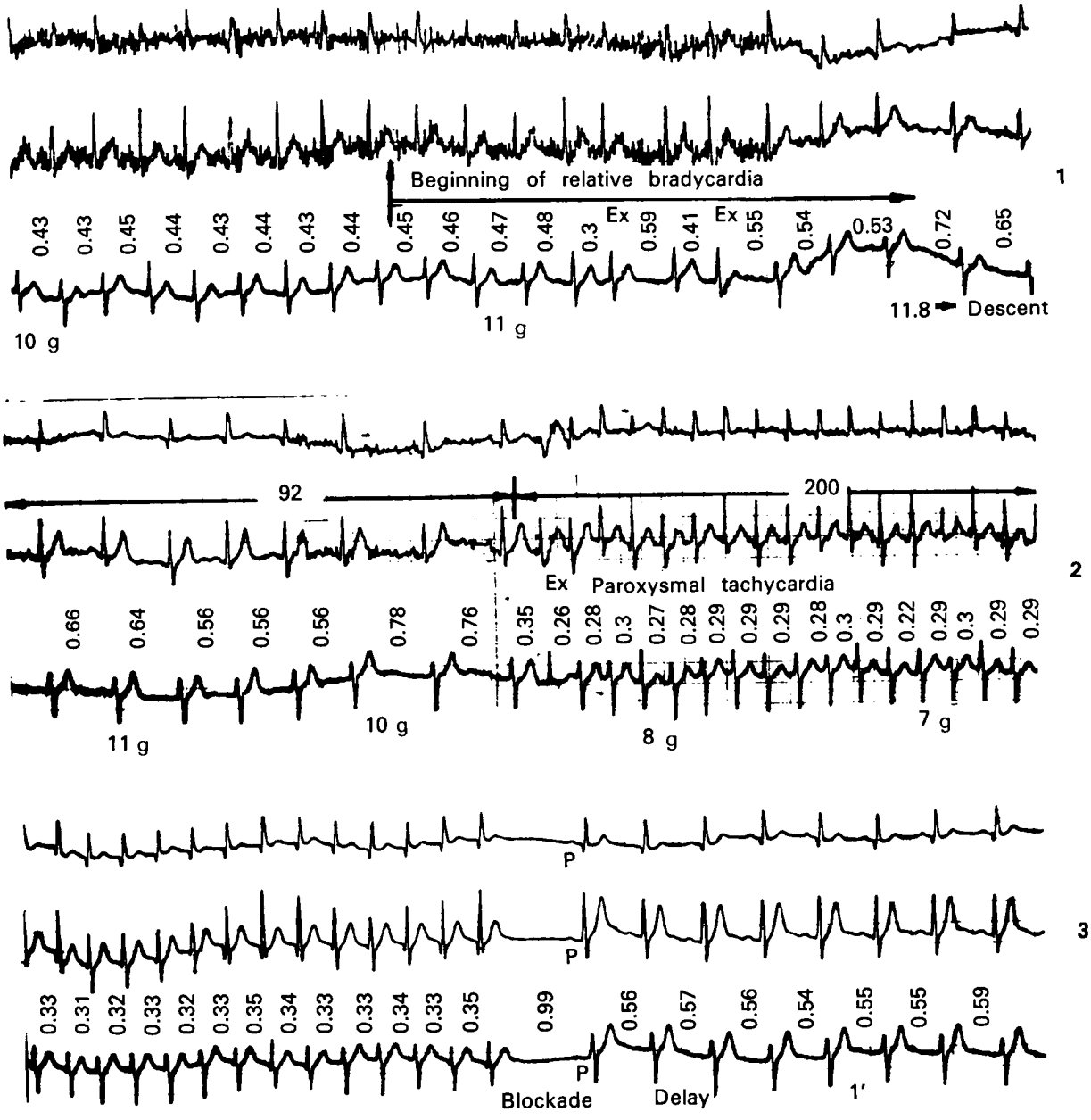

FIGURE 15.—Paroxysmal tachycardia in man under transverse $+G_x$ acceleratory stress [113]. 1: Dynamics of change of cardiac rhythm under + 10.0–11.8 G_x acceleratory stress, againt a background of relative bradycardia (arrow); extrasystoles of atrioventricular type (Ex) were recorded. 2: Relative reduction in cardiac rhythm suddenly replaced by acute paroxysmal tachycardia (200 beats/min), ECG shows no P-wave. 3: Before stopping centrifuge, paroxysmal tachycardia suddenly stopped, and after block, was replaced by sinus rhythm; P-wave reappeared on ECG.

disruption and glycogen content in myocardium and liver [26].

Cardiovascular system regulation is governed significantly by peripheral receptors. A reduction in blood volume per minute to 73–77% of its initial level was observed during exposure of narcotized animals to +9 G_x, whereas in intact dogs, blood volume per minute increased by 52–53% [190]. In all experiments on narcotized dogs, with forces of 5.0–6.0 G_x and more, there were reductions in blood volume per minute and systolic blood volume, with insignificant changes in arterial pressure at heart level. In intact animals and humans, a regular increase in blood volume per minute was observed and an increase in arterial pressure during spaceflight acceleration [76, 118, 228].

Brain blood changes slightly at +7.0–8.0 G_x [150]. At accelerations of +8.0–10 G_x with the seat back inclined at 25° from the horizontal, the pulse blood filling the brain is lower than the initial level, although arterial pressure at heart level increases. The cerebral vessel's blood content during transverse acceleration is determined by the longitudinal component in the head-pelvis direction (+G_z). An increase in blood is observed when this component is 1.6–1.8 G_x, while at +3.0 G_z, it is equal to the initial level, and at +5.0 G_z, begins to decrease.

Thus, acceleration causes changes in frequency and force of cardiac contractions, in cardiac output per beat and per minute, in arterial and venous pressure, and in the general and regional speeds of blood flow. It redistributes circulating blood and causes many physiologic changes.

Respiratory System

The influence of acceleration on external respiration is determined not only by the value and time of application, but also by direction of the acceleration vector in relation to the vertical axis of the body. The principal effects are from changes in respiration biomechanics and increases in hydrostatic lung pressure.

With +G_z forces up to +5.0 G_z, progressive increases in respiration frequency, volume per inhalation and per minute have been observed [10, 63, 73, 210]. There were increases in O_2 consumption, CO_2 liberation, and other respiratory factors [22]. Reduction in lung extensibility was noted at this level, plus a slight increase in functional residual volume [21]. Diaphragm lowering and increased intraperitoneal pressure become significant under these conditions. Increase in pulmonary ventilation with +G_z stress is accompanied by less increase in effective alveolar ventilation [22]. With constant recording of lung volume and pressure gradient, neither elasticity nor resistance to air flow changed up

TABLE 4.—*Change in Hemodynamic Indicators in Dogs Under Transverse +G_x Acceleration* [207]

Indicators	Control	5.0 G_x–2 min	10.0 G_x–2 min	15.0 G_x–1 min
Arterial pressure in aorta, mm Hg	140	164	186	207
Arterial pressure in left ventricle, mm Hg	154/3	171/8	200/24	217/48
Rate of blood flow in ascending aorta, v, cm/s	25	25	20	16
Rate of blood flow in left coronary artery, v, cm/s	43	55	54	81
Rate of blood flow in carotid artery, v, cm/s	31	28	31	37
Pulse rate, beats/min	124	144	70	60

Resistance of vessels was calculated by dividing mean pressure in aorta by various blood flow rates in arteries.

to +3 G_z. However, the total workload of the respiratory apparatus increases due to reduction in elasticity of thorax walls and increase in intraperitoneal pressure.

X-ray studies on men and animals have shown increased transparency of the lung image in the upper portion and increased image density in the lower portions [145, 152]. These changes result from hydrostatic effects of acceleration on pulmonary parenchyma. The alveoli in the upper portions of the lungs expand greatly, and tissue anemia sets in, to the point of total cessation of circulation at forces of 6.0–7.0 G_z, while edema, atelectases, and blood pooling are in the lower portions. Therefore, in spite of increase in respiration volume per minute and alveolar ventilation, uneven air flow distribution in the alveoli and hemodynamic changes resulting from +3 G_z and more cause disruptions in arterial oxygenation [21].

External respiration is most significant for transverse $+G_x$ stress, tolerance for which is frequently limited by respiratory disorders. An increasing external pressure resulting from the transverse acceleration component causes thorax deformation, changes in positions of organs, and difficulty in normal respiration. Respiratory reaction to $+G_x$ stress is characterized by a moderate increase in the volume of respiration per minute (VRM), due primarily to sharp increase in respiration frequency (Fig. 16). The respiratory volume increases up to +6 G_x, then begins to decrease. For this reason, at high accelerations, in spite of the rather high level of VRM, the alveolar ventilation deteriorates. Mechanical compression of the thorax causes a reduction in all pulmonary volume, with some increase in residual air (Fig. 17).

The vital capacity of the lungs decreases, approaching 0 at high accelerations, at which time the tolerance for accelerations is determined by the respiration delay time [47]. The shifts observed originate to a great extent from the increased work of the respiratory apparatus, due to the elastic component and significant reduction in dynamic extensibility of lungs [233]. Thus, the effects of high transverse $+G_x$ forces are ac-

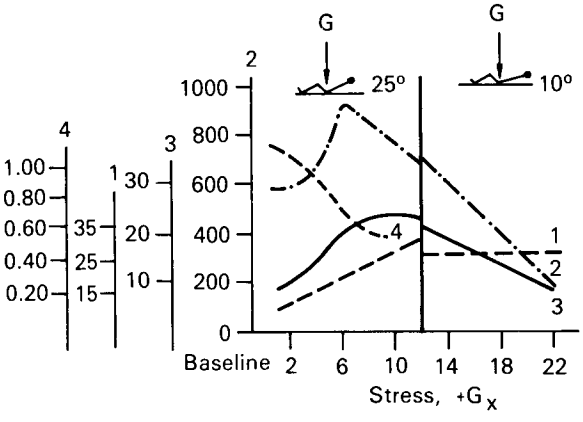

FIGURE 16.—Dynamics of change in man's respiration with $+G_x$ acceleration [17]. 1: Respiratory rate per min; 2: respiratory volume, ml; 3: respiratory volume per min; 4: ratio of vital capacity of lungs during acceleration to value in initial state.

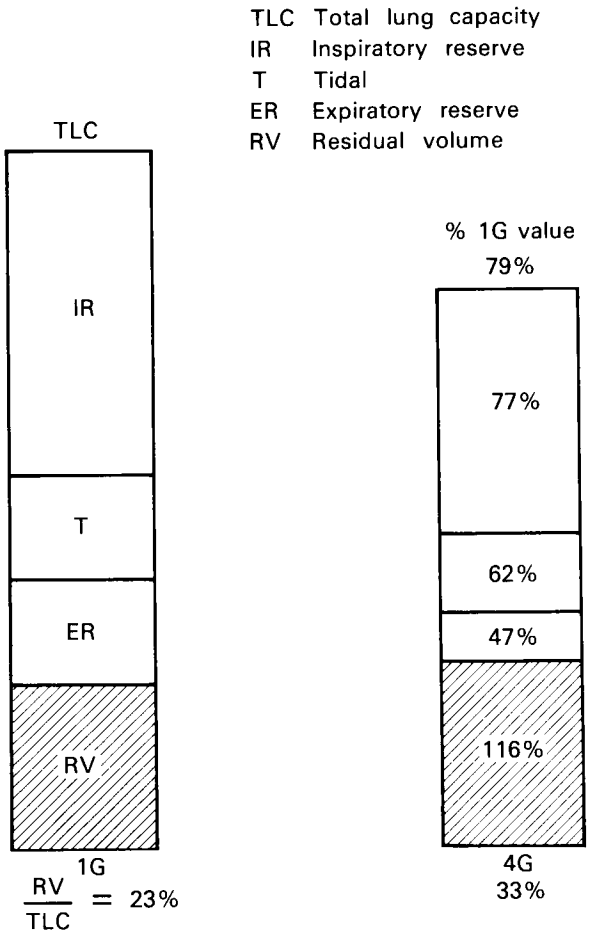

FIGURE 17.—Change in pulmonary volume with $+G_x$ accelerator stress at 4.0 g [47].

companied by significant reduction in pulmonary reserve and deterioration of the effectiveness of ventilation, which is confirmed by experimental data indicating a reduction with increasing acceleration in the oxygen utilization factor, i.e., the quantity of oxygen absorbed in the lungs from each liter of ventilated air (Fig. 18). The hydrostatic effects in the lungs from $+G_x$ are similar in principle to those for $+G_z$ stress. The differences are purely regional, i.e., hypoperfusion and hyperventilation in the anterior portions of lungs, with hypoventilation and hyperperfusion in posterior portions. These effects become obvious after analysis of the relationship between the gradient of alveolar pressure and pressure in lung vessels under acceleration (Figs. 19, 20).

Thus, the hydrostatic effects of acceleration in any direction cause unevenness of ventilation and blood circulation in lungs and, consequently, lead to disruption of arterial oxygenation of blood (Fig. 21). Damage to lung tissue is also possible (congestive hyperemia, perivascular edema, hemorrhage, and atelectases), which has been established in animal experiments [108, 119, 162].

Direct results of disruptions in respiratory system functioning under $+G_x$ stress include shifts in gas metabolism, manifested in reduced O_2 intake and extraction of CO_2 during the actual application of acceleration, with subsequent sharp increases during the aftereffect [17, 193, 200]. These effects are accompanied by increases in the oxygen debt with increasing acceleration (Fig. 22) and apparently are related to the significant deterioration in hemocirculation during acceleration. Deterioration in the diffusion capacity of the lungs might also be significant [247], although this requires further study.

The oxygen debt also reflects an increase in organic metabolic processes during acceleration and is caused by a reduction in anaerobic metabolic products [80].

When transverse forces in the opposite ($-G_x$) direction are applied, respiratory changes are less manifest and approximate those for $+G_z$ forces. With $-G_z$, a slight increase in the respiratory depth and rate is observed up to -3.0 G_z [9]. With accelerations of -6 to -8 G_x, pulmonary ventilation increases due to increased respiratory rate and volume with moderate de-

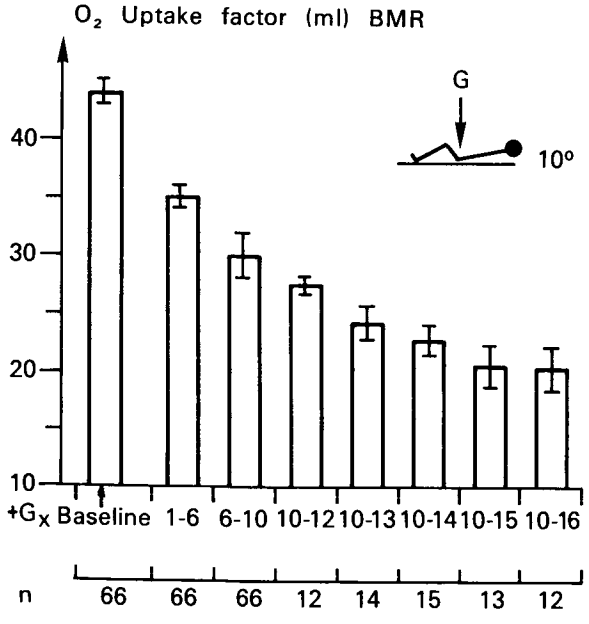

FIGURE 18.—Oxygen uptake factor in lungs under various $+G_x$ acceleratory stresses of peak type [193]. Acceleration rise rate 0.2 g/s; n = number of persons.

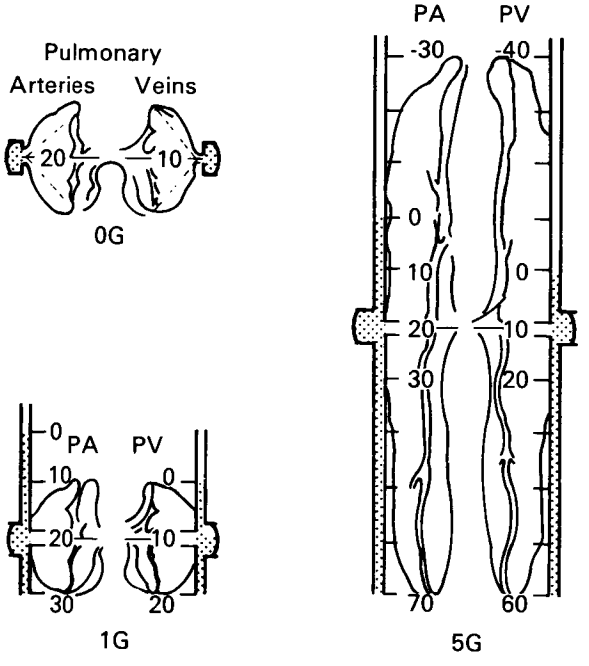

FIGURE 19.—Hydrostatic effects of $+G_x$ acceleratory stress on pulmonary hemodynamics [139]. Numbers show pressure of water column, cm. 0: atmospheric pressure in central portion of thorax; dorsoventral dimension of lungs, 20 cm.

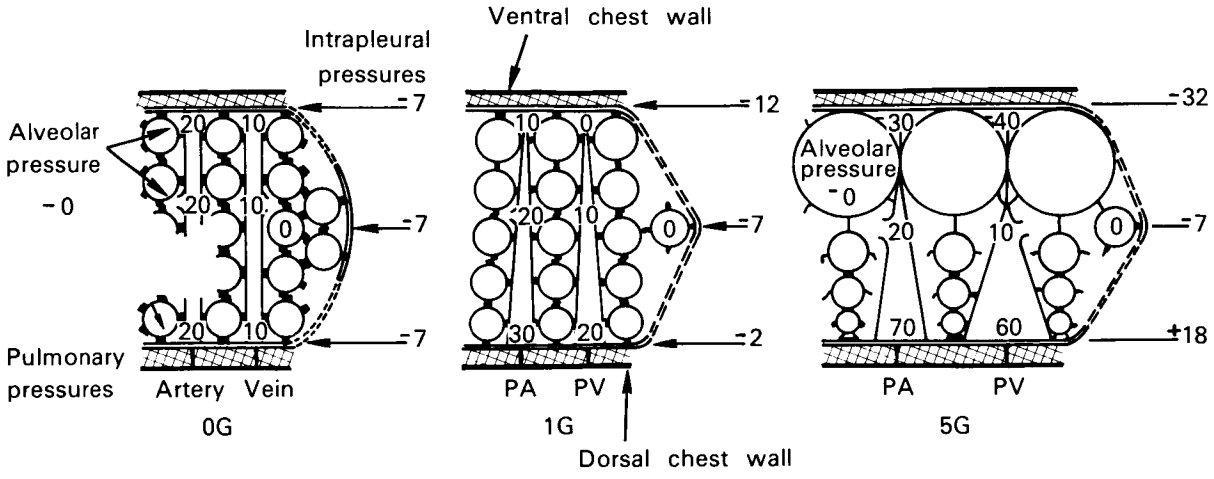

FIGURE 20.—Influence of transverse $+G_x$ acceleratory stress on intraperitoneal pressure [242]. Dorsoventral dimension of lungs, 20 cm; numbers show pressure of water column in cm; 0 shows atmospheric pressure in central portion of thorax in plane of heart.

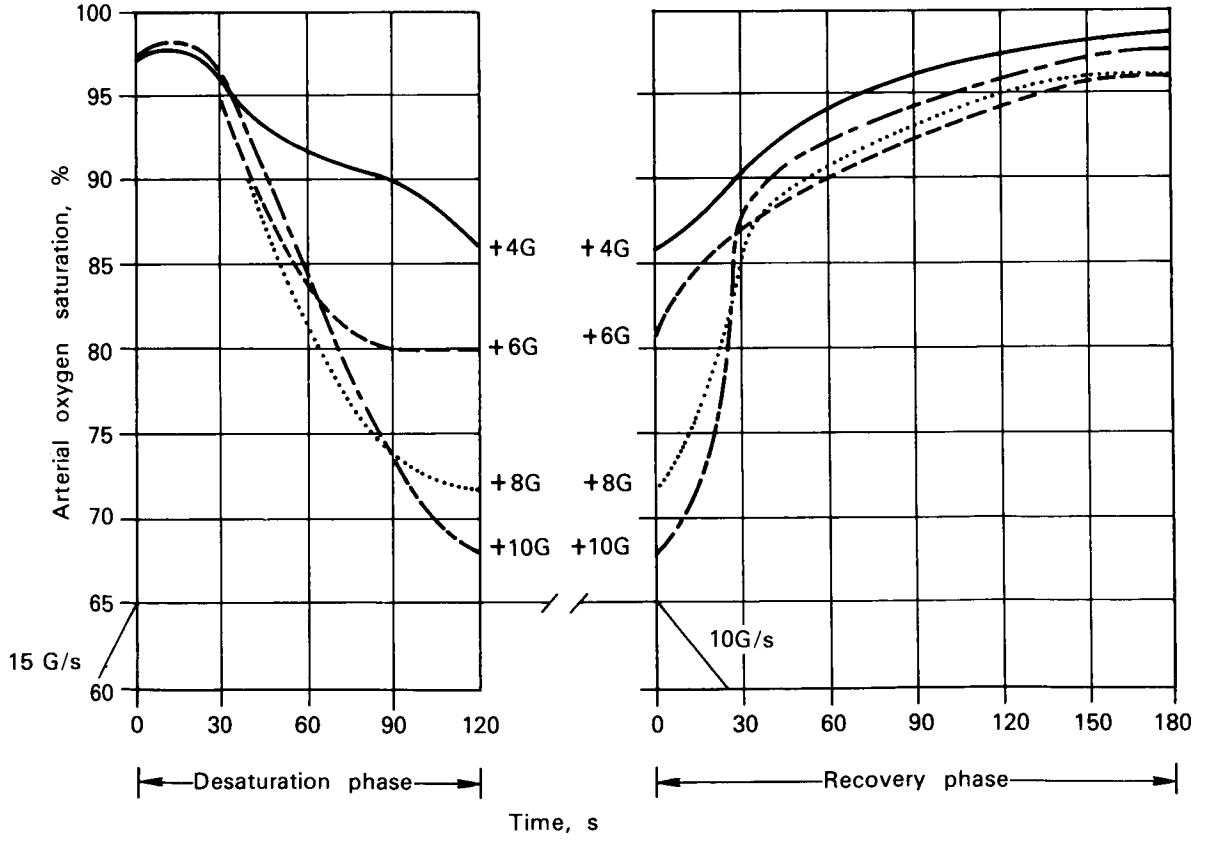

FIGURE 21.—Oxygenation of arterial blood during breathing of air [5]. Ordinate shows arterial oxygenation in %; abscissa shows reduction phase and restoration phase of blood oxygen saturation.

crease in the vital and functional residual capacities of lungs [172, 196].

The arteriovenous shunting and deterioration of gas metabolism in lungs during accelerations unavoidably lead to disruptions in arterial blood oxygenation. This factor, added to the insufficiency of blood supply, is the most important in the mechanism of tissue hypoxia present under long-term exposure to acceleration. Detailed information is available on the $+G_x$ direction of the acceleration vector. There is reduced oxygenation of arterial blood after as little as 30 s exposure to +3.0 G_x or more [4, 104, 201, 232, 242]; such changes are shown in Figure 21. Reduction in oxygenation of blood is never as great as for hypoxic hypoxia, and at high acceleration values is partially compensated by respiration of 100% oxygen [4].

Thus, disorders in the external respiration system are significant in the pathogenesis of disrupted functions of other body systems under the influence of acceleration.

Visual Analyzer

The reliability of astronauts' work depends to a great extent on the functional state of the visual organ. However, vision has proved susceptible to the effects of long-term acceleration in various directions.

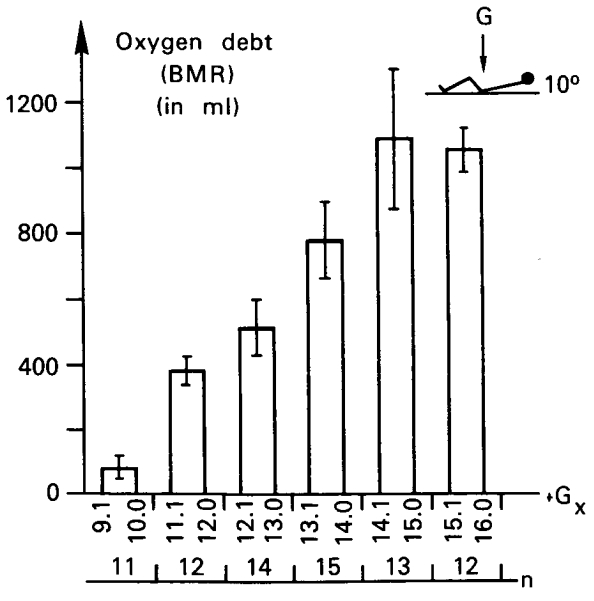

FIGURE 22.—Oxygen debt in man following exposure to $+G_x$ accelerations of various values [193]. Acceleration rise rate: 0.2 g/s; n = number of persons.

In aviation medicine, visual disorders serve as a reliable criterion for the tolerance limit to $+G_z$ forces [11, 33, 38, 73, 114, 189, 210] because disruptions in visual function under $+G_z$ precede loss of consciousness resulting from reduced cerebral blood circulation. Depending on the gravitoinertial value and duration of application, disruptions of vision go through successive phases: constricted field of vision, grayout, then blackout, and finally total loss of vision. The sensations of those who have been subjected to acceleration include: gray veil, fog, whitish fog, looking through rain or fog, and so forth, followed by total blackness but with retention of consciousness and hearing. The threshold of grayout and blackout depends on the subject's position in relation to the inertial force vector, value and duration of its force, and the body's functional state. Visual disorders frequently start at the beginning of acceleration application, then, despite continued acceleration, disappear after 8–12 s, with vision sometimes fully recovered. This is explained by the delayed development of compensatory reactions, primarily those of the cardiovascular system, for which the latent period of engagement is the same (8–12 s).

The thresholds of vision disruption for 1000 test subjects under the influence of $+G_z$ forces [52] are presented in Table 5.

With transverse acceleration, visual disruptions also result. The thresholds of grayout and blackout for $+G_x$ are determined by the subject's position. Calculation data in Figure 3 provide for determination of the relative percentage values of components on the $+G_z$ and $+G_x$ axes from the resulting acceleration vector, as well as the relative retinal-aortal $+G_z$ component (along the axis between the retinas and the arc of the aorta) for various positions of the seated body—from lying-on-the-back to sitting positions. The absolute retinal-aortal component can be used to predict the probability of visual disorders.

The threshold for development of grayout for various effective physiologic angles (Fig. 23) has been established experimentally [22]. With the

TABLE 5.—*Thresholds of Visual Disorders and Loss of Consciousness Under* $+G_x$ *Acceleration* [52]

Symptoms	Mean threshold, G_z	Standard deviation	Extreme values
Loss of peripheral vision	4.1	±0.7	2.2–7.1
Blackout	4.7	±0.8	2.7–7.8
Loss of consciousness	5.4	±0.9	3.0–8.4

Erect "seated" position, muscles relaxed, acceleration rise rate 1.0 g/s.

seat back angle ($SA+\epsilon=20°–25°$) so that inertial forces along the head-pelvis axis are significant, visual disruptions precede loss of consciousness. Under these conditions, similar to $+G_z$ longitudinal forces, the visual function correlates definitely with disruptions in general hemodynamics. With the body in a more horizontal position ($SA+\epsilon=10°–12°$), visual disruptions do not precede loss of consciousness, but indicate disruptions in retinal circulation. Thus, in the optimal position ($SA+\epsilon=10°$), vision is completely switched off at levels of +14.0–16.0 G_x, without loss of consciousness [16, 24, 38, 110, 113]. Consequently, visual disorders caused by the influence of $+G_x$ forces in various body positions have different significance for evaluating the body's condition.

With increasing acceleration, visual acuity decreases, and the width of the vision field narrows with a drop in absolute light contrast sensitivity, and reaction time to light signals increases [15, 70, 73, 97, 196].

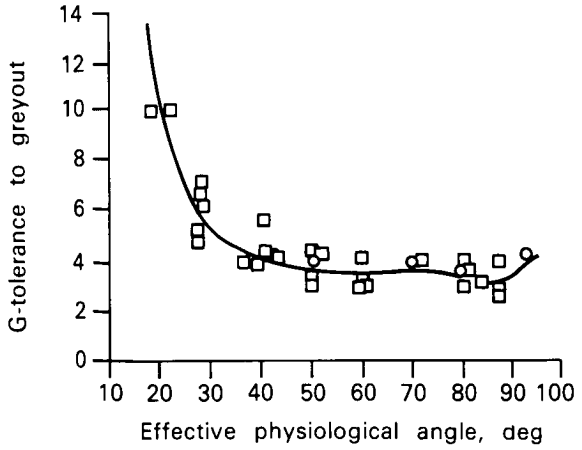

FIGURE 23.—Development of grayout as a function of subject's posture [45].

Visual acuity changes with different directions of acceleration ($+G_z$ and $+G_x$) [222] (Fig. 24). When the limiting $+G_z$ forces are reached (over 6.0 g), visual acuity drops sharply, usually due to visual disorders. Under transverse acceleration, the reduction in visual acuity is less pronounced.

A reliable reduction in visual acuity was observed under transverse forces beginning at +6.0 G_x with the seat back at an angle of 25°, and at +10.0 G_x with the seat back at a 10° angle. In $-G_x$ visual disruptions become distinct at 6.0—8.0 G. It is assumed that fogging and reduction of acuity vision with $-G_x$ might be caused by displacement of the cornea. However, when a special optical device was used [196], there were no changes indicating deformation of the cornea; these visual disorders probably result from abundant lacrimation.

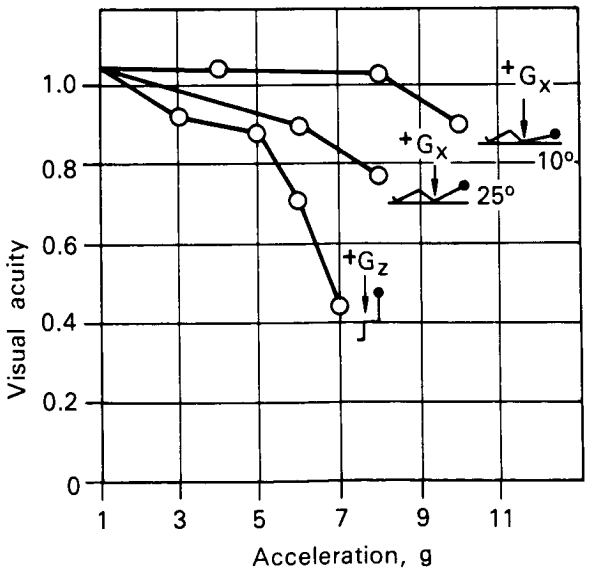

FIGURE 24.—Visual acuity of man during exposure to accelerations in various directions [222].

Visual Disruptions

A contribution to reduction of visual acuity under acceleration might be by the contrast or discrimination sensitivity of the eye, the basis of object vision. High contrast sensitivity is essential for adequate perception of visual information. The thresholds of the eye's contrast sensitivity increase with decreasing background illumination and increase for illumination level with increasing $+G_z$ and $+G_x$ forces. With $+G_z$, the thresholds of contrast sensitivity are higher than with $+G_x$.

Shifts in visual functions were apparent long before hemocirculatory disorders appeared, causing grayout and blackout, according to studies of contrast sensitivity and operators' reaction time [222]. The earliest changes were at $+4\,G_x$ (in the position $SA+\epsilon=10°$). As acceleration increased, reaction time to light signals increased, and finally, a reduction in visual acuity. Another area of interest is the gradual change of absolute visual threshold with acceleration, i.e., the minimum light stimulus which can be perceived. The threshold of central vision at $+3.0\ G_z$ is almost double, and at 4.0 G_z, 3.4 times higher than at 1.0 G_z (with a 50% level of probability) while the threshold of peripheral perception increases 1.5 times at 2.0 G_z, 3 times at 3.0 G_z, and 4 times at $+4G_z$ [236, 237]. Pupil reactions do not change under the influence of acceleration [196]; dilation of the pupil was noted, accompanied by loss of peripheral vision [24].

Thus, long-term acceleration causes constriction in the field of vision, limitation of voluntary motion of eyes to the point of ataxia, deterioration in recognizing low-intensity signals and contrast sensitivity, and in differentiation of fine details. Disruptions in vision are usually explained by disorders in regional hemodynamics and retinal hypoxia [6, 11, 64, 65, 66, 126, 129, 174]. However, such developments are sometimes related to changes in activity of the visual analyzer's cortical portion [87, 165], and finally, a few researchers do not differentiate these mechanisms [239].

Vision is clearly disrupted under the influence of altered hydrostatic pressure, and symptoms of disruption appear at levels preceding loss of consciousness. Under conditions of acceleration, blood supply to the eye can continue normally only if blood pressure in the central retinal artery is greater than the level of pressure in the eye, normally equal to 22–23 mm Hg (with fluctuations from 18–30 mm Hg). This was confirmed by application of a negative pressure of 30–40 mm Hg to the eyeball by means of suction goggles which increased the threshold of blackout [125]. These experiments were later confirmed [101]. In a sealed chamber, when pressure was reduced in front of one eye, this eye regained clear vision, but when pressure was not reduced in front of the other eye, it remained blind.

Direct ophthalmoscopy of the fundus oculi was performed on men and apes during application of $+G_z$ forces at the moment of blackout, and arterial pressure in the radial artery was measured with the arm at eye level [65]. A correlation was established between changes in visual function and morphologic changes in the area of the fundus oculi. Data from this study are presented in Table 6. Photographs were made of the fundus oculi of human subjects during $+G_z$, with and without visual disruption [135, 153]. A definite dynamic sequence of changes of retinal circulation was recorded similar to that obtained by ophthalmoscopy [65]. When vision was clear, practically no ophthalmoscopic changes were observed on the fundus oculi, but were maximally expressed while in blackout, up to cessation of blood flow in the retinal vessels (Fig. 25).

Since the inner layers of the retina are highly sensitive to hypoxia, it can be assumed that hypoxia in these layers starts during retinal ischemia [137]. The critical point of application of hypoxia is at the sympathetic connections of the ganglionic and bipolar cells of the retina. Visual disorders such as grayout appear under the influence of $+G_z$ when the systolic arterial pressure at the head level falls below 50 mm Hg [126, 129, 210]. With transverse $+G_x$ forces and the test subject in the optimal position, when inertial forces along the head-feet vector are slight (not over 18–20% of the total acceleration), visual disorders also indicate disruptions of blood circulation in the retina. These disruptions are apparently related primarily to disruptions of regional circulation in eye vessels, but are not

precursors of a critical reduction in the cerebral circulation level or, consequently, loss of consciousness.

In studies of vascular reactions in the retina following $+G_x$ stress, two phases were differentiated in fundus oculi changes in the aftereffect [123]. During the first phase, directly after termination of acceleration and during the first few hours, reactive hyperemia predominates (hyperemia and blurring of the boundaries of the visual nerve discs, ectasia of the capillaries, expansion of the retinal veins and arteries). During the second phase—several hours to several days—phenomena related to disruption of permeability of the vascular walls in the retina predominate (perivascular edema of the retina, increased dimensions of the physiologic scotoma). The degree of changes manifested in the vascular system of the retina depends on the value and application time of acceleration [111, 245].

Disruptions in regional circulation in the eye's vessels under transverse acceleration may also result from the inertial force component along the forehead-occipital axis.

Visual disorders arising during acceleration are generally thought to result from anoxia of the retina and brain cells due to hemodynamic disruptions, although there are other opinions. Disruption of visual analyzer activity during acceleration could be ascribed to a mixed cortico-retinal mechanism with enforcement of inhibitory processes in neurons of the retina, reduction in neuron excitability of the cortical part of the visual analyzer, and retardation of synaptic transmission in neurons of the visual tract [179].

Central Nervous System

In the last 30 to 40 years, much experimental work has been concerned with the influence of acceleration on various portions and levels of the central nervous system (CNS), using various animal species and man as subjects. A detailed summary of this research is contained in a monograph by Savin [179].

The first studies concentrated primarily on the effects of positive $+G_z$ and, to a lesser extent, negative $-G_z$. It was established that $+G_z$ stress significantly disrupt perception, increase simple and complex motor reaction time, and elongate latent response periods to sound and light signals [38, 231]. These results were later deepened and expanded [56, 105]. Soviet researchers subsequently investigated higher nervous activity (HNA) using conditioned reflexes, and established that even at slight $+G_z$ stress, there is a clearly expressed elongation of latent reaction periods to conditioned stimuli, and that restoration of normal latent conditioned motor reflex usually occurs in waves [180], beginning 20 to 30 s after cessation of acceleration at 3.4–4.0 G_z, and 1.5–2 min after cessation of acceleration at 5.0–7.0 G_z. Experiments with animals are probing the nature and mechanism of higher nervous activity disruptions during acceleration. Experiments with motor-defense reflexes [231] and with food reinforcement [180] indicate that conditioned reflex changes are observed as early as 1.5–3.0 G_z. These acceleration levels primarily damage internal inhibition, cause phase phenomena, and, as accelerations become higher, full inhibition of conditioned reflexes. At the beginning of acceleration, an increase in excitability of the cerebral cortex is observed. These investigation results have been confirmed and expanded [156].

The application of $+G_z$ forces also causes significant changes in brain bioelectric activity [1, 98, 99]. Slight accelerations of $+2.0$–3.5 G_z result in a significant increase in frequency and

TABLE 6. — *Disruptions in Visual Function and Changes in Fundus Oculi with* $+G_z$ *Acceleration* [65]

Stage	Subjective sensations	Objective data
I	Loss of peripheral vision	Pulsation of arterioles, periodic discoloration
II	Blackout	Evacuation and spasm of arterioles
III	Restoration of central and peripheral vision	Restoration of pulsation of arterioles and temporary expansion of veins

amplitude of rapid fluctuations and depression of slow waves, while greater accelerations of +3.0 to 6.0 G_z initially cause δ-waves, which are later replaced by full depression of bioelectric activity.

An analysis of available materials leads to the conclusion that $\pm G_z$ forces cause phasic changes in CNS functions, determined by value and time of accelerations, direction of the inertial force vector, animal species and their initial functional condition.

The effect of transverse $\pm G_x$ forces on CNS functions is characterized by the same changes recorded for $\pm G_z$. Experiments with human subjects established that with an acceleration of +3 G_x, latent conditioned reflex periods are slightly shortened. When G forces increase to +5 G_x, conditioned reflexes pass through two phases. First, there is a significant elongation of latent present reflex periods, while latent periods of trace reflexes are shortened. Subsequently, with greater elongation of latent periods of present reflexes to both light and sound stimuli, there is some elongation of latent periods of trace reflexes with simultaneous sharp increases in numbers of errors. Pronounced inhibition of conditioned reflexes arises. In some experiments, following elongation of latent periods of trace reflexes, visual disorders or even fainting arose [36]. These results were later amplified in experimentation with both humans and animals.

Phasic changes in the functional state of the CNS were found applicable to various conditions in a number of later experiments using electroencephalograms (EEG) [20, 74, 75, 221]. In the first phase, immediately after application of acceleration, there was a significant increase in the number of fast potentials, with simultaneous decrease in amplitude—the reaction of EEG desynchronization [96]. In the second phase, there were high-amplitude slow waves—the reaction of EEG synchronization. The third phase, occurring only with accelerations over 6.0 G_z, showed deepened synchronization of cortical bioelectric activity with decompensation of cardiac activity and respiration.

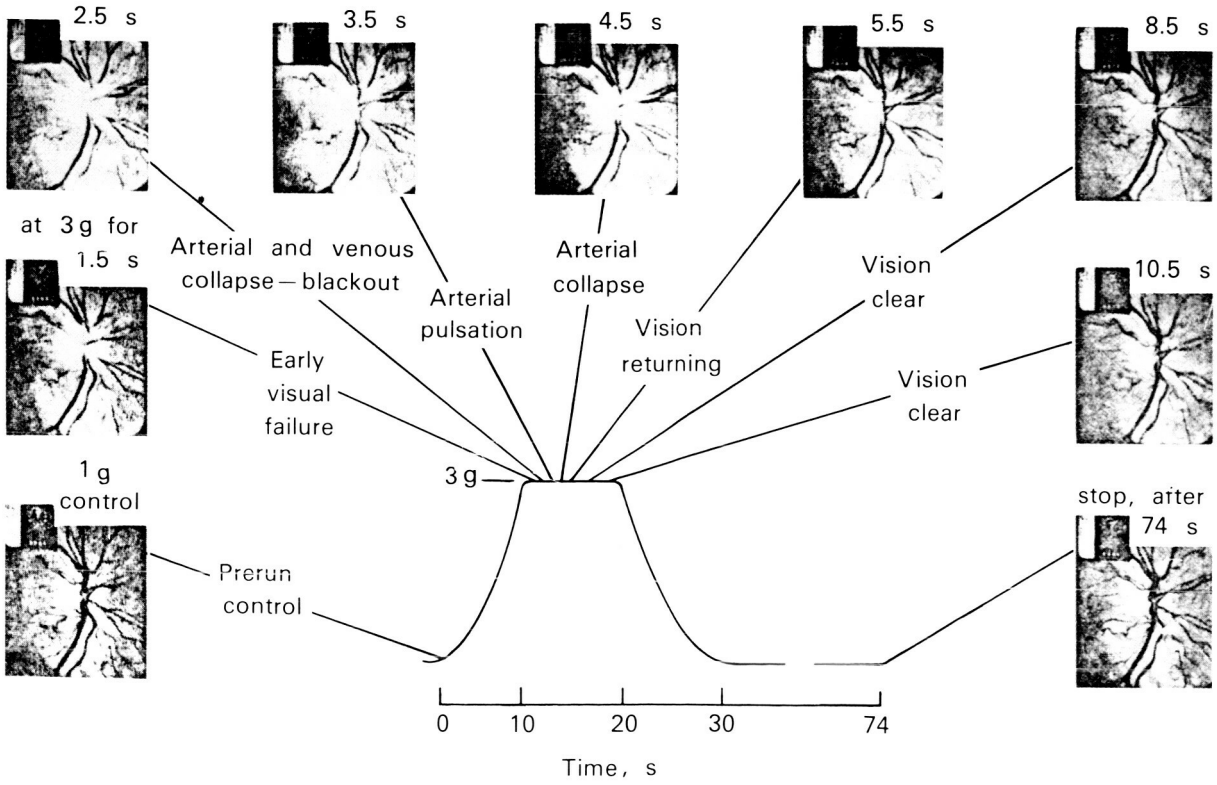

FIGURE 25.—Dynamics of change in circulation in retinal vessels of human subjects during exposure to $+G_z$ acceleratory stress [153].

The desynchronization phase in human subjects was observed with longitudinal forces of 3.0–4.0 G_z, and transverse forces of 5.0–8.0 G_x [75]. The phase of exalted α-rhythm began during longitudinal forces of 5.0–7.0 G_z and transverse forces of 8.0–10.0 G_x. With further increases in acceleration, the slow θ- and δ-waves predominated, usually preceded immediately by visual disorders. Rabbit experiments showed that during the first phase, when there was desynchronization in the cortex, synchronous oscillations of the primary rhythm (5–6/s) increased in the reticular formation and hypothalamus. Under accelerations of + 7.0 G_x, high-amplitude slow waves appeared in the cortex. At this time, slow high-amplitude activity was also noted in the hypothalamus, while reduced amplitude of the primary rhythm, compared to initial data, was recorded in the reticular formation. Then a significant shift in the direction of faster oscillations occurred in the potentials recorded from the hypothalamus. During aftereffect, first the cortex was restored, then the hypothalamus, and finally, the reticular formation.

Functional disorders are often accompanied by histochemical and histological changes [119, 122].

The disruption mechanism of CNS function during acceleration has not been conclusively clarified. Most authors place primary significance on the developing of hypoxia [4, 21, 73, 186], but some believe that the most important aspect of the mechanism is strengthened afferentation from deformed organs and tissues [179]. Thus, accelerations cause functional disorders not only in the cerebral cortex, but also in many other CNS formations [154]. These functional shifts lead to disruptions in regulation and coordination of the CNS, and often reduce man's working capacity.

Endocrine Glands

There are numerous reactions in the endocrine apparatus under the influence of acceleration. The combination of changes is sometimes protective and adaptive, at other times, pathologic. Study of the influence of acceleration on endocrine gland functions must place emphasis on the condition of the sympathetic-adrenal system and the hypophysis which is significant in the body's reactions to various stresses [184].

A one-time application of acceleration causes an increase in the content of adrenalinelike substance in the blood, while repeated exposure to acceleration may cause a significant decrease [14, 81, 102]. No definite correlation between the organism's resistance to acceleration and changes in adrenaline content of urine has been determined [81]. According to observations, however, secretion of noradrenaline is always greater when there is high resistance to acceleration than when resistance is low. However, the secretion of catecholamines increases in both types with increasing acceleration [157].

Decreased resistance to acceleration in adrenalectomized animals has been noted [67, 163, 167] (Fig. 26) and restoration of resistance after parenteral injection of cortisone and hydrocortisone. Data on the effectiveness of the use of deoxycorticosterone acetate (DOCA) are contradictory [34, 167]. Morphological and histofunctional studies [119, 143, 162] indicate cyclical restructuring and stress on adrenal function under acceleration influence. The stressed function often leads to damage of medullary substance cells, with degenerative vacuoles, and indications of other serious damage. Following extended and repeated application of acceleration to white rats and guinea pigs, the weight of the adrenals increased and the relationship between cortical and medullary substances changed, predominantly the latter [59, 136].

The reaction of the hypophysis to acceleration is a complex, multiphasic process. Following 1 to 2 hours' spinning on a centrifuge, the content of corticosteroids in blood plasma usually increased in all animals studied [68]; subsequently, depending on the degree of acceleration, there was either further decrease or increase. In experiments with rats under 4.5 G acceleration, an increase was noted during the first hour in corticosterone concentration by a factor of 4; after 2.5 hours, the content increased by a factor of 7; longer exposure to acceleration resulted in a gradual reduction in its content. Under maximum tolerable negative G (– 25.0 G_z), an increase was noted in synthesis and secretion of hormonal substances by the somatotropic and

adrenocorticotropic cells, with almost total cessation of secretion of thyrotropic and gonadotropic cells.

In studies on rabbits and white rats under $+G_z$ acceleration, there were deep phasic changes in neurosecretory processes in cells of the supraoptic and paraventricular nuclei of the hypothalamic area. In the first phase (increase in functional stress), the antidiuretic activity of the blood plasma increased. Neurosecretions of the anterior portion of the hypophysis decreased [158], which was considered an indication of increasing concentration of antidiuretic hormone in the blood [158]. Acceleration resistance of hypophysectomized animals increased (Fig. 26) and acceleration tolerance decreased upon injection of ACTH before rotation [163].

The reactions and roles of the other endocrine glands during acceleration remain physiologically insufficiently studied. In rat experiments, removal of the thyroid increased survival rate by approximately 38% compared to intact animals, while injection of thyroidin (unpurified extract) decreased survival [167]. This change in resistance to acceleration was considered a result from change in intensity of metabolic processes, in particular, oxygen uptake. Similar data are available on the role of the thyroid gland in animal resistance to $-G_x$ [67].

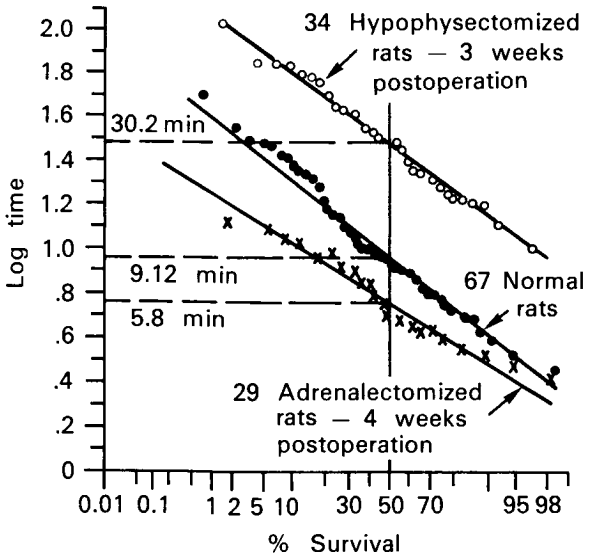

FIGURE 26.—Influence of hypophysectomy and adrenalectomy on survival rate of rats under $+20$ G_z acceleratory stress [163]. Ordinate shows logarithm, of survival time, abscissa shows survival rate, %; horizontal dashed line shows mean survival time, min.

The functional state of the hypothalamus-hypophysis-adrenal system and the other endocrine glands may change significantly under the influence of acceleration; yet, these glands are important in the organism's reaction to acceleration effects of various magnitudes and directions.

Acceleration influences blood distribution in the body, as well as indicators of morphological, chemical, and physical properties of the blood [186]. That acceleration causes hyperglycemia was established some 20 years ago [34]. In later studies with comparatively low values of $+G_z$, changes were noted in the content of acetylcholine [14, 102, 212], adrenalinelike substances [81, 119, 212], histamine [102], serotonin [102], electrolytes [14, 78], transaminase [176, 241], and a number of enzymes, proteins, and other indicators [119] in the blood. The nature and depth of these changes vary primarily with the value and time of acceleration.

There are changes in the composition and values of formed elements in animals and man subjected to $\pm G_x$ forces [14, 69, 186]. Studies on apes [132] under accelerations up to $+10$ G_x showed decreased erythrocytes and hemoglobin, segment-nuclear leukocytosis, and damage to genetic mechanisms of bone marrow cells. Similar data resulted from experiments with mice, rats, and dogs [58, 62]. In addition to changes already noted, these experiments revealed a depression in the mitotic activity of bone marrow cells and increased frequency in disruptions of the nuclear apparatus (adhesion and restructuring of chromosomes).

Different data were obtained in experiments on white mice exposed to -25.0 G_x [213]. Increases were detected in hemoglobin and in the number of erythrocytes in the experimental animals' blood, as well as pronounced leukopenia, reticulocytosis, and an 8–10% increase in polychromatophils. The leukocytic composition showed neutropenia, lymphopenia, and some eosyinopenia. There was an increase in erythrocyte volume with simultaneous decrease in the mean corpuscular concentration of hemoglobin, as well as expansion of osmotic resistance boundaries of red blood cells.

Morphologic studies of bone marrow [246] indicate activation of the erythropoietic and granulopoietic functions following $+G_x$ stress. Erythropoiesis normalizes 1.5–2.5 months later [132, 246], and after the same time, normal values of hemopoiesis in the regional lymph nodes are restored [119]. Under the influence of $-G_x$, anticoagulation properties of the blood increase (activation of fibrinolysis, increase in content of heparin, decrease in quantity of procoagulants) [187]. There is normalization of these indicators 5 days after rotation is stopped. These data are not in agreement with findings of pronounced tendency toward thrombosis in experiments with apes [14]. In spite of intense studies on acceleration influence on the blood system, unsolved problems require further experiments.

Gastrointestinal Tract

The influence of acceleration on the function of the digestive organs has not yet been sufficiently studied. In experiments on cats which were given barium sulfate with food, there was delay in evacuation of stomach contents after exposure to moderate accelerations. A direct dependence was noted between the duration of holding food mass in the stomach and the degree of acceleration [186]. Similar results were obtained in experiments on rats [34, 230] (Fig. 27).

The classical methods of Pavlov were used in experiments on dogs, with clinicophysiologic observations of humans, to study the influence of positive ($+G_z$) and negative ($-G_z$) forces on the evacuatory function of the stomach, as well as the secretory function of the salivary, gastric, and intestinal glands [208, 211]. It was established that the $\pm G_z$ inhibited hunger contractions of dogs' stomachs for 1–1.5 hours. The nature and direction of changes in secretion of digestive tract glands were similar for $+7$ and $+9$ G_z for 20 s and -3 and -5 G_z for 20 s, consisting of initial inhibition of secretion, later replaced by excitation. An increase in intestinal secretion, accompanied by an increase in the dense portion of the juice and change in amylase and phosphatase activity, were observed a few days to a few weeks after exposure to acceleration. These results were confirmed in later studies [164] on the secretory function of the stomach and the small intestine under transverse forces ($+G_x$). Changes in enzyme activity and duration of enzymatic disruption under this type of acceleration was less than with longitudinal acceleration.

Studies on humans with $+G_z$ and $+G_x$ also showed a multiphase secretory reaction – initial inhibition, followed by stimulation. Motor activity of the stomach under ± 5 G_z did not change significantly [208]. With repeated application of accelerations at intervals of 4–5 days, adaptation phenomena developed: inhibition time of salivary secretion was significantly shortened, while the dense residue in the saliva decreased less; changes in amylase content were not observed, nor secretion of acid stomach juice of the empty stomach. The primary genesis of these changes in the secretory-motor function of the gastrointestinal tract is in disruption of interrelations between tonus of the sympathetic and parasympathetic nervous system and nervous-humoral regulation [166].

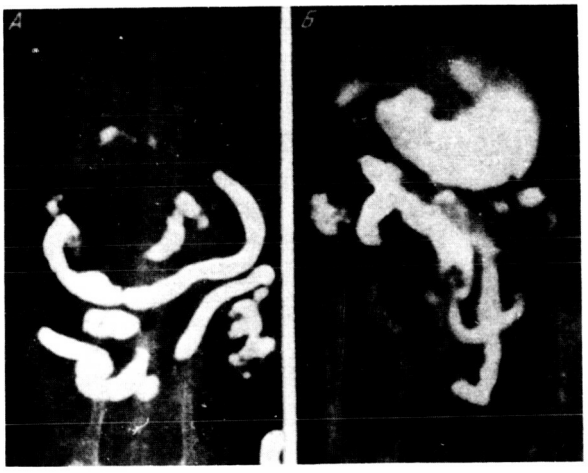

FIGURE 27. – X-ray of gastrointestinal tract in rats following $+G_x$ acceleratory stress [230]. Three hours after injection of barium sulfate: A, control animal; B, following stress.

In a study of the influence of G forces on activity of the digestive glands [37], systematic studies were first performed on the juice and enzymatic functions of the pancreas during and following $+G_x$. In experiments with dogs subjected to $+8$ G_z for 3 min, disruption of the

secretory function of the pancreas was observed: hypersecretion alternated with hyposecretion; the secretory reaction to food stimulus was distorted; and quantitative and enzymatic composition of secretions was disrupted. Restoration of the function required 4 weeks or more. Adaptive reactions of the pancreas following repeated exposure to acceleration appeared to be significant.

In experiments on dogs subjected to positive transverse forces of 4.0–10.0 G_x, there was reduction in bile released and slight increase in concentration of bilirubin and bile acids, retained for 2 weeks. These changes subsequently became uneven, and were restored to the initial level only after 50–60 d [155].

Comparatively slight accelerations cause significant changes in functions of the digestive organs, due to structural and biochemical changes [119]. The literature should probably be referred to in developing regimens and rations for feeding, particularly in the days and weeks following takeoff and landing.

Renal System

Pilots subjected to a stress of 6.0–8.0 G_z frequently manifested erythrocytes in the urine, and in some cases granular cylinders [133]. Similar results were obtained in 10% of experiments with humans [71] and animals [185] rotated on a centrifuge.

Diuresis following +2.0–5.0 G_z was studied in rats, which established that polyuria developed and was maintained for 5–6 h, and concentration of chlorides in the urine was significantly reduced [186].

Contradictory results were obtained in other experiments [198] —stresses of+3 G_z caused the quantity of urine following ingestion of water to decrease from 12.5 ml/min to 7.5 ml/min, while its specific gravity increased from 1.0008 to 1.0086. These data were confirmed with transverse acceleration; however, under these conditions, oliguria developed only after exposure to forces of +7 G_x and more.

Seven dogs were fitted individually with tapped ureters (method of Orbeli) for a study of glomerular filtration, capacity of kidneys for osmotic concentration, and liberation of sodium and potassium before and after exposure to loads of +5.8 and +12.0 G_x. Immediately after acceleration, there was a brief period of oliguria followed by increased diuresis [225]. The degree of these changes is determined largely by the value of the $+G_x$ force. Exposure to twelvefold G-loads causes increases in urine production, excretion of potassium and sodium, and reabsorption of osmotically free water. However, these changes are usually normalized after 1.2–2 h, and all indicators return to their initial levels.

The water-loading experiments indicate that ability of the kidneys to pass water does not change under repeated acceleration: the function of kidneys for hypotonization of urine, reabsorption of sodium and potassium (and as indicated by other factors) is not disrupted. Protein appears in the urine in slight quantities and disappears after 1.5–3 h. The urine precipitate contains leukocytes, epithelial cells, and fresh, unleached erythrocytes. The data would appear to indicate that the changes resulted primarily from activation of the hypothalamus-hypophysis system.

The importance of neurohormonal mechanisms in changes of kidney function was also noted in experiments with six healthy males subjected to $+4G_x$ [235]. The starting mechanism was considered to be stimulation of volume receptors of vessels in the thorax when fully filled with blood. Under acceleration, similar to the experiments with dogs, brief inhibition of diuresis (20–35 min) was followed by a slight transient increase in glomerular filtration.

Humans subjected to loads up to +10 G_x showed a slight increase in diuresis, clearance, endogenic creatinine, and erythrocytes [109]. Diuresis was attributed to changes in kidney hemodynamics and increasing glomerular filtration. Accelerations also caused various morphologic changes in kidneys of experimental animals [120] which, as a rule, were transient following single exposure to acceleration.

Hematuria following acceleration is believed to result from disruption of blood circulation in the kidneys, increase in the permeability of the capillary walls of the glomeruli, the main membrane, and internal layer of the capsule [107].

WORK CAPACITY UNDER THE INFLUENCE OF ACCELERATION

Studies of work capacity under the influence of acceleration are significant in regard to astronaut activity. During space flight, the astronaut must be in control of the spacecraft, perform diverse maneuvers during various flight stages that require rapid reactions, solve a number of problems, and maintain precise coordination of motions and physical strength. Acceleration effects may cause unfavorable organic and systemic reactions and finally be reflected in the operator's work capacity. Such phenomena relate primarily to disrupted processes of afferent perception, changes in functional state of CNS, and limitations in mobility of operating organs.

Changes in visual perception are vital in an operator's work under acceleration. Depending on the value, duration, and direction of acceleration, a delay in reaction to light may relate to the value of the acceleration, or to the period of acceleration immediately preceding grayout, or to reduced perception of contrast in visual images, particularly with low light levels and diminished ability to distinguish colors [41, 206, 238]. With sufficiently high $+G_z$ and $+G_x$ forces, deterioration in visual perception may lead to total loss of vision.

Processes of auditory perception under the influence of acceleration have received limited study. It has been established that with $+G_z$ and $+G_x$ loads, auditory perception, based on reaction time to sound, is retained significantly longer than the visual function [43, 220].

While the significance of proprioceptive and vestibular stimuli under the influence of acceleration in flight is acknowledged, this problem remains open concerning questions of work capacity. Centrifuge experiments revealed reduced ability to solve arithmetic problems and perform psychological tests, reductions in the critical flicker fusion frequency and short-term memory capacity [93], and deterioration in the results of compensatory tracking [60]. The severest disruption in brain functions, and consequently, work capacity, is under the influence of $+G_z$ forces before loss of consciousness. The condition of motor functions is important in maintaining work capacity under acceleration.

Mechanical forces make the work of the muscle groups more difficult, thereby limiting the motions of working organs. In a centrifuge experiment, large-amplitude motions and generalized locomotor acts such as walking, running, and crawling suffered the most [53]. For example, straightening the trunk becomes impossible at $+4$ G_z; while at $+8$ G_x and higher, it is impossible to raise the body and the extremities. However, motion of arms in the carpal joint was possible up to $+25$ G_x. Under these conditions, professional activities are possible only by systematic repetition of motor skills already well-learned.

Another aspect of work capacity under acceleration is determining the operator's effectiveness and reliability in a "man-machine" system, which was studied in detail [72]. An effort was made to coordinate the characteristics of a man-machine system under conditions of acceleration in order to increase the reliability of the operator's work [19]. In a system simulating manual control of the spacecraft's descent to Earth, it would be expedient to include an auditory signal indicating a mismatch with the desired return trajectory in addition to a visual signal. Such a combined system is necessary due to the possibility of vision loss at forces of $+14.0$ to $+16.0$ G_x, in order to assure satisfactory control quality up to loads of $+18$ G_x (Fig. 28).

Finally, the problem of man's working capacity under the influence of acceleration requires broad experimental studies to establish requirements for control systems to be used when the operator is subjected to long exposure to acceleration.

REACTIVITY OF THE ORGANISM DURING AFTEREFFECT OF ACCELERATION

Reactivity, in the generally accepted meaning, is the body's property of responding to the effects of the external environment. Reactivity, then, expresses the relationship (balance) between the body and the environment [2].

The secretory and motor functions of the gastrointestinal tract show, for an extended period following acceleration, alternately reduced and

increased response reaction to mechanical, chemical, and food stimuli [37, 166, 211].

The organism's reactivity also changes sharply relative to pharmacologic agents [160, 181, 224]. After extended exposure to transverse accelerations, animals exhibited increased sensitivity to cardiac glycosides (Fig. 29), narcotics, and other preparations, and decreased sensitivity to analeptics and analgesics. There are changes in the body's reactions to ingestion of radiation protectors (Fig. 30) and autonomic nervous system mediators. For example, the increase in motor activity of white mice following injection of Phenamine (Benzedrine, amphetamine) following application of acceleration is less clearly expressed (Fig. 31) than in control animals, indicating a decrease in the specific effect of this preparation. The analgesic effect of 1, 2, 5-trimethyl-4-phenyl-4-propionyloxypiperidine hydrochloride (Promedol) and certain other pain-relieving substances is reduced. Acceleration significantly changes the reaction of an animal's body to ionizating radiation [181, 248].

Preliminary application of stress (−10 G_x for 15–30 min) increases by 15–23% the survival rate of mice irradiated at a dose of 700–750 R in air [181]. Animals which were subjected to various values of acceleration and subsequent irradiation with x-rays or γ-rays, as well as high-energy protons, provided the conclusion that sequential exposure to acceleration and radiation, with intervals of 4 to 24 h between, results in an increase in $LD_{50/30}$ by 100 R in comparison to radiation alone. This is explained by an increase in activity of the hypophysis-adrenal-cortical link of the neuroendocrine regulation system under the influence of acceleration, manifested by increased catacholamines and serotonin in the blood, with increased ceruloplasmin activity and other biochemical indicators.

During the aftereffect following acceleration, there are changes in endurance of physical loads, increase in resistance to acute hypoxia and electric trauma, and a decrease in resistance to overheating and overcooling [192]. In centrifuged mice, there is definite correlation between changes in content of ceruloplasmin, biological activity of the blood, and physical endurance [7] (Fig. 32).

Immunobiological reactivity is disrupted in

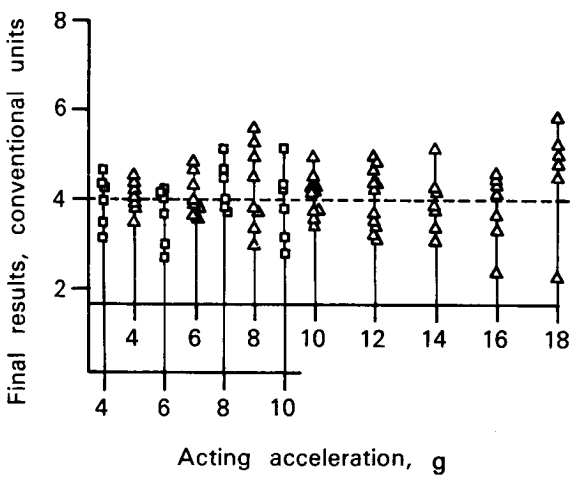

FIGURE 28.—Deviation of final regulation parameter from calculated value with $+G_x$ acceleratory stress [19]. Dashed line (----): calculated value of final result; □: value of final result using light-sound indication; Δ: value of final result using only sound indication.

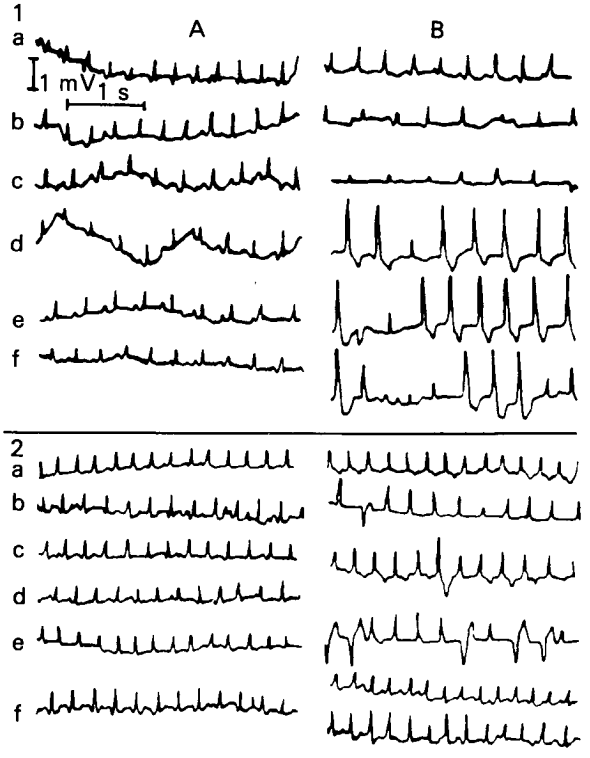

FIGURE 29.—Change in ECG of apes [2, 3] following injection of strophanthin after exposure to +12 G_x acceleratory stress [224]. A: before stress; B: 20 min following stress; a: before injection of strophanthin, dose 0.05 mg/kg body weight; b, c, d, e, f: 1, 3, 5, 7, and 15 min following injection of strophanthin, respectively.

animals subjected to acceleration [3, 188]. A clear dependence on the value and time of acceleration is noted by the nature and degree of changes in the phagocytic function of neutrophils, and bactericidal activity of the blood and saliva. With slight or brief applications of acceleration, immunobiological activity is stimulated, while greater accelerations cause its depression. For example, with forces of -9 G_x and particularly, -12.0 G_x, the absorptive function of the neutrophils and bactericidal properties of skin and saliva were reduced, thus reducing the body's resistance to pathogenic microbes. In experiments with artificially induced acute *Staphylococcus* infection, the death of mice subjected to -30 G_x acceleration was 38% greater than in the controls.

Thus, during aftereffect following acceleration, reactivity of the organism is altered, despite almost complete restoration of basic somatic and autonomic functions recorded at rest (cardiovascular system, respiration, and CNS) to their initial level. Reactivity is increased relative to some environmental stimuli, decreased relative to others, and distorted relative to still others. Knowledge of the nature and depth of possible changes in reactivity during various stages of aftereffect following acceleration, and of the incompletely understood physiologic mechanisms, is necessary for proper selection of medical tactics (recommendations and requirements, preventive and therapeutic measures).

ADAPTATION AND CUMULATION EFFECTS OF ACCELERATION

The influence of adaptive and cumulative effects of acceleration on humans and animals is of scientific and practical significance in preparing man for space flight. The literature indicates that resistance of the organism may increase following repeated exposure to acceleration [34, 71, 72, 164], which, on the other hand, may cause cumulative negative effects [78, 191].

Trained pilots can better tolerate the effects of acceleration in flying than can untrained pilots. Repeated exposure to longitudinal $+G_z$ during several days helps to increase resistance of the organism, but frequent repetition during a single day may have the opposite effect [9]. However, the literature contains as many or more reports indicating the possibility of negative effects and damage to the body following repeated exposure to acceleration.

Daily exposure of apes to acceleration for 3 weeks led to pronounced pathologic changes in kidneys [191], disruptions at the cellular membrane level [78], and dystrophic changes in walls of the cerebral vessels [102]. Extended and repeated exposure to acceleration produced damage to the right ventricle myocardium in rats and apes, which appeared in both ECG and autopsy (myocardial hemorrhage) [86, 98]. The degree and nature of disruptions described by various authors were not the same, and resulted from differing experimental conditions. Repeated application of acceleration caused increased resistance in some animals and significant decrease in others [179]. Frequent repetition of acceleration led to profound morphologic changes in the organs, but long intervals between experiments helped to decrease the pathologic changes [103].

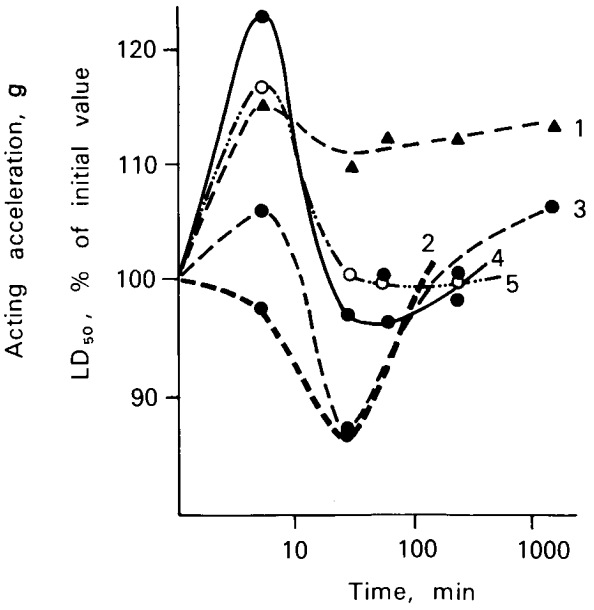

FIGURE 30.—Influence of transverse acceleration on mortality of white mice injected with toxic doses of radiation protectors [7]. 1: 5-methoxytryptamine (-10 G_x, 15 min); 2: s-β-aminoethylisothiuronium bromide hydrobromide (-10 G_x, 15 min); 3: cystamine (-10 G_x, 15 min); 4: cystamine (-30 G_x, 15 min); 5: cystogen (-10 G_x, 15 min).

The duration of acceleration is considered highly significant. For example, it was shown that forces of +8.0 to +12.0 G, lasting up to 15 s, caused no cumulative effects in dogs, even though repeated daily for 26 d [239]. However, when these accelerations were applied for a longer time, significant deterioration in the animals' condition resulted. A combined study of body processes in dogs under the influence of $+G_x$ forces (3.0 to 12.0) applied repeatedly revealed indications of adaptation reactions [112]. Upon repeated application of acceleration, changes in the dogs' respiration, energy expenditures, and hematological and biochemical indicators showed development of adaptive reactions. However, pathomorphological studies indicated structural disruptions in various organs and tissues [106, 108, 119, 120]. Consequently, with repeated exposure to $+G_x$, various effects are adaptive, but on the other hand, clearly show cumulative damage [112].

Thus, incomplete data in the literature do not indicate any conclusive agreement on aftereffects of repeated acceleration. While data indicate the possibility of adaptational changes, possible cumulative negative effects must also be acknowledged. Findings indicate manifestation not only of functional changes, but also of significant structural damage to tissues. However, various body changes doubtlessly result from the modes used in acceleration: value, direction of vector, duration, gradient of increase, frequency of repetition, and intervals between application. It is important to clarify the various aspects of this problem for the development of systems to train man, prior to space flight, to tolerate acceleration.

In designing a system of training on the centrifuge, it is not feasible to draw a complete analogy with sports training. Under acceleration, an abnormal factor acts on the body, while in sports training the organism experiences elevated loads—for which it is adequately adapted through evolution. The solution of this problem requires an approach that must take into consideration the establishment of optimally tolerable acceleration modes, repetition frequencies, individual resistance, and conservation of training effects.

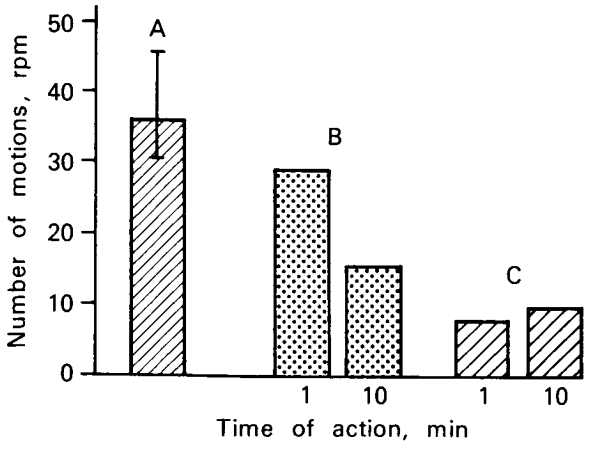

FIGURE 31.—Motor activity of white mice following injection of Phenamine, dose: 10 mg/kg [224]. A: Control animals; B: following exposure to -10 G_x acceleratory stress for 1, and 10 min; C: following exposure to -40 G_x acceleratory stress for 1, and 10 min.

MECHANISMS OF THE INFLUENCE OF ACCELERATION

Acceleration causes functional and morphologic changes in various systems in the body.

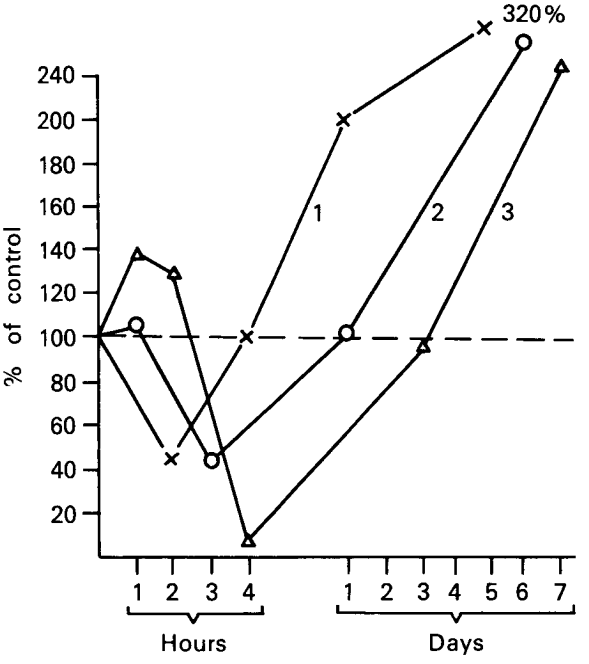

FIGURE 32.—Comparative data on changes in activity of ceruloplasmin. 1: Biological activity of blood; 2: mean effective floating time; 3: following application of acceleratory stress [7].

The most important direct effects of acceleration are blood redistribution in the vascular system, lymph flow impairment, organ displacement, tissue deformation, disruption in respiration, and stress reactions. The specific significance of these primary acceleration mechanisms will change depending on the direction of the acceleration vector. Thus, during longitudinal acceleration, circulatory hypoxia of the brain is the most significant development. Application of acceleration produces visual disorders and when continued or intensified, loss of consciousness and convulsions. At the same time, a decrease is noted in the blood flow to the heart, causing it to overwork.

During transverse acceleration, respiration difficulties are important in the mechanism of disruption. Hypoxemia also develops as a result of strong pressure on the thorax, as well as disruption of blood oxygenation in the lungs from hemodynamic disorders. When the heart cavity and blood vessels of dogs were probed [104, 232, 243] after forces of +2.0 to −9.0 G_x, it was found that venous blood is first pooled, then shunted to pulmonary veins, and oxygenation disrupted, causing reduced volumetric content of oxygen in arterial blood. Consequently, respiratory disruption and hemodynamic disorders lead to hypoxemia and hypoxia of such important organs and tissues as the brain and heart [121, 197]. The unusual flow of afferent impulses facilitates development of central regulatory disorders, which in turn reduces the body's compensatory-adaptive capabilities. Changes in the endocrine glands resulting from disruptions in CNS regulatory activity and hypoxia cause still greater disorders in the body's various systems.

The primary components of the mechanism by which acceleration influences the body's functional systems are schematically presented in Figure 33. Accelerations sometimes become extremely irritating, severely disrupting normal vital processes with a traumatizing or even destructive effect on biologic objects.

Two phases of reaction to G forces have been distinguished [175]: (1) compensatory changes in the body in which primarily the vital functions are reinforced, while some are adaptively suppressed temporarily and others somewhat disrupted; (2) decompensation, in which there is depression and suppression of vital bodily systems.

During the first phase, there are increases in heart rate, blood pressure, volume of blood pumped per minute, regional blood flow, pulmonary ventilation, oxygen uptake, and even an increase of oxygen tension in brain tissues. At the same time, endocrine gland activity is

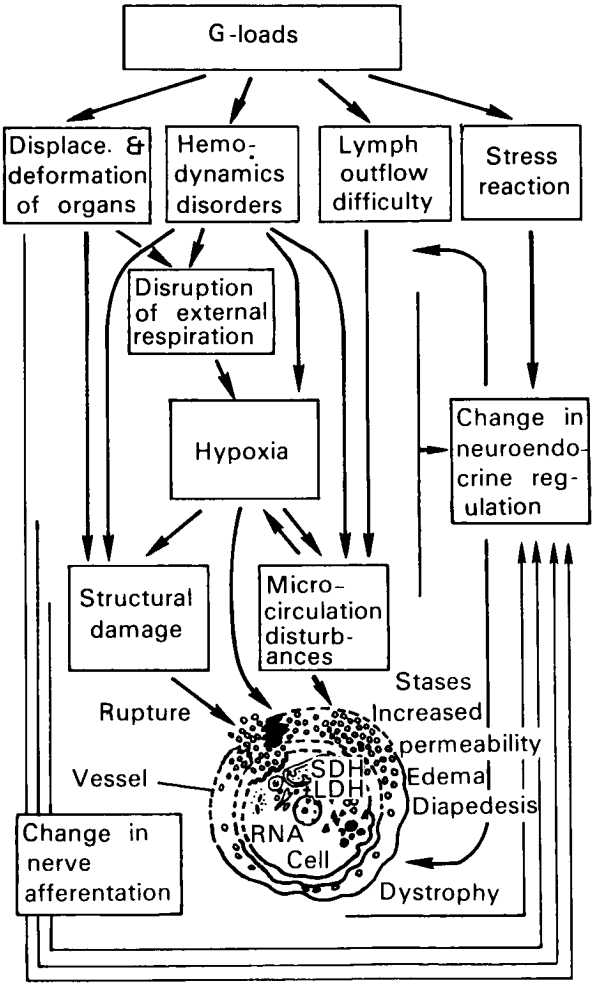

FIGURE 33.—Basic mechanisms of acceleration action on the organism [120]. Changes in the cell: increased activity of lactate dehydrogenase (+LDH); reduction in activity of succinate dehydrogenase (−SDH); reduction in quantity of ribonucleic acid (−RNA) in cytoplasm.

strengthened as judged from an unmistakable change in peripheral blood composition, increase in cholesterol content of blood, and other indications [119, 246]. Changes in the volume of histamine, adrenaline, acetylcholine, potassium, and sodium as reactions to slight and moderate accelerations are also believed to be indications of adaptive reactions [14].

The second phase, interruption of compensation, is manifested by relative or absolute bradycardia, disruption of heart rhythm and conductivity, drop in blood pressure, disruption in redox processes of vital organs [197], regulatory disorders of nervous and endocrine systems, and so forth. These lead to extreme functional and morphologic changes not only at the body, organ, and tissue levels, but also at cellular and subcellular levels [119, 120]. Long-term exposure to high G forces may cause death, usually as a result of cardiovascular or respiratory insufficiency. Another phase of nervous and emotional stress has been suggested [210]: increases in frequency of pulse and respiration, cardiac minute volume, EEG desynchronization, and so forth, immediately before acceleration application, and an aftereffect phase of restoration and normalization of functions. Other models have been described in the literature, establishing relationships, sequence, regularities, and periodicity of the organism's reactions to acceleration effects.

METHODS OF INCREASING RESISTANCE TO ACCELERATION

The search for methods to increase the body's resistance to long-term acceleration has become particularly important since maneuverability of aircraft is now limiting the body's physiologic tolerance.

The rapid development of rocket technology and space flight requires further investigation of anti-G-load measures. The development of effective methods would affect the mode of spacecraft injection into orbit by more fully utilizing the power of rocket engines, increasing the working capacity of crewmembers during the injection into orbit and descent to Earth, and providing more reliable protection in emergencies. These are particularly important in the return of spacecraft to Earth and landings on other planets following extended periods of weightlessness, which may cause pronounced disorders in blood circulation, general asthenization of the body, and other problems.

Increased resistance to accelerations is being sought a number of ways:

1. Mechanical methods
   - anti-G compensating suits
   - special seats for maintenance of optimal position to the acceleration vector
   - individual contoured supports
   - immersion systems
   - breathing under elevated pressure
2. Physiologic methods
   - physical training (specific, nonspecific), general toughening of the body, centrifuge training
   - adaptation to hypoxia
   - changing body reactivity through pharmacological agents and cooling (hibernation)
3. Combined methods

There are advantages and drawbacks to each of these methods.

Anti-G suits (*G-suits*). The primary pathogenic link during $+G_z$ acceleration is displacement of blood from the head and upper sections of the trunk to vessels in the abdominal cavity and lower extremities. The first G-suit models were designed in the early forties to hinder such redistribution of blood under the influence of inertia. G-suits in use at present operate by creation of counterpressure on portions of the lower half of the body. As accelerations increase, pressure in the rubber chambers surrounding the stomach and legs is automatically increased: the greater the G forces, the higher the pressure in the suit.

A detailed physiologic explanation of methods for increasing resistance to accelerations is not necessary since there are many such studies [72, 73, 95, 186, 189, 219, 240]. The use of G-suits has been effective in maintaining many of the body's functions. Arterial pressure in the carotid and brachial arteries is maintained at a higher level, the influx of blood to the brain and heart is improved, and fewer changes are observed in

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vision, bioelectric activity of the myocardium, conditioned-reflex activity and energy expenditure, and so forth. Results from testing in centrifuges, as well as during aircraft flights using various criteria of evaluation have shown that man's resistance increases by 0.8–1.3 G_z when such suits are used [127, 128].

Modern G-suits and improved methods for their use can increase resistance by 2.0–2.5 G_z [42]. In spite of many design studies, further improvement in the effectiveness of G-suits is not likely; at present, they are used primarily for $+G_z$ acceleration. However, the protective influence of G-suits, including decrease in visual disorders, is effective for transverse accelerations of up to $+15.0$ G_x [48]. Other methods of increasing acceleration tolerance are being investigated.

Seat back angle inclination and subject position. The greatest tolerance for acceleration is observed when it is applied transversely to the main blood vessels in the human body (noted previously). Special studies to find the optimal position of a subject under acceleration [31] have established that strict observance is required to the relationship between inclination of the seat back and head support and acceleration vector, as well as between hips, shins, and trunk. The most significant variable is in the trunk and head position. Physiologic studies have established that the optimal inclination of the seat back is 78–80° with regard to the acceleration vector [72, 117, 234].

A tolerance of $+12.0$ G_x with the trunk position inclined to the horizontal plane at 80° was 2–3 times greater in application time than with 65° inclination position [17]. Cardiovascular and respiratory reaction was less intensive in the former case, allowing a higher body resistance as a whole.

Contoured supports. Individualized contoured supports (Fig. 34), which provide a large area of counterpressure, can increase tolerance to 25.0 G_x when the body is in the optimal position in regard to the acceleration vector [48].

Breathing pure oxygen. Respiration and circulation disorders leading to hypoxemia and hypoxia are leading pathogenic factors resulting from transverse acceleration. Experiments on animals and humans have tested the effectiveness of breathing pure O_2 at normal and elevated pressures. If test subjects breathe pure O_2 or a gas mixture under excess pressure, there is a significant increase in acceleration tolerance [12], which is a result of improved gas metabolism in lungs and, consequently, oxygen deficiency is prevented.

Optimal excess pressure for the gas mixture [234] is 2–3 mm Hg/G unit. This helps to prevent changes in respiration indicators and increases tolerance time by 67%, although chest pains do not decrease significantly. On the other hand, some authors are skeptical that breathing under increased pressure will heighten resistance to acceleration. Breathing pure O_2 while undergoing acceleration may cause adverse aftereffects, similar to oxygen poisoning [131].

Immersion systems. There is substantial interest in immersion systems developed by Tsiolkovskiy [217] as a means of increasing acceleration tolerance. Experiments with white mice have produced exceptionally favorable results [149]. When immersed in water, they tolerated forces up to 1300 G for 60 s. Similar data were produced by other researchers [24]. Experiments have also shown that immersion of human subjects in a water tank can significantly increase resistance to acceleration [241]. Effectiveness is determined to a great extent by depth of immersion. Human subjects immersed to the third rib reached accelerations of $+16$ G_z, whereas under ordinary conditions loss of peripheral vision began at 3.25 G_z [48, 82]. When totally immersed in water in a special container

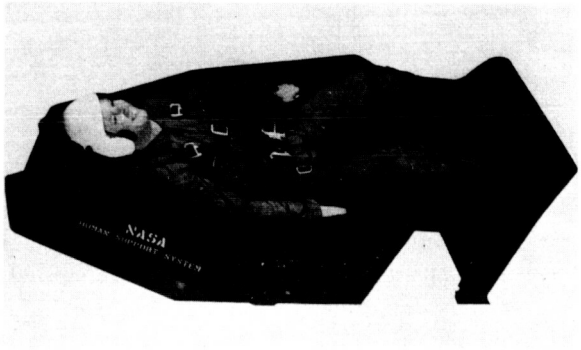

FIGURE 34. – Position of human subject in individual contoured support [48].

(Fig. 35) using special breathing apparatus, resistance to gravitoinertial forces was increased to +26.0–31.0 G, although stomach pains and slight damage to the frontal sinuses were noted. A significant increase in resistance to acceleration from immersion has been corroborated in other experiments [30].

In spite of the great effectiveness of this method, its practical use in modern flight is impossible due to the great complexity and cumbersomeness of immersion systems. Furthermore, placing the pilot in a container filled with liquid sharply reduces his capability to observe and control the spacecraft. Thus, although protection from acceleration by hydraulic systems is valid, other methods to solve this complex problem must be sought. Although some effective methods of protecting the body from acceleration effects have been developed, all physical methods of increasing resistance developed so far depend upon complex devices. Consequently, physical methods using the body's reserves have been studied by means of training, stimulation, and medications.

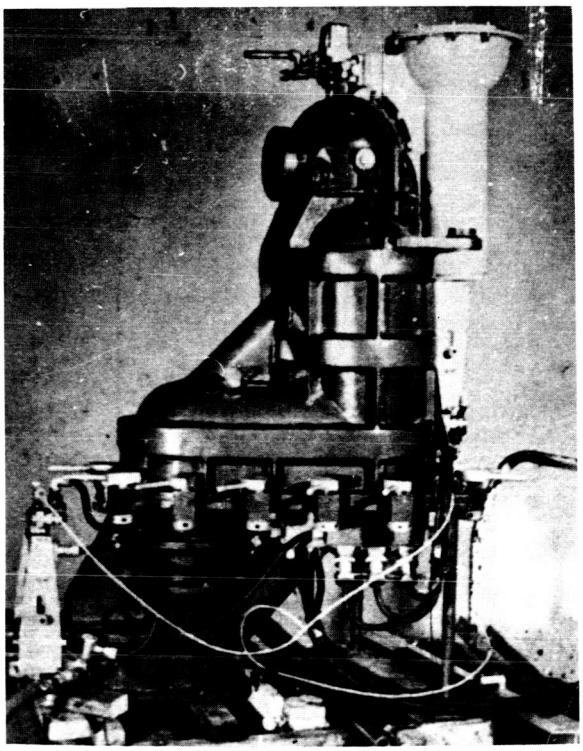

FIGURE 35.—Container used for immersion protection of man from acceleration [48].

General toughening, physical training, and adaptation to accelerations. From observations of many flight physicians, general toughening of the body by special physical exercises to improve the regulatory mechanisms of circulation and respiration, strengthening of abdominal and leg muscles, development of skills in shifting from abdominal respiration to chest type and vice versa, and extended tonic tension in groups of muscles can increase pilots' acceleration tolerance [12]. In studies of sportsmen, it was found that gymnasts, boxers, weight lifters, and sprinters were most resistant to $+G_x$ accelerations [203]. These sports require, by submaximal and maximal work intensity, strength and speed-strength exercises, and a broad range of complex coordinated motions. Data [57] indicating that physical training to develop resistance to acceleration has no positive effect are correct only for specific conditions reproduced in centrifuge testing (total muscular relaxation of subjects). However, it is believed that muscular tension can increase resistance to acceleration, and therefore, regular physical training is probably an important part of the training of both pilots and astronauts.

An increase in the body's acceleration resistance can also be achieved by centrifuge training [11, 34, 71, 142]. Systematic training on the centrifuge can increase man's tolerance by approximately 1.5–2.0 G [32]. In experiments on dogs [202] using physiologic, morphologic, and histofunctional investigation methods, it has been established that with the use of training regimens based on repetition and gradually increasing loads, plus warmups and maximal and submaximal loads, tolerance for transverse acceleration can be significantly increased. In studies with human subjects, centrifuge training using the optimal plan helps increase tolerance by 1.6–5.8 G_x. The effect of training was retained for at least 6 months. Histomorphologic indications of the degree of training for acceleration were also studied [161, 169]. The literature indicates that in addition to training mechanisms for adaptation, exposure to great acceleration for long periods may cause pathologic changes in the body [119, 162].

Adaptation to hypoxia. One of the primary pathogenic mechanisms in $\pm G_x$ forces is oxygen deficiency and hypoxia in the circulatory mechanism. [21, 104, 113, 159, 232]. Therefore, adaptation to hypoxia has been successfully used as one of the nonspecific methods for increasing body resistance to acceleration [114, 194, 227]. Adaptation to hypoxia has been performed both in barochambers and under high mountain conditions.

Animal experiments have convincingly proven that the survival rate of adapted white mice, rats, and guinea pigs under high acceleration was 1.5–2 times greater than the survival rate of a control group. Active adaptation of the animals to hypoxia by systematic physical training was found to be more effective than passive exposure at high altitude. Disruption in the cardiac activity of experimental animals, shown by electrocardiography, began later and was less pronounced [218].

Studies of humans have established that after a stay in the mountains, resistance to $+G_x$ stress of individuals previously unexposed to hypoxia was increased by 2.4 ± 0.2 G_x [114, 227]. The increased resistance of those thus trained, was retained, for the first time, up to 3 months, and significantly longer in mountain climbers who spent vacations in the mountains each year. This method of increasing acceleration resistance might also prove promising for extended space flight [124, 134, 226, 229].

Pharmacologic agents. Pharmacologic agents for increasing acceleration endurance are currently being studied. Although the first experiments started more than 20 years ago [34, 35, 130], such usage was not developed until recent years. In aircraft flights it is not always possible to predict the precise time acceleration begins, which is important for the use of pharmaceuticals, and the specific effects of a number of preparations prevent their use in flight medicine (soporifics, narcotics, phenothiazine series preparations, and so forth). A number of these limitations is eliminated in space flights since spacecraft can be controlled automatically without astronaut participation.

Medicines studied for action on the resistance to acceleration are in these pharmacologic groups: vasoconstrictors [34, 88, 130, 160, 182, 224], vasodilators [129, 183, 224], ganglioplegics [54, 134, 224], narcotics [160, 224], hormones [167, 185, 204, 224], CNS stimulators [34, 183, 224], and other substances [72, 224]. Positive effects resulted from various medicines.

The most favorable results have been obtained with Lucidril (meclofenoxate) and strychnine, sympathomimetic amines, and certain combinations of these substances. Pharmaceuticals (strychnine + caffeine + phenamine) given to test subjects before revolving on the centrifuge after long-term (70–100 d) hypokinesis restored their lowered resistance to acceleration to the initial level or even above it [113, 227]. Thus, pharmaceuticals may be not only effective, but also in certain cases necessary, particularly during descent after extended flights and weightlessness. A complete summary of pharmaceutical influence on human and animal resistance to acceleration (as well as to other spaceflight factors) is in the monograph of Vasil'yev et al [224].

Hypothermia

Deep cooling, in order to save the body under spaceflight conditions, particularly in emergency situations when various factors including acceleration may reach extreme values, is a subject that has received increasing attention recently [27, 29, 44, 226]. A pronounced protective effect was observed in rats cooled to 5–20° only for accelerations over 30.0 g; for accelerations of 20.0 g and less, cooling caused reduced resistance [205]. This difference in the effects of hypothermia is explained by the different mechanisms of animal deaths during different values of acceleration. The positive effect of artificial hibernation in rats, by reducing body temperature to 24–22°, was observed [215]. In these experiments, the survival rate in the experimental group during accelerations of -31 G_x was twice that of the control group. Similar results have been obtained in other studies [61].

Combined methods. The combined application of anti-G forces is the most effective method. In aeronautics, this principle has been used by selecting the proper seat position for the pilot, use of voluntary muscular tension, and the anti-

G suit. The combined application of protective methods against acceleration can be further developed, and effectiveness greatly increased. For example, in experiments on white mice and hamsters, water immersion combined with narcosis and deep cooling of the body increased acceleration tolerance to as much as 1800–2300 g [29]. Water immersion combined with optimal position achieved human acceleration tolerances up to 32.5 g [48]. A comparatively simple means, such as selecting the optimal inclination of the seat back, contoured supports, and respiration under increased pressure, achieved an acceleration tolerance of $+26.5\ G_x$ with a rise rate of 1g/s [17].

These data prompt anticipation that further development of anti-G forces methods will lead to future achievement of more effective protection from acceleration.

PROBLEMS AND METHODS OF FURTHER STUDY

Acceleration, an integral part of space flight, may cause adverse effects in various systems of the body under certain situations. A pathogenetic mechanism primarily producing these disorders must be considered the hypoxic and circulatory form of oxygen starvation.

Man's resistance and his work capacity are of great concern under long-term acceleration. Resistance and work capacity depend on the interaction of a combination of factors, which are not inherently comparable and consequently, can be evaluated only with considerable caution [72].

Sufficient information is not available on permissible limits for a healthy man to maintain work capacity under the influence of various modes of acceleration. Such information is lacking completely for individuals with variations in health.

Further studies are needed for objective criteria to evaluate resistance and for standardization. Objective criteria for longitudinal $+G_z$ forces should probably be the state of regional circulation at head level (in the ear) and the EEG; for $+G_x$ stress, the level of oxygenation of blood and development of bradycardia should be the criteria. Fatigue in connection with acceleration deserves attention, which is particularly important in flight landing, when various environmental factors may cause functional changes.

The effects of lateral $+G_y$ forces have not been sufficiently studied. With proper support, tolerance for $\pm G_y$ or $-G_x$ might be no worse, and respiratory disruption might be less, than for $+G_x$ force vectors ordinarily used.

Studies are needed on a centrifuge with variable radii. The significance of short-radius centrifuges for creating artificial gravity has not been established. Technically, this type of centrifuge is most suitable for solving the problem of acceleration effects in space flight. Theoretically, evaluation must be made of the pressure gradient which arises along the body during rotation in a centrifuge with short radius.

The effects of slight accelerations during long periods must also be studied. Physiologic effects, and resistance and working capacity should be determined under loads of 2.0 G during many days and perhaps months.

Studies should be continued on the effects of various acceleration rise rates. There are probably different optimal rise rates for long-term acceleration, for peak-type acceleration modes, and plateau-type modes. There are apparently optimal combinations of rise rate and relief rate, peak and plateau values, which can assure higher resistance of astronauts to accelerations expected under actual flight conditions. These combinations have not yet been determined. Studies on reactions of cardiovascular and respiratory systems should be continued. Broad investigations are needed on the influence on acceleration resistance of varied composition of the gas media used (or which has been suggested for use) in spacecraft cabins.

The positive effect of breathing oxygen with increased content, or under excess pressure, requires explanation of practical problems such as determination of the optimal time for applying this protective measure, and the values of positive pressure.

Information should be obtained on man's resistance to the effects of $+G_x$ loads in various modes (value, rise rate), as well as combinations of various types of accelerations. This is important when considering the possibility of accidental

rotation of a spacecraft. There should be further studies to develop methods of protection, mechanisms of physiologic reactions at both cellular and subcellular levels, and treatment methods for pathologic disorders. Study of the combined influence of acceleration with other flight factors is a pressing task for physiologists, biochemists, morphologists, and other specialists. Further studies should, hopefully, supplement insufficient information on acceleration influence on the human body, data that will prove highly beneficial for space flight.

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Chapter 6

IMPACT ACCELERATIONS[1]

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IMPACT HAZARDS

Impact acceleration may be encountered during normal as well as emergency phases of spacecraft operations. The impact loads experienced during normal flight phases occur primarily on spacecraft landing upon its return to Earth. Recovery systems used or considered for spacecraft designs have included conventional single and multiple parachute canopies, retrorockets, inflated fabric spheres, and parawings or parasails. Within existing technology and primarily weight limitations, it has not been practical to allow descent and horizontal drift rates to be adequately controlled within the range of impact velocities that would not be hazardous to the crew under all adverse circumstances. Exact knowledge of the physical environment to which the astronauts might be exposed with a particular spacecraft and its recovery system for all potential environmental variables, that is, impact surface, wind, impact angle, and others, is absolutely essential for realistic risk analysis and evaluation of protective requirements.

The severity of the impact experienced during spacecraft landing can be reduced considerably by controlling the landing site. With such control, the impact surface and wind conditions that are most favorable may be selected. Water, or flat, soft terrain have generally proven to produce less severe impacts. Data are available on the dynamics of water impact and, more specifically, on the water and land impact characteristics of the Apollo spacecraft [5, 98]. The descent rate at impact may range up to 8.5 m/s if the recovery system deploys properly. In a design such as the Apollo spacecraft where three recovery parachutes were used, the descent velocity could be as high as 15.2 m/s. The resulting impact pulses under even nominal conditions are typically high amplitude, short rise time accelerations, which are shown in Figure 1.

If a catastrophic failure occurs on the launch pad during final portions of the preflight preparations, short-duration, high-amplitude acceleration may be required to catapult the space vehicle crewman safely away from the launch vehicle. This same emergency escape system may be required during the initial phase of launch vehicle acceleration if there is failure of the propulsion or guidance systems. The acceleration environment associated with use of the escape system is more complex as the launch vehicle achieves higher velocities while it is still within the Earth's atmosphere. This more complex environment is due to interaction with the windstream and rapid deceleration of the escape system immediately after separation from the launch vehicle. In addition, the

[1] The authors are indebted to the Soviet compiler, S. A. Gozulov, and USA compilers, E. M. Roth and A. N. Chambers, for the material which formed the basis for this chapter.

impact of the opening of the recovery parachute may be quite severe at these higher airspeeds.

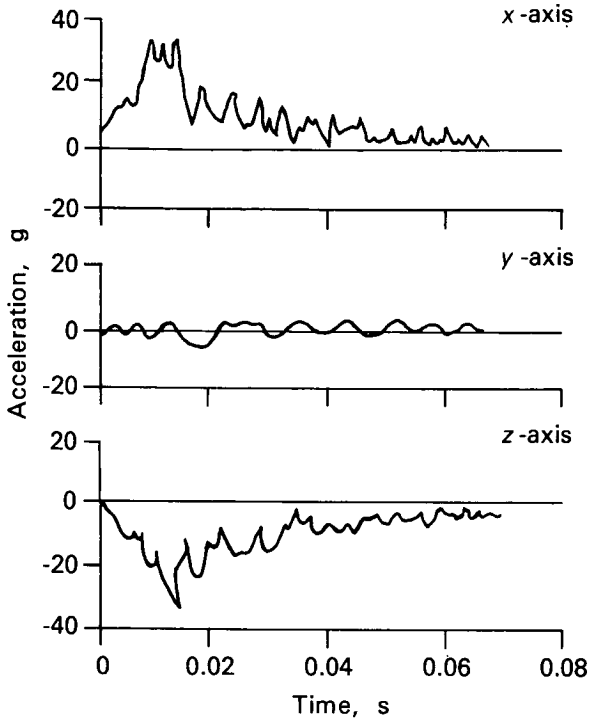


FIGURE 1.—Accelerations recorded during impact tests of the Apollo Crew Module [98]. Impact occurred at a pitch attitude of −27.5°, a roll attitude of 0°, a horizontal velocity of 11.4 m/s, and a vertical velocity of 10.5 m/s.

Two basic types of emergency escape systems have been used to assure spacecraft crew safety. The impact environments associated with each type are different in many aspects. The first type, the individual ejection seat which is used in high-speed aircraft, generates short-duration acceleration pulses throughout its entire sequence. These pulses are created during ignition of the ejection catapult, firing of the sustainer rocket, impact with a high-velocity airstream, parachute opening shock, and landing impact. The second type of escape technique involves propulsion of the entire spacecraft away from the launch vehicle. The catapult acceleration required with this type of escape system is generally of lower magnitude, usually no greater than 8 to 12 g, and longer duration than that required if an ejection seat is used. The alinement of the propulsion system thrust vector and center of gravity of the vehicle are more easily controlled than when the conventional ejection seat is used. A large portion of the ejection velocity must be imparted to the ejection seat while it is still stabilized by ejection rails, because of this problem. Therefore, the ejection acceleration may be as high as 18 to 20 g.

When the entire spacecraft is used as an escape system, it causes two other notable differences in the impact environments. The first, a beneficial difference, is elimination of the problem of impact with the windstream and rapid deceleration. The spacecraft is generally optimally designed for aerodynamic deceleration upon reentry into the Earth's atmosphere, and thus, the deceleration forces tend to be low. The second difference occurs at landing. Landing without the spacecraft is usually accomplished without incident by a properly trained crewman. A crewman descending under a personal parachute may judge his drift rate and even control his direction of drift, whereby he can position himself and use his legs to minimize landing impact effects. A difficult design problem is assuring an equally safe landing of the spacecraft under emergency and even normal conditions.

The relatively complex tasks performed by an individual prior to a parachute landing (which are not easily accomplished without adding undesirable weight and complexity to the spacecraft) are, sensing drift rate and direction and alining himself to obtain the best use of his legs to attenuate the impact. Impact accelerations that are experienced during capsule landing impact are quite variable due to lack of control of these factors. Furthermore, variabilities of the spacecraft structural rigidity, stiffness and contour of impact surface, and oscillation induced by the recovery parachute, coupled with the possibility of multiple impacts in different directions, add to the difficulty of providing a safe landing.

An escape system composed of several of the most desirable attributes of each of the basic escape system approaches represents another alternative. This approach uses the spacecraft to achieve separation from the launch vehicle

but individual ejection seats are also used after the required separation distance is achieved, and spacecraft velocity has decayed to an acceptable level. This approach avoids ground-landing impact problems associated with crew recovery within the spacecraft; however, it may not be the most effective approach in terms of spacecraft weight and complexity except in cases where there is no requirement to recover the spacecraft.

Impact environments may also be encountered during other portions of the space mission. For example, acceleration associated with spacecraft docking operations, that is, coupling the spacecraft to another spacecraft or propulsion unit, will result in transient acceleration. The ground-landing problem in spacecraft recovery after mission completion or emergency escape is also present during extraterrestrial landing. The impact environments of docking and extraterrestrial landing must necessarily be mild, to prevent injury to the crew or spacecraft equipment that might compromise success of the venture.

Each potential or actual impact hazard associated with the mission must be assessed to determine the degree of risk that may be allowed for injury or equipment failure. A mission risk analysis of this type cannot be carried out without a relatively detailed understanding of the human response to each level of impact stress. A primary objective of research in this technology area has, thus, been the development of human exposure limits in terms suitable for such a risk analysis.

Definition of Impact

Impact is generally defined as an acceleration with a pulse duration of not more than 1 s. The acceleration-time history is defined in terms of its magnitude in m/s^2 or usually in g units and its time parameters. Included in time parameters are rise time (duration from start of acceleration to peak acceleration time), and pulse duration (total time of the individual pulse). Acceleration derivatives such as rate of onset of acceleration (g/s) and rate of offset of acceleration are also commonly used as descriptors. However, it must be kept in mind that these descriptors give approximations only to the true acceleration-time history and that the limits within which they are meaningful must be examined.

For purposes of frequency domain analysis, an impact pulse is composed of energy density distributed over a spectrum of frequencies. Thus, a particular acceleration-time history may be reduced to terms of the power spectral density.

Impact accelerations might occur as linear or rotational accelerations, all together in 6 degrees of freedom.

Terminology used in the study of the human response to impact is varied [19, 48, 49, 87, 88, 96]; however, terminology that is generally understood has been selected for this discussion. Terms such as "overload" used in USSR literature and "dynamic overshoot" used in US literature are not used, in order to permit a more universal understanding of the text. The direction of linear and rotational acceleration vectors is defined with respect to the human body by use of the coordinate system shown in Figure 2, which is standardized for biomechanics.

Physiologic and Pathologic Effects of Linear Impact

Most human impact research has been conducted in connection with general automotive or aviation crash research, not in support of specific space requirements. Impact exposures experienced during emergency escape maneuvers have been studied during the last 30 years in connection with emergency escape from aircraft. Impact situations similar to space capsule landing impacts have been of interest for the last 15 years in the development of aircraft capsule escape systems [12].

Primary physiologic and pathologic effects of impact are caused by localized pressures and resulting relative displacements of body tissue. Massive stimulation of the entire nervous system in an extremely short time results in various sensations and reactions immediately after impact due to activation of pressure and stretch receptors. These sensations will vary in magni-

tude depending on the magnitude of the insult and will vary in seriousness from momentary stunning and mild cardiovascular reactions to cardiovascular shock, unconsciousness, and concussion—the latter probably always connected with pathologic injury. Direct injuries to body tissues result when relative displacements of body tissue exceed mechanical stress limits of the particular tissue involved.

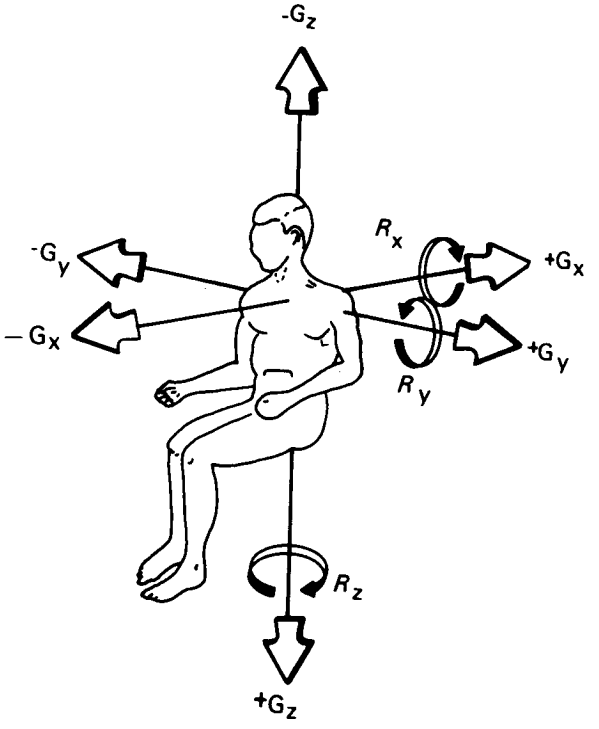


FIGURE 2.—Coordinate system for description of impact inertial response vector direction.

Such injuries may be at a cellular or subcellular level with no gross evidence of shear, tensile, and/or compressive stresses. Damage due to blood movement has not, in general, been observed, although conjunctivitis and retinal symptoms observed in $-G_x$ impact may be related to this phenomenon. This type of injury would not be expected for very short duration impact since the duration of exposure to acceleration is too brief to allow significant shifting of blood volumes. Injuries may also occur with more acute pathologic effects such as: abrasions, contusions, hematomas and laceration of soft tissues; strains, sprains, failure of cartilaginous structure and joint derangement; and various fractures or subluxations within the skeletal system. The seriousness of these injuries will vary from simple, reversible disabilities to chronic, irreversible impairment of anatomic structures or physiologic functioning of the body, and major trauma which may be either immediately or eventually fatal.

Physical response of the body and its organs, i.e., stress distribution along the body and stress severity, is dependent upon the acceleration-time history of the impact environment. Other major factors influencing the response include acceleration direction [52, 66], restraint degree [68], and body condition, that is, age, physical state, and others [44, 82]. The pathologic manifestations described rely heavily on analysis and interpretation of aviation, automotive, sport, and home accident data as well as data collected from suicides [91, 92]. Causes and mechanisms leading to these effects are derived from low-level noninjurious human tests or animal experiments.

Research conducted so far has shown different mechanisms of injury and symptoms for each impact direction studied. Much information that is available on these injury mechanisms has been collected from studies of accidents as well as laboratory experiments. In accident situations, head injury is the most frequent and most severe manifestation [74].

Head Injuries

More than 75 percent of aircraft crash fatalities result from head injuries. These injuries usually result from heavy blows to the head rather than from acceleration of the head structure as a whole [2, 3]. Neck injury from indirect acceleration of the head is not as well understood; these injuries may include ligamentous, disk, and vertebral damage as well as involvement of the spinal cord. Concussion may result from either neck hyperflexion or hyperextension if the head is not supported during impact [18, 43, 70]. Other concussion types are observed after concentrated

blows to the head that deform or fracture the skull [31, 32, 60] and cause deformations throughout the brain tissue [10, 33, 55, 67].

Head impact studies have been conducted with anesthetized monkeys and dogs to relate the severity and duration of concussion to intracranial pressure change and its duration [34]. Pressure changes were recorded with intracranial pressure transducers. Moderate to severe concussion effects were observed in the range of 2.1–6.3 kg/cm^2 intracranial pressure change concurrent with head impact. Observations of concussion effects in humans are limited to clinical investigations. Accuracy of such studies is greatly limited by the ability to estimate impact conditions associated with trauma.

Case histories of 317 patients with head injury have been studied and related to impact velocity, impact direction, and rigidity of the impact surface [75]. Severity of the trauma was evaluated on the basis of the patient's condition immediately after impact and during the affliction. Severity of the trauma resulting from impact velocities in the range of 3.0 to 10.5 m/s depended, to a considerable degree, on occurrence of fractures in the cranial base and degree of pathogenic involvement of the intracranial structures adjacent to the cranial base. Frontal region impacts resulted in a less severe clinical picture than impacts in the temporal and occipital regions. Cranial base fractures and damage to adjacent cerebral tissues almost always resulted if the impact velocity was greater than 5.0 m/s.

Spinal Impact

Damage to the vertebral column is a common mechanism of injury where the impact is applied parallel to the spine in the $+G_z$ direction such as in seat ejection maneuvers [17, 102]. Compression fracture of individual vertebral bodies is frequently observed in radiographic examination of individuals who have used aircraft ejection seats [38]. These fractures are usually confined to the upper lumbar and lower thoracic areas of the vertebral column. Although such injuries to the upper thoracic and cervical spine are relatively uncommon, they are observed when the ejecting crewman is poorly positioned prior to ejection. Immediate symptoms of this injury may range from slight, to severe, incapacitating pain. Ileus, persistent neuralgic and sciaticlike pains are common lingering symptoms. Compression fractures or fractures of spinal processes may, in extreme cases, be sufficiently extensive to result in intrusion of bone fragments or the disk into the spinal cord canal. Such instances may result in paralysis or other neurologic symptoms.

Physiologic and pathologic effects of impact in the $-G_z$ direction have not been identified in humans [17]. Investigators have speculated that intracranial hemorrhage would be the limiting factor, on the basis of results of longer duration acceleration experiments conducted on centrifuge facilities. However, impact tests with animal subjects have not supported this theory. Dogs exposed to accelerations up to 15 g from a duration of 0.05 s and 7 g for up to 1 s showed only petechial hemorrhages, generally in the mucous sinus membranes. Autopsy of dogs revealed no indication of intracranial hemorrhages. Experiments with volunteers have been limited to tests required to support development of the downward ejection seat and evaluation of Project Apollo crew protection designs [9, 40].

Transverse Impact

When impact is transverse to the longitudinal axis of sitting, in a well-supported and restrained body, the first signs of limiting human tolerance [94] have been various degrees of shock, i.e., pallor, perspiration, and transient elevation and subsequent drop of blood pressure. In one test, brief attacks of low blood pressure and albuminuria were observed for about 6 h after impact. More severe impacts will result in unconsciousness. Effects of maximum voluntarily tolerated impact levels were at times not pronounced, but delayed effects occurred with gradual onset in the following 24-h period. Subtolerance impact exposures in this axis normally cause elevation of pulse rate to approximately 150–170 pulses/min with respiration rate of 30–40 breaths/min followed by a rapid drop in these rates. Upon repeated exposures, the degree of these functional changes before and immediately after impact is decreased [24, 67, 68].

Bradycardia and extrasystoles in the first seconds after impact may be indicative of traumatic effects. Disturbance of cardiac rhythm in white rats, as a rule, accompanied damage to internal organs [26, 67]. However, bradycardia has been observed immediately after exposures of human subjects to $-G_x$ and $+G_x$ impact levels as low as 15 g [101]. This response was related to activity of the vagus nerve, since atropine blocks bradycardia. Test subjects also exhibited transient neurologic symptoms for brief periods after exposure to impacts in the 15 to 25 g range in the $\pm G_x$ direction.

Although physiologic stimulation may be of hormonal or neural origin, immediate onset of bradycardia in response to impact is consistent with neural stimulation. Cardio-inhibitory body reflexes can be initiated from baroreceptors in the aortic arch and carotid sinus. Visceral afferent nerves originating in nearly all tissues and organs except the skin may produce bradycardia [83]. Stretch receptors in the lung can initiate reflex cardiac slowing [16]. Stretching or distortion of lung tissue can occur during $-G_z$ impact and may be the cause of bradycardia observed in tests in this axis. Vascular fluid shifts are an unlikely source of stimulation to the cardio-inhibitory reflex areas because of the brief duration of impact. However, it is apparent that the inertial effects of $-G_z$ impact would produce a transient increase in the hydrostatic pressure sensed by the baroreceptors, which in turn respond to this pressure increase by reflex slowing of heart rate.

Evidence of damage to the respiratory system is also evident in impact studies. Injury ranges from minor functional changes in maximum ventilation of human subjects within voluntary exposure levels [35] to contusion and hemorrhage in animal subjects at near-lethal levels [6]. Restraint straps and structures may be responsible for lung damage noted in some of these experiments [6, 22, 84].

Biochemical Changes

Biochemical changes following impact have been studied in an effort to develop indices that would correlate with stress imposed by the acceleration environment, and forewarn and/or refine the definition of the injury threshold [4]. Transient hematuria and reduction in the number of circulating blood platelets has been observed after exposure of human subjects to impact [37, 101]. Urinary excretion of vanillylmandelic acid has been measured prior to and after volunteers were impacted in the $+G_x$ direction at a level of 25 g with a rate of onset of 1000 g/s and an impact velocity of 10 m/s [36]. Sham tests of each subject served as a control. Average urinary excretion of vanillylmandelic acid increased in both instances, with the greatest increase after true impact.

Impact experiments with white rats have been conducted to study the activity of aspartic aminotransferase, alanine aminotransferase, aldolase, and lactate dehydrogenase in blood serum [90]. Statistically, significant changes, rapidly appearing and prolonged in duration of activity, were noted in test groups where specific organ damage occurred. An increase in aspartic aminotransferase activity in blood serum of volunteer subjects has been found following both $+G_z$ and $+G_x$ impact tests with acceleration profiles of very short rise time and magnitudes in the range of 25 to 38 g and 22 to 40 g respectively [80]. Measurements of serum myocardial enzyme levels (creatine phosphokinase, hydroxybutyric dehydrogenase, lactic dehydrogenase, glutamic oxalacetic transaminase, and glutamic pyruvic transaminase) after $+G_x$ impact tests with human subjects at magnitudes ranging from 11.7 to 24 g have been accomplished without detecting levels outside normal ranges [43].

In this same work, a study was included of 40 accident victims, with the conclusion that serum myocardial enzymes are of no value as an index of cardiovascular injury in accident victims with mixed bodily injuries. Use of biochemical indices has proved useful in detecting the presence of general tissue damage; however, considerable research remains to provide methods to indicate specific tissue damage. Such specificity is required before a truly practical tool becomes available for clinical and impact injury research applications.

There is a general lack of controlled experimental data on physiologic and pathologic effects

of lateral ($+G_y$) impact. Prior to the emphasis placed on this particular problem by space vehicle designers, knowledge of lateral impact effects had been limited to data from accidents and from centrifuge experiments where long-duration acceleration up to 10 g was shown to be tolerable [39]. Radiographs collected during these experiments showed extensive displacement of thoracic and abdominal viscera at acceleration levels as low as 6 g.

In support of specific spaceflight requirements, rhesus monkeys were subjected to impacts up to 75 g at velocities up to 9.8 m/s, with and without contoured lateral support, and with no observation of postmortem evidence of injury [78]. Electrocardiographic evidence of transient changes in both conduction and rhythm was noted at higher accelerations and impact velocities. Comparison of radiographs taken before and after impact revealed a heart displacement in the direction of the inertial response; however, sequential radiographic observation indicated that the heart returned to a normal position within about 3 h after impact.

Response to Angular Acceleration

Angular impact acceleration may occur during the initial phase of ejection when the escape system separates from the ejection rails or during landing impact of the spacecraft [12, 98, 102]. Studies of physiologic and subjective response of volunteer subjects have been limited to the environmental ranges that have been explored with motion simulation devices. One study, conducted with acceleration durations of 0.2 to 0.22 s and braking durations of 0.25 to 0.26 s, explored acceleration levels up to 534 rad/s^2 with rotation about a "side to side" axis close to the seat-man center of gravity [100]. Limiting symptoms were manifested as hyperemia, indicating that the limiting factor for the range of acceleration amplitudes and durations explored thus far is the inertial force within the cardiovascular system acting within the head. Angular accelerations up to 1089 rad/s^2 with a duration of 0.2 s (braking deceleration was 816 rad/s^2 for 0.25 s) were well-tolerated when the rotation was about the longitudinal axis of the body.

The effects of angular velocities up to 13.1 rad/s have been studied with exposure times of several seconds [104]. These velocities were tolerated when the axis of rotation was through the center of gravity of man, i.e., through the abdomen at the level of the iliac crest. Symptoms in the head approached subjective tolerance at 8.8 to 9.4 rad/s. The development of conjunctival petechiae was found to be a reliable measure of the stress imposed on the unsupported peripheral vasculature. The curve for conjunctival petechiae, when the center of rotation was at the iliac crest, varied from 3 s at 9.4 rad/s to 2 min at 5.2 rad/s. With the center of rotation at the heart, petechiae appeared only at velocities of 2.7 to 3.1 rad/s higher for the same durations.

Cumulative Effects of Omnidirectional and Repetitive Impact

The unpredictability of the impact vector and the possibility of repetitive impacts during capsule landing in rough terrain or severe sea conditions necessitated various studies with oblique impact vectors. Although these results are by no means conclusive or exhaustive, they proved the safety of limited, anticipated impact profiles and precluded unexpected biological effects [66, 95, 103]. These studies are discussed in more detail later in the chapter.

Evidence of cumulative effects of several successive impact exposures of human subjects in the same or different directions close to voluntary limits has not been reported so far. The number of subjects and exposures are too limited, and physiologic and psychologic tests are too crude to permit valid differentiation of subtle effects of such stress from the changes with time in individuals not exposed to impact.

Experiments designed to study the pathology associated with repeated impacts have been carried out with white rats [23, 29]. This study was performed with impacts up to approximately 600 g at 1.2 to 0.8 ms durations. Accelerations of 450 to 600 g were applied at 2 to 3 min intervals in one series of experiments and in 1 and 24 h intervals in a second series. The animals were impacted 2 to 14 times. Impact velocities were

varied from 4 to 7 m/s. Cumulative lesions resulting from repeated exposures at 1-h intervals were detected as primary lesion of the lungs. Lesions developed after a comparatively small number of repeated exposures.

Another study was carried out with white rats and dogs exposed to repeated impacts at lower levels [26]. The rats were exposed to 300–350 g three times at 10-min intervals. Respiratory and heart rate changes intensified with repetition of the impact. Disturbances of cardiac rhythm (extrasystoles, atrioventricular block) became most marked. Dogs were exposed to 4 to 5 impacts at levels less than 200 g of 0.01 to 0.015-s duration at 2 to 5 d intervals without marked increase in functional disorders which had been observed in white rats [26]. The investigators concluded that the length of the impact interval reduced the degree of functional deviations and apparently caused some adaptation.

RESEARCH STUDIES OF TOLERANCE LIMITS

Numerous approaches have been used in research to determine the physiologic effects of impact and to quantify impact exposure limits. Early studies of man's reaction to impact, conducted during and immediately after World War II, were directed toward answering questions concerning the safety of ejection seat catapults [1, 17, 81, 86]. Extensive experimentation was also undertaken to study effects of aviation crash landings and the short-duration $-G_x$ deceleration encountered during ejection from a high-speed aircraft [94]. Most of this early experimentation was with human subjects—often the investigators themselves. Anthropomorphic dummies were used to evaluate adequacy of the experimental apparatus prior to tests with volunteer subjects, but the usefulness of data collected with dummy subjects was very limited. Animal tests were also performed but their value was minimal and at best, qualitative, due to the paucity of information that might be used to relate the relative impact tolerances of man and animals.

The significant work accomplished at this stage in the development of aviation medicine was, for the most part, based on subjective comments of volunteers, symptoms that were usually mild and often vague, and judgments of investigators. This approach continues to be used to define voluntary tolerance limits and evaluate the relative merits of protection systems, but refinements of methodology and more substantial scientific literature have reduced somewhat the risk associated with this approach.

Impact testing with animals has become a more meaningful approach to assess the effects of specific impact environments and to recognize and analyze specific injury patterns as the volume of data collected with each species has increased. Experiments with animals provide a basis for estimating injury types that might be expected for different acceleration directions and variations in protective equipment configurations [26, 45, 56, 59, 65, 93]. Animal tests to determine frequency of lethal injury have served to substantiate theories of the biomechanical effects of impact, that is, deformation of load-bearing tissues and effects of impact-time parameters on the attainment of injurious levels [50, 51]. While animal data originally were only of qualitative use in identifying injury patterns and mechanisms, their quantitative usefulness had to wait for the establishment and verification of dimensional scaling laws based on broad progress in biomechanics. The validity of these scaling relationships is supported by tests with various types of mechanical stimuli such as airblast, vibration, and sustained acceleration [6, 105, 106].

Despite advancements made in this aspect of impact research, data collected from animal experiments must be approached with more than an ordinary degree of caution. Basic differences in anatomical geometry on both a macro- as well as a microscopic level undermine the fundamental scaling requirements for similitude of structural geometry and material properties. Furthermore, not only may the dimensional proportions of the animal be significantly different from those of man, but also, perhaps more importantly, physiological responses may be manifestations of other dissimilarities.

The use of human cadavers or tests on their tissue or organs constitute another approach used to determine impact limits without actually

endangering living subjects. This approach has been more successful in studies of the breaking strength of bone since postmortem changes in bone are less pronounced than in soft tissue. Impact exposure limits for the $+G_z$ direction have been developed, partially based on tests conducted on cadaver vertebral segments [27, 81, 97]. A great deal of the findings available on head injury [31, 33, 53, 55, 85] has been obtained from tests with cadaver skulls.

Biomechanics Research

Contemporary biomechanics research has become progressively directed more toward establishment of impact exposure limits in terms of probabilities of injury and/or fatality instead of the oversimplified concepts used earlier of "limit of tolerance" or "zone of injury." Such relationships can only be obtained by the integration and correlation of all six basic approaches:

1. Experimentation at low-impact levels using volunteer subjects to establish basic kinematics of the living body and its relationship to kinematics of animal and cadaver bodies;
2. Discovery of areas of injury, mechanisms of injury, and severity of local impact using cadavers at high-impact levels;
3. Experimentation with animals to study the full range of physiologic and pathologic responses in various species;
4. Analysis of human accident data to verify laboratory research and clinically evaluate severity of the injury and the longer term outcome of these injuries;
5. Testing of isolated components of the human body such as vertebral segments or skulls to determine mechanical properties, i.e., breaking strength, stiffness, and others.
6. Integration of results from approaches (1) to (5) into a theoretical framework or mathematical model, which allows prediction of response dynamics and injury probability for exposure parameters not yet experimentally tested.

One major difficulty in determining useful impact exposure-limit criteria is that impact levels are not determined by the biological system alone, but are strongly influenced by, and coupled to, the body support or restraint system used in applying mechanical force to man. A definition of impact-exposure limits without definition and accurate description of this support and restraint is meaningless. The physical dimensions and mechanical properties of all contact areas, that is, seat, backrest, restraints, head support, and others, must be controlled and described with test data. With animal experiments, these "mechanical components" must also be scaled dimensionally, dynamically, and in strength to allow meaningful extrapolation to the human case.

Mathematical Models

The application of models to represent dynamic responses of the human body and support and restraint systems can be of great value in determining relative effects of specific characteristics of the human, or his mechanical protection system elements in impact environments [71, 72, 89]. Their use further enables analytic determination of the detailed effects of complex waveforms that could not be obtained using such simple parameters as peak acceleration, rise time or rate of onset—parameters which are meaningful only as descriptors of relatively simple waveforms.

Various models developed have had one or more of these purposes:

1. Understanding the basic pathologic, physiologic or anatomic dysfunctions resulting from impact;
2. Extrapolating from environments evaluated in the laboratory to operational environments not yet tested;
3. Determining optimum protection system designs for a given set of environmental parameters;
4. Using the model to evaluate and interpret tests on human surrogates, i.e., animals or anthropomorphic dummies;
5. Providing a technique to describe human tolerance to impact in a format that can be more easily understood by aerospace equipment design engineers.

General types of biodynamic models may be categorized as models that describe properties of tissue, human body subsystems such as the head and neck, total body response, or kinematic response of the whole body. Models developed to describe experimentally obtained tissue properties provide some understanding of basic physical processes by which mechanical energy is transmitted through the body tissue in various frequency ranges [20, 47]. Subsystem models of the human body such as mathematical representations of the head [10] and spinal column [9, 27] have the greatest degree of practical usefulness. Models of this type account for the statistical variability of failure modes and effects of parameters such as age of the individual [97].

The total body model is composed of several of the subsystem models and allows more complete understanding of interaction of various responses. Kinematic models depict individual segments of the body as a linkage system with individual components having the geometric shape and inertial properties of human body segments and the degree of joint mobility as well as muscle forces derived from experimentation [62]. Such models are useful in determining crewmen's motion of the body segments during specific impact conditions and in predicting interaction of body segments with the restraint system and interior surfaces of the spacecraft.

Model Response to Impact Forces

Most of the total body and subsystems models used to describe human response to impact forces are of the lumped parameter type, presenting the body or body segment as a mechanical system composed of masses, springs, and dampers. These models assume a simple stress-strain relationship. More complex models have been suggested and mathematically described; however, available data on mechanical properties of the body are not yet sufficient to justify their use in evaluation of practical operational problems. Such models can be used successfully to describe main tissue motions such as head, upper torso, or abdominal viscera motions. At higher frequencies, lumped parameter representation becomes increasingly less valid when wave phenomena (transverse shear waves as well as compression waves) become apparent. However, gross body deformations and organ motions leading to major injury patterns observed under impact accelerations occur in time periods corresponding to frequencies below several hundred Hz and are well-described by lumped parameter representation.

The model shown (Fig. 3) is an example of a total body model developed to combine the body's response characteristics in the G_z direction as measured in both vibration and impact exposures. Only the airways are represented by their fluid dynamic properties and not by lumped parameters. Spinal compression, interthoracic pressure, and chest and abdominal motions can be calculated for this model and exhibit typical resonance phenomena observed on these systems under impact or steady-state vibration. For example, the upper torso mass combined with the spinal spring has a resonance of 5.6–8.4 Hz and the abdominal mass undergoes maximum displacement, i.e., is most sensitive, in the 4–6 Hz region. For a more detailed analysis of specific injury modes, it is often preferable to use subsystem models where further refinements and nonlinearities can be investigated more easily. An example of the application of such a simple lumped parameter model to describe spinal injury under $+G_z$ impact loads will be discussed later.

Total body models usually are a complex coupling of simple second-order subsystems, each representing individual dynamics of a body segment or organ system. Although the acceleration transmitted to a specific subsystem may be modified by the dynamics of intervening and surrounding subsystems, the tolerable (noninjury producing) acceleration level is determined primarily by the individual response of each subsystem. Thus, the dynamic response characteristics of the system, i.e., natural frequency, damping properties, and the like, determine sensitivity to impact.

A complete discussion of how differing impact environments produce different maximum strain or peak force level in a second-order system is beyond the scope of this chapter. Detailed discussions of these effects are available in the

technical literature [51, 71, 97]. However, certain basic principles of dynamic systems should be understood. First, the maximum strain or peak force in a dynamic system is related to velocity change associated with impact acceleration-time history when the acceleration time duration is less than the natural period of the dynamic system. The force that will cause equal strain increases as the acceleration pulse duration decreases. Second, for a given pulse shape, the maximum strain or force level in the dynamic system is primarily related to acceleration magnitude when acceleration duration is greater than the natural period of the system. If the

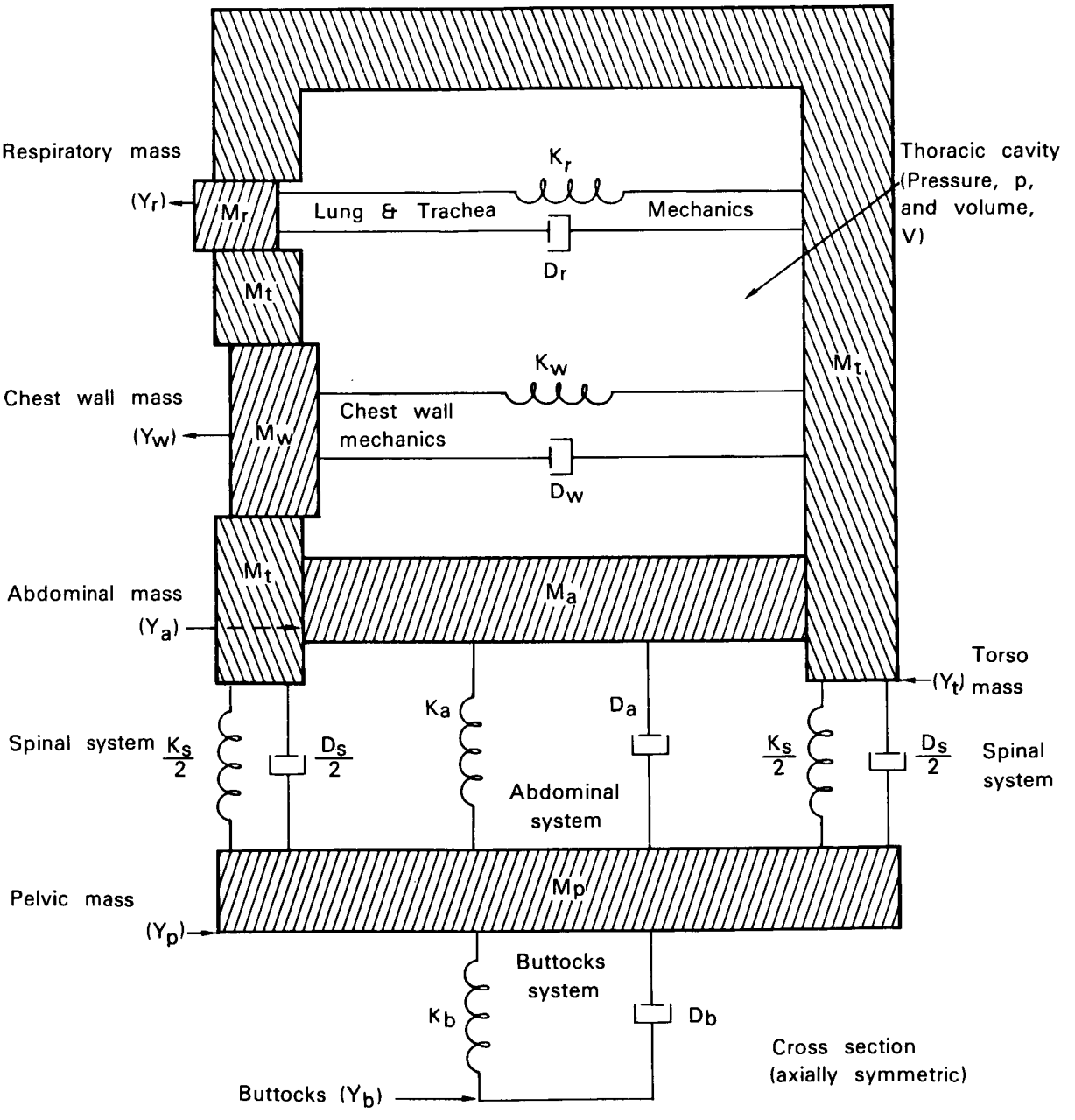


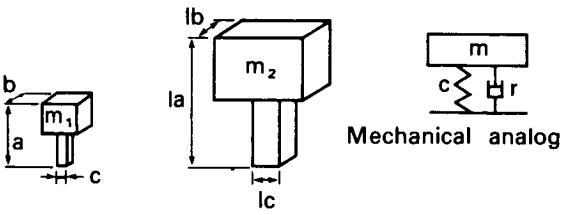
FIGURE 3.—Multidegree of freedom model to depict whole body response to impact [21].

impact pulse duration is comparable with the natural period of the system, the peak strain or force is a complex function of velocity change and acceleration level. (The natural period of the dynamic system depends upon its natural frequency and damping coefficient.) Therefore, in later sections of this chapter dealing with these parameters, velocity change and g level are used as descriptors of human exposure limits.

Subhuman Primates Response to Impact Forces

Interpretation and application of the relatively large amount of available data on the effects of impact on subhuman primates and other mammals is vitally dependent upon the use of model scaling techniques. The basic assumption of this approach is that an impact environment will lead to similar injury mechanisms in animal and man when dynamic similarity or scaling laws are applied. This assumption must be continually verified with efforts to use this approach, in light of the geometric dissimilarities between species. Methods commonly employed in such verification include evaluation of the similarity of the mechanical properties of tissue; steady-state vibration response analysis of various species of different size; kinematic response to impact; and evaluation of injury mechanisms observed in clinical investigations of humans involved in accidents where the impact environment can be reasonably estimated.

The anatomic and physiologic differences between various species and assumption of similarity of injury mechanisms may present sizable obstacles; however, valuable first approximation results can be obtained by using scaling laws. By applying the scaling laws (in Fig. 4), approximate resonant frequencies may be obtained for chest, spinal, and abdominal systems for various animal species (shown in Fig. 5). Smaller species generally have higher natural frequencies for the same organ, which involve two important consequences; in a somewhat oversimplified statement, these are: (1) equivalent injury patterns in smaller animals are produced by correspondingly shorter duration impact patterns, which leads to the requirement for "scaling" the impact pattern for experiments with small animals in order to make results interpretable in terms of human injury; and (2) smaller animals in general have lower impact sensitivity, i.e., they can stand higher G-loads.



	Tissue	Airspace
$\frac{m_2}{m_1}$	l^3	l^3
$\frac{c_2}{c_1}$	l	l
$\frac{r_2}{r_1}$	l	l^2
w_0	$\frac{1}{l}$	$\frac{1}{l}$
Damping $\frac{r}{w_0 m}$	$\frac{1}{l}$	Constant

FIGURE 4.—Scaling laws for geometrically similar structures such as mammals of different size [21].

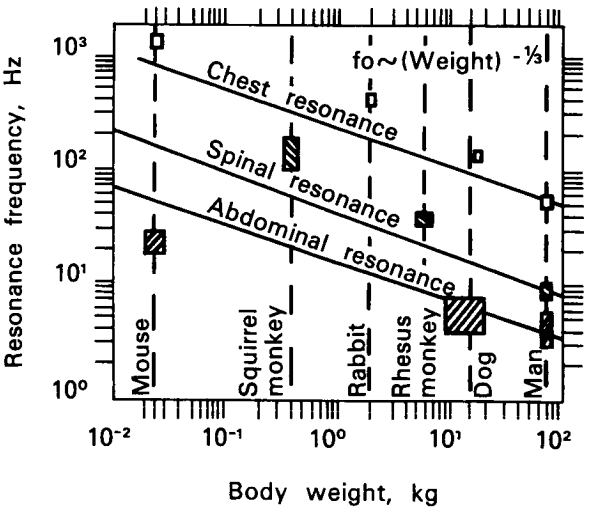


FIGURE 5.—Approximate resonance frequencies of total body response models as a function of body size (weight) [21].

Impact Simulation Techniques

Mechanical facilities in a wide variety have been used to simulate the impact environments anticipated in normal and emergency spaceflight operations. To assure broad usage of test data, their mathematical interpretation, and easy application to biodynamic models, most work has not been conducted with the complex acceleration waveforms encountered in actual operational situations, but with simple approximations to these patterns such as rectangular, triangular, and half sine pulses. The simplest of the facilities are the vertical deceleration towers—devices which use gravity to assure the reproducibility of the impact velocity. The impact-time history may be controlled by using hydraulic decelerators [11, 103], crushable materials such as paper or aluminum honeycomb [37, 46], or energy storage devices such as elastomeric materials or liquid springs.

Ejection towers, which have been used since immediately after World War II to study man's response to $+G_z$ acceleration, evaluate personnel protective equipment, and provide crew training [1, 17], have incorporated both pyrotechnic and pneumatic devices to accelerate ejection seats and subjects. Rocket-powered sleds, propelled along horizontal tracks into water brakes, have been used to study combined effects of short-duration decleration and windblast encountered during emergency escape from high-speed aircraft [1, 94]. More precise studies have used a pneumatically propelled sled and water brake decelerator, designed for conducting human tests [11]. This facility is shown in Figure 6.

Other impact simulators include simple pendulums and pneumatically powered strikers. Pendulum impact devices have been used to study impact protection systems [94], head impact tolerance, and to evaluate protective headgear. Special small-scale pneumatic strikers have been developed to study head and thoracic trauma [70].

Impact simulators must be designed to provide precise control of the impact environment parameters, if human subjects are to be used at impact levels approaching tolerance. Reproducibility of the test environment is especially critical in experimentation where impact stress is increased in small increments until voluntary tolerance is reached. Furthermore, the test apparatus used with the simulator must be given extraordinary care in design and in understanding its contribution to test results. Where prototype hardware, such as an astronaut ejection seat, is used, it must be recognized that the design of the structure of the seat may include only a small margin of safety, for example, a factor of 1.25, since the impact environment under study would be encountered only under emergency conditions. This margin of safety, while suitable for a low occurrence probability such as emergency escape, is normally not considered adequate for experimentation with volunteer subjects.

Rigidity of the structure, or lack of it, is important not only in considering the safety of the apparatus, but also in the fidelity with which it transmits the simulator impact to the subject. The acceleration transmission characteristics of the apparatus and component articles such as seat cushions and padding are, unfortunately, often ignored. Under these conditions, it is usually difficult, if not impossible, to draw any general conclusions about the work or to extrapolate to other equipment configurations. Where determination of human tolerance is the primary objective of the experimentation, it is often simpler to assure that the structure is rigid and to eliminate elastic padding. Furthermore, the rigid structure lends itself to repetitious use common for impact testing.

Beyond the more straightforward considerations of experimental procedures and apparatus design are the fundamental ethical questions surrounding impact experimentation. Perhaps the most basic question: "Is the information value resulting from the test commensurate with the risk to the subject?", should be answered not only in the initial planning stages of the research program but also immediately before initiation of testing when the scope and adequacy of data to be collected are more completely defined. In any case, investigators are ethically bound to minimize risk to the subject. Actions which can achieve this end include thorough

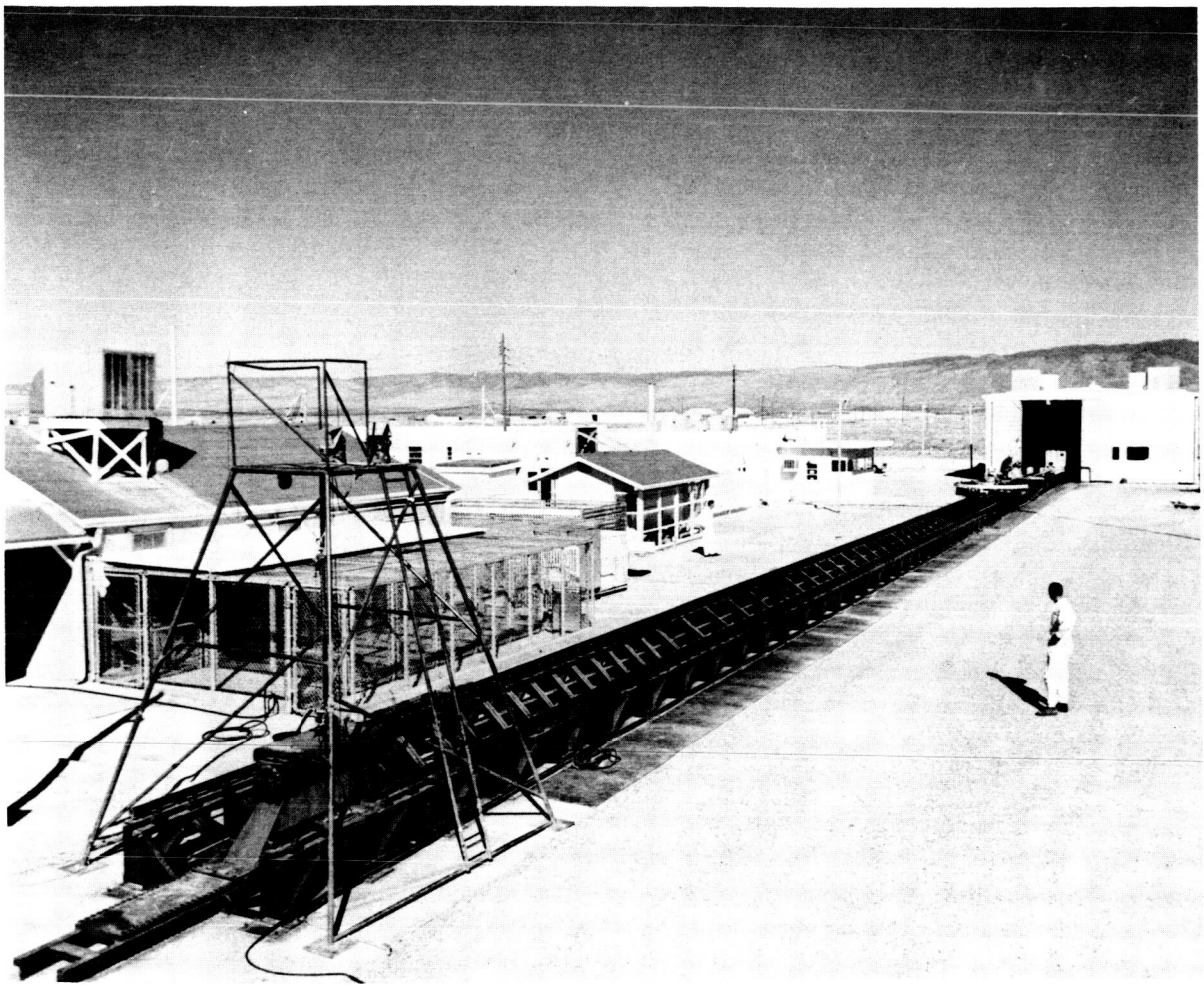


FIGURE 6.—The daisy decelerator.

physical examinations prior to, and after testing, and careful medical monitoring throughout the experimentation and posttest period as well as meticulous attention to operation of impact simulation equipment and emergency procedures. Posttest examination and followup of subjects depends on specific test goals, subject symptoms reported, and the medical investigator's report.

HUMAN IMPACT TOLERANCE AS RELATED TO SPACE MISSIONS

During early work on manned spacecraft designs, there was recognition of the necessity to acquire more complete data on human response to impact. Available literature reflected that the majority of impact research had been directed toward solution of aviation problems. First, acceleration exposure limits for the z-axis had been developed as design criteria for ejection seat catapults, and thus were defined in terms of the acceleration waveforms that are normally obtained from such ballistic devices. Second, x-axis limits were similarly defined for pulse shapes that were anticipated during the deceleration of ejection seats immediately after ejection into high-velocity windstreams. Third, practically no data were available to assess effects of impact vectors acting in the y-axis. Furthermore, information available pertained only to the

cardinal axes and thus, the effects of impact vectors acting in directions other than these axes could not be evaluated.

The work of Eiband summarized data available at that time within the US [17]. These data are summarized graphically in Figures 7 and 8. While these data have been of inestimable value in developing design criteria for manned spacecraft, they were inadequate for evaluation of specific impact problems associated with both normal and emergency astronautic operations. It was mentioned previously that providing escape from the launch pad with an ejection seat requires use of a high-magnitude, short rise time acceleration pulse.

It is also most important that landing impact environments anticipated during the recovery phase of space missions presented a set of potentially severe conditions, characterized by high-magnitude, short rise time impact pulses of varying direction and irregular waveform. The impact exposure environments, unfortunately, are hard to predict as long as the prototype space system is not available for test and always subject to large statistical fluctuations depending on details of landing conditions. Tolerance limits presented in Figures 7 and 8 are only available in terms of idealized trapezoidal waveforms. Deduction of a plateau level and time duration from a complex acceleration-time history encountered in actual practice is not an easy task, and in some instances impossible.

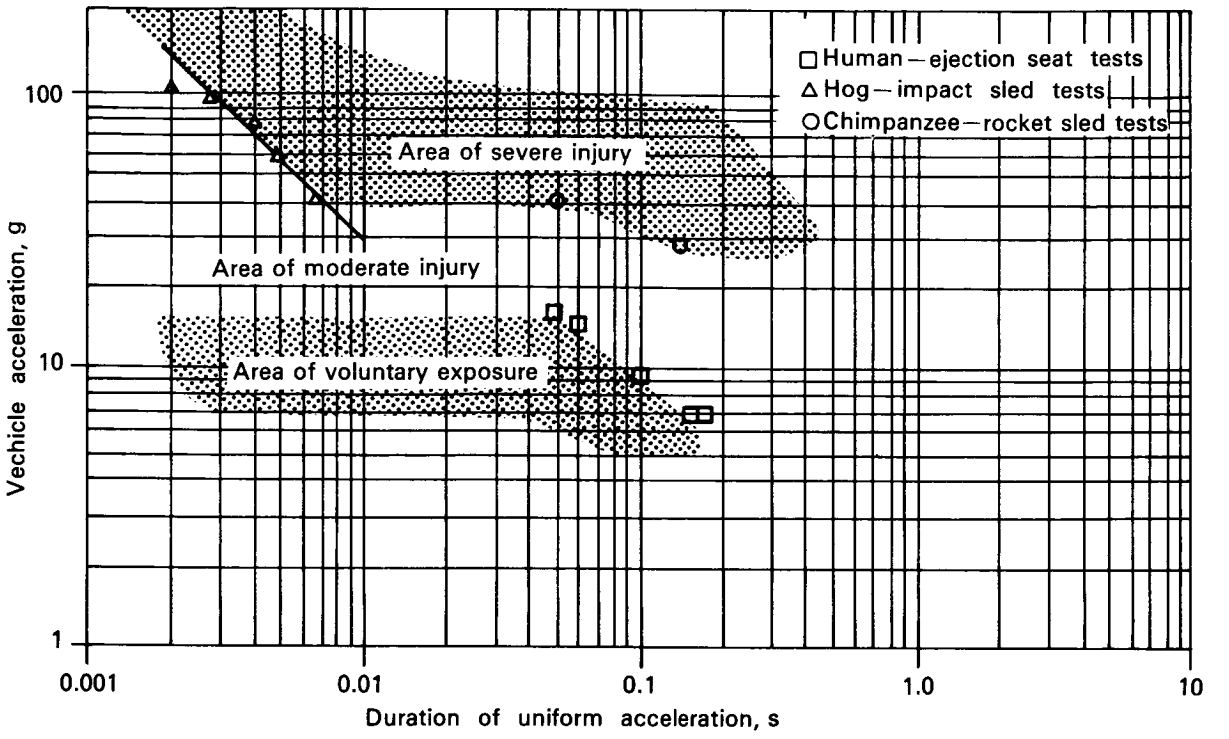
$+G_z$ Impact Exposure Limits

Evaluation of the Eiband summaries shows that there is a considerable unknown region between the areas of voluntary human tolerance and injury. In the $+G_z$ direction (Fig. 7a) the unknown area shown covers over 20 g in the ordinate and does not show human exposures for time durations less than 0.04 s. It is unfortunate that this unknown region includes impact environments of greatest interest in space operations. It is clear that boundaries are not well-defined and a few more data points might change the shape of the curves. Although plotted data are too limited in numbers of tests and control of variables to provide a basis for accurate interpretation [69], the general form of the curve shown in Figure 7a merits some comment to provide insight into the general form of the tolerance curve in the short duration region. It should be noted that for impact plateau durations up to 0.007 s, data points dividing areas of severe and moderate injury decrease in nearly linear fashion on the log-log scale as time duration increases. The relationship of these data points is as it should be, if viewed in terms of the dynamic response of a mechnical system. Use of a mechanical analog seems appropriate here, since the injury mechanism that is operationally important is mechanical in nature, that is, compression fracture within the vertebral column.

The simplest analog developed for the study of impact applied parallel to the vertebral column ($+G_z$) is a mechanical model composed of a mass, a spring, and a viscous damper [97]. The mechanical elements are lumped parameter elements, e.g., all the human body mass that acts upon the vertebrae to cause deformation is represented by the mass element. The model, shown diagrammatically in Figure 9, is used to predict maximum deflection and associated force within the vertebral column for any given impact environment. Compression fracture occurs when the force in the spring exceeds its breaking strength. Properties of model elements have been derived from existing data. Spring stiffness and breaking strength have been determined from cadaver vertebral segments, and damping ratio calculated from measurements of mechanical impedance during vibration tests [15, 97]. Response of the model can be determined for any given acceleration-time history by solution of a second order, differential equation with terms representing the positions of mechanical elements in regard to time.

Injury Prediction

The mechanical model also provides a basis for a probabilistic approach to injury prediction. Since the model reduces the effect of the impact environment to a single parameter, that is, peak deflection or force in the spring element, a correlation can be determined between this parameter and injury. For example, the breaking strength of vertebrae is variable but it can be statistically described in terms of failure prob-



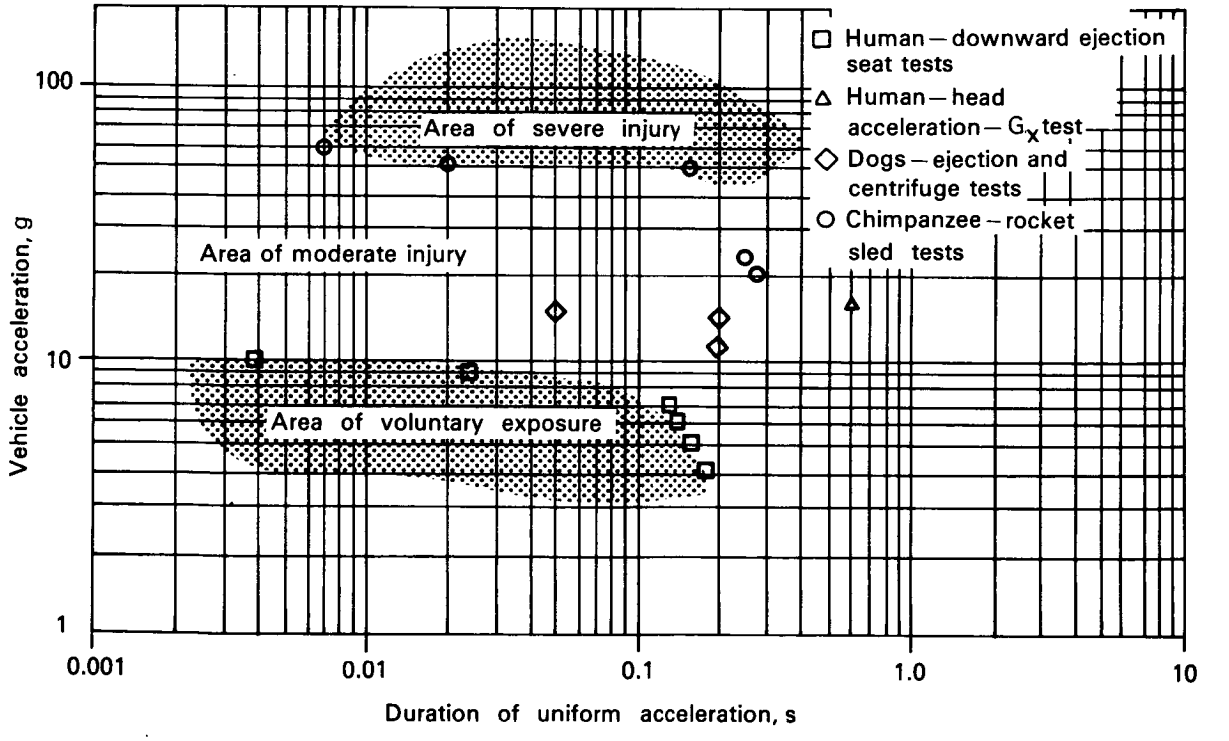


FIGURE 7, a and b.—These two graphs show durations and magnitudes of abrupt decelerations in the G_z direction which have been endured by various animals and man, showing areas of voluntary endurance without injury, moderate injury, and severe injury marked by shading. Graph "a" shows data of $+G_z$ acceleration (headward) and "b" shows data for $-G_z$ acceleration (tailward). (After [17])

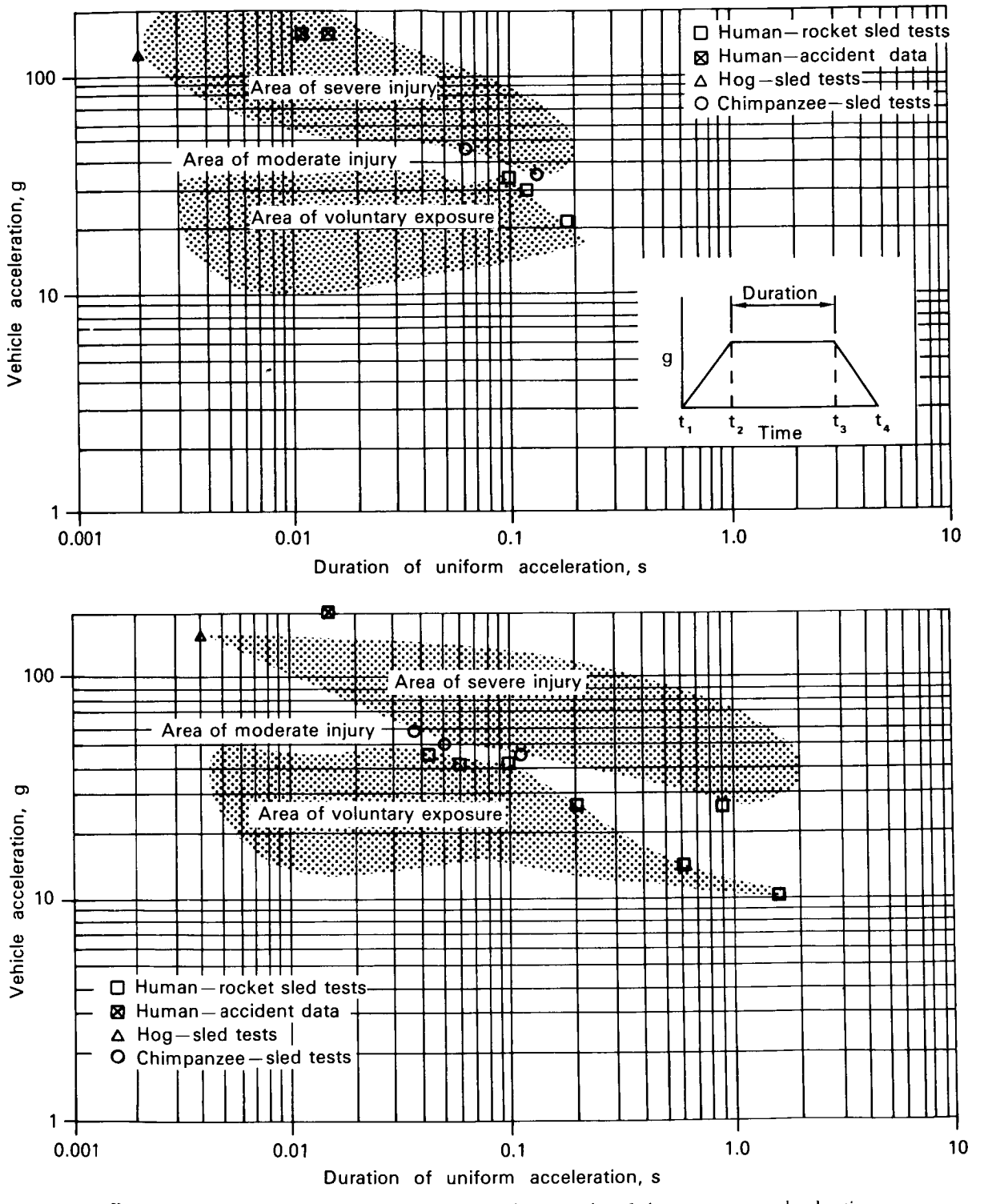


FIGURE 8, a and b.—Two graphs show durations and magnitudes of abrupt transverse decelerations endured by various animals and man, showing areas of voluntary endurance without injury, moderate injury, and severe injury. Graph "a" summarizes ($+G_x$) data (chest to back acceleration) and "b" shows ($-G_x$) data (back to chest acceleration).

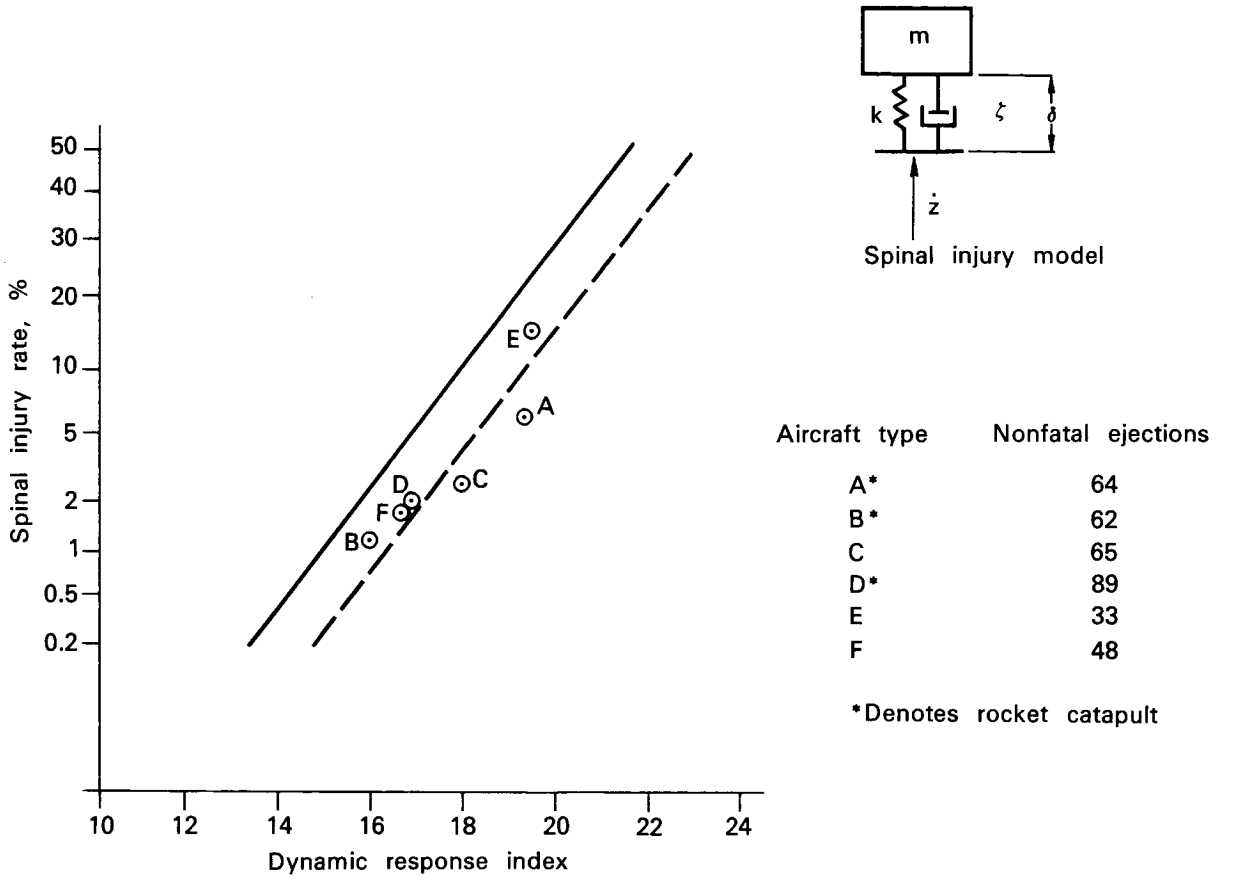


FIGURE 9.—Probability of spinal injury estimated from laboratory data compared to operational experience. (After [8])

ability [97]. This same approach provides estimates of the relationship between age and breaking strength [73, 97].

An analytical effort was made to determine the degree of correlation between the spinal injury model and injuries experienced in operational aircraft ejection seats [8]. The relationship between operational acceleration environments and actual spinal injury rates of the ejection systems included in the study are shown in Figure 9. The response of the model is expressed in terms of dynamic response index (DRI) values. The initial estimate of injury probability as determined from cadaver data is compared to operational data. The slope of the line drawn through operational data points was established on the variance of vertebral strength used to establish the initial estimate. The spinal injury model and this injury probability estimate have been used to assess risk of spinal injury associated with the Project Apollo mission impact environments.

Vertebral and Intervertebral Strengths

The vertebral failure process has best been described by a mechanical deformation and effect sequence, shown in Table 1.

Extensive studies of vertebral and intervertebral disk strength have been conducted to determine more precise estimates of $+G_z$ impact tolerance [27]. This work significantly increases the number of data points, since a total of 530 vertebrae was studied, which included tests of cervical vertebral segments. Only a few data points were available previously to provide

an estimate of the breaking strength of the cervical spine. The mean ultimate strength of vertebral segments tested in this study are in Table 2. The values indicate the same general change of breaking strength as a function of position of the vertebral segment, as do similar collections [73], but the breaking strength is approximately 18% higher. Data were obtained from vertebral specimens in men ranging in age from 19 to 40. Less than 30 h elapsed after death before the start of the experiment. Data shown were obtained at a deformation rate of 10 mm/min. From 6 to 16 observations were used to compute arithmetic means.

TABLE 1.—*Mechanical Failure Sequence of Vertebral Body Under Axial* ($+G_z$) *Compression* [27]

Deformation, %	Effect
6–10	Within elastic range of deformation No macroscopic structural changes
12–13	First macroscopic irreversible changes Compression of limbic zone
17–18	Cracks and compression in area of wrist of vertebral body
25–26	Fractures within vertebral bodies without displacement of hips
36–37	Fractures with dislocation

Average mechanical characteristics of intervertebral disks of cervical, thoracic, and lumbar sections of the vertebral column are in Table 3. The ultimate strength was identified by rupture of the disk fibrous ring and extrusion of a jellylike substance.

Physical Inactivity/Immobilization and Weightlessness

In connection with longer space missions, potential effects on impact tolerance to prolonged immobilization, physical inactivity, and weightlessness have been of considerable interest and speculation [30, 82]. Cardiovascular and metabolic effects of simulated and actual weightlessness are treated in a separate chapter; it will only be mentioned here that cardiovascular changes observed must have some effect on the cardiovascular impact responses described. Quantitative data on this subject are not available and these changes are not usually considered to limit human tolerance. However, decrease in bone strength from osteoporosis of disuse is established; bone loss has been measured on astronauts after space missions and in simulated weightlessness studies on man and animals [61]. Although bone loss, per se, cannot yet be related directly to bone strength, there is good reason to assume a noticeable reduction in bone strength after prolonged space missions.

In rhesus monkeys immobilized for 240 d by plaster of Paris casts, a reduction of 25% in overall spinal impact tolerance was observed, the main decrease in strength having already occurred after 60 d immobilization, which is shown in Figure 10 [46]. These data cannot yet be applied quantitatively to an estimate of strength reduction in human subjects. However, they obviously call for further studies and conservative application of all bone strength/bone impact limits data obtained on "normal" human subjects adapted to the Earth's gravitational field.

Tolerance to $+G_z$ impact applied to the standing subject has been studied to determine the effects of explosions beneath a vehicle floor [41]. With impact on the sole of the foot with leg extended, fracture of the distal tibia in the human leg resulted at a load of 680 kg applied in axial compression between knee and foot [42]. Limiting velocity change for impact transmitted to a stiff-legged subject is 3 m/s; the resulting impact exposure limit curve is shown in Figure 11. A few empirical studies on cadaver legs are plotted. Such exposure criteria are of value in the design of lunar or planetary landing vehicles where the crew may be standing upright during landing.

After the initial compressive phase of impact motion response of the floor, the unrestrained man will be thrown and propelled off the floor with some velocity that will not cause injury; however, it will have bearing on his velocity at the termination of his motion when injury can occur. The kickoff velocities of men in the standing and seated positions have been measured for various impact pulses [41]. Ratio of peak deck velocity,

TABLE 2.—*Ultimate Strength of Vertebrae Compressed Vertically* [27]

Vertebra segment	Strength, kg	Vertebra segment	Strength, kg	Vertebra segment	Strength, kg
C1	800	T2	436	T10	860
C2	510	T3	467	T11	917
C3	404	T4	522	T12	1054
C4	408	T5	551	L1	1059
C5	453	T6	619	L2	1175
C6	563	T7	681	L3	1269
C7	464	T8	824	L4	1296
T1	475	T9	840	L5	1286

TABLE 3.—*Mechanical Characteristics of Intervertebral Disks Compressed Vertically* [27]

Vertebra section	Ultimate strength, kg	Elastic deformation, mm
Cervical	486	1.2
Thoracic	1270	1.6
Lumbar	1502	2.1

V_d, to kickoff velocity, V_k, was plotted as a function of the ratio of rise time to peak velocity (t_p) to natural period of man (T) (Fig. 12). The curves follow the form:

$$\frac{V_k}{V_d} = 2.7 \left(\frac{t_p}{T}\right)^{0.44}$$

where T is 0.1 s for the standing man and 0.167 s for the seated man.

Transverse ($\pm G_x$) Impact Exposure Limits

Impact effect in the $-G_x$ direction is critically dependent upon the type of restraint and body posture at impact time. Volunteers have been exposed to impact levels to approximately 45 g for 0.09 s with an onset rate of 413 g's [94]. Subjects were restrained by 7.5 cm-wide shoulder straps, lap belt, and thigh straps, and the subjects' head and neck were preflexed prior to impact. Onset rate or rise time was instrumental in production of perceptible subjective differences and cardiovascular shock symptoms. Under operational conditions where only 5 cm-wide shoulder straps and lap belt are used, and the crewman wears a helmet weighing from 1.5 to 2 kg, moderate injury may be expected at as low as 30 g. In an open ejection seat, even higher acceleration levels can be tolerated because of the counteracting effects of aerodynamic forces. If the crewman is protected only by a lap belt, impact tolerance is reduced further. Volunteers have tolerated short $-G_x$ impacts up to 32 g where the impact velocity was 4.69 m/s and the acceleration duration was 0.001 s with an onset rate of 1600 g/s with no significant injury [94]. In other experiments, the volunteer was restrained only by a lap belt; impact velocities ranging from 5.8 to 8.8 m/s with accelerations from 11.4 to 20.0 g produced more pronounced subjective complaints and minor trauma [94].

In transverse $+G_x$ impact direction, human tolerance is potentially higher than in any other axis, if the crewman is restrained by full body

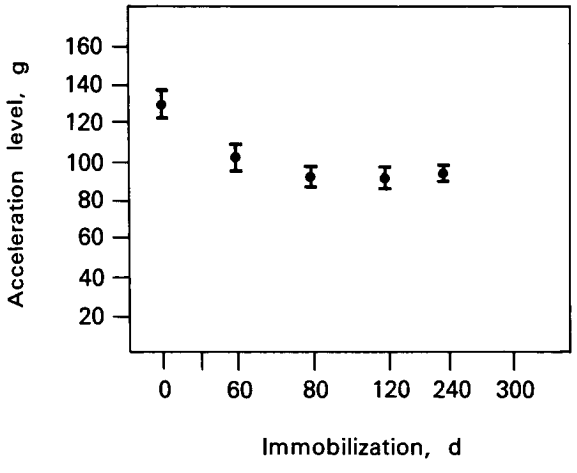


FIGURE 10.—Spinal impact tolerance of normal and osteoporotic primates. (After [46])

support. Impact levels up to 35 g for 0.16 s with an onset rate of 1115 g/s were tolerated by a volunteer subject with only relatively mild symptoms [94]. Shock symptoms—pallor, vertigo, no readable blood pressure, and loss of consciousness—were the results in a volunteer test at 40.4 g from 0.040 s duration with a velocity change of 14.8 m/s and a rise time of 0.083 s, resulting in an onset rate of 2140 g/s [94]. Human subjects exposed to $+G_x$ impact in the range of 35 to 40 g for 0.03 s with onset rates of 4000–5000 g/s complained of pelvic pain and changes in cardiovascular system activity, that is, bradycardia and decreases in systolic and diastolic blood pressures were recorded [4]. The impact exposure limit for the $+G_x$ direction, based on available data, is estimated at 35 g for acceleration durations up to 0.1 s to prevent injury [17]. Higher accelerations have been estimated as tolerable, if moderate injury is acceptable.

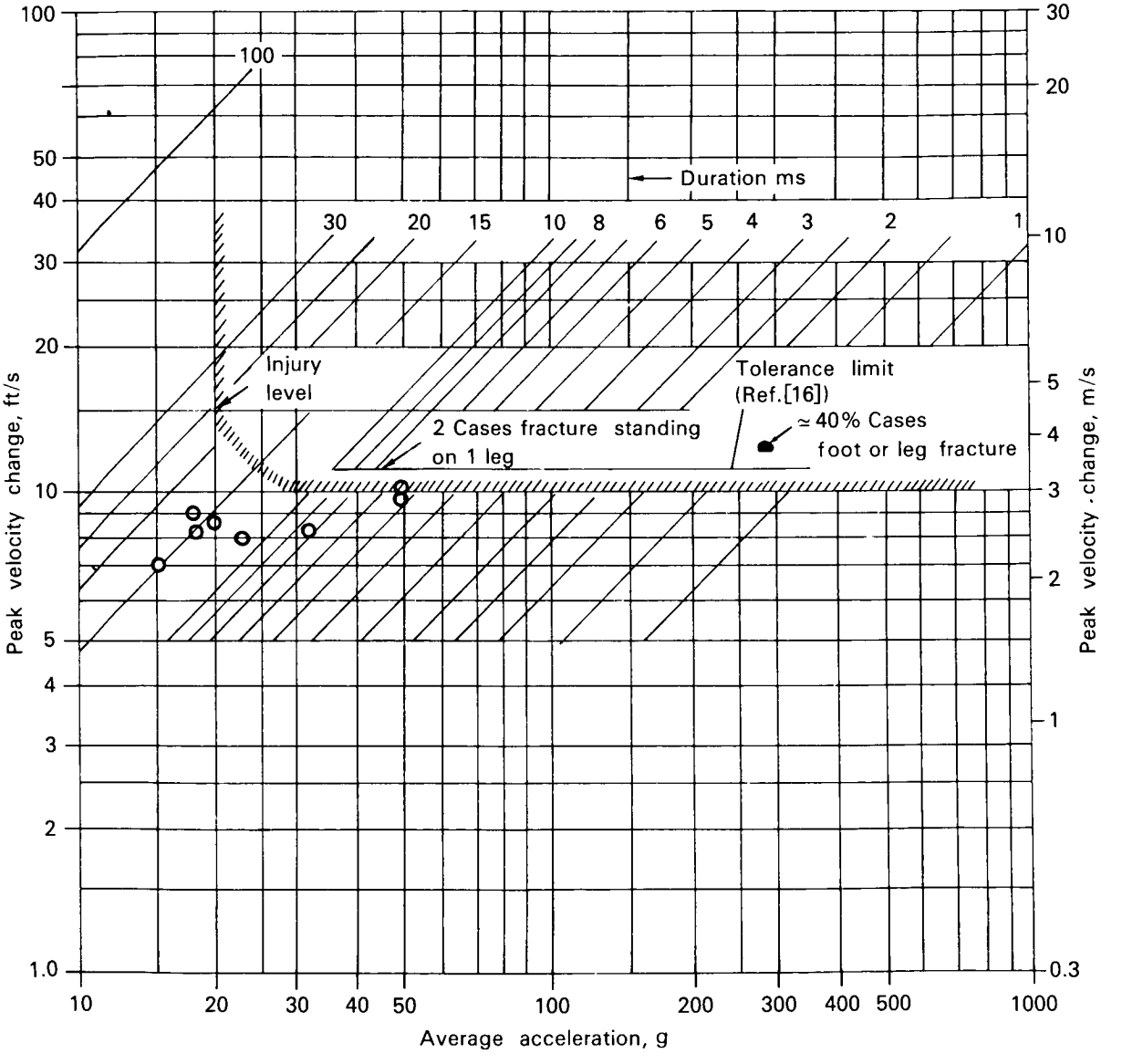


FIGURE 11.—Tolerance of stiff-legged standing men to shock motion of short duration. (After [41])

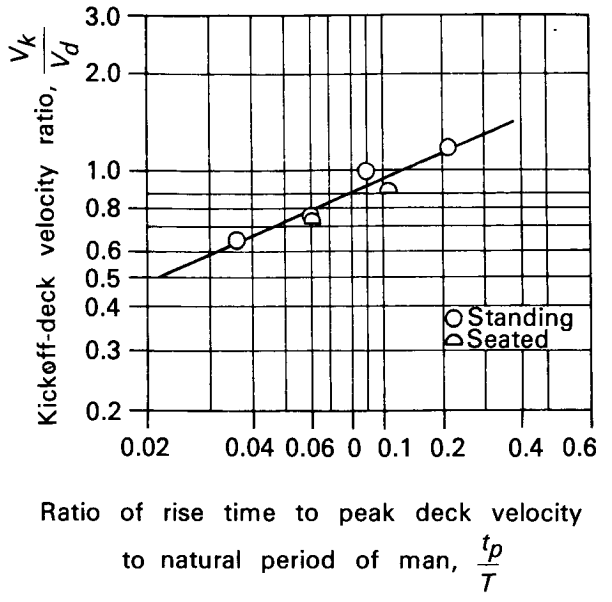


FIGURE 12.—Ratio of kickoff to peak deck velocity as a function of ratio of rise time to peak deck velocity to natural period of man. (After [41])

Lateral (+ G_y) Impact Tolerance

Human tolerance to lateral (+G_y) impact environments is not well-defined. A rather narrow range of acceleration pulse durations has been explored in tests. Volunteer subjects supported by a fully contoured couch were exposed to impacts up to 22 g with an onset rate of 1350 g/s where impact velocity was 5.9 m/s (19.3 ft/s) [13]. In another series of tests, volunteers were supported laterally by flat plates on which their shoulders would bear during impact [7]. The acceleration-time patterns used are discussed in detail in the section dealing with off-axis tolerance.

Tests with volunteers were conducted with more conventional restraints and seats, but the acceleration levels found tolerable were more moderate. A lap belt, shoulder harness, and crotch strap configuration were tested with human subjects up to 17.7 g without irreversible injury [76]. Tests have also been run with volunteers restrained only by a lap belt [107]; these tests were terminated when an acceleration level of 9 g was reached due to prolonged pain symptoms in the neck musculature.

Off-Axis Impact Tolerance

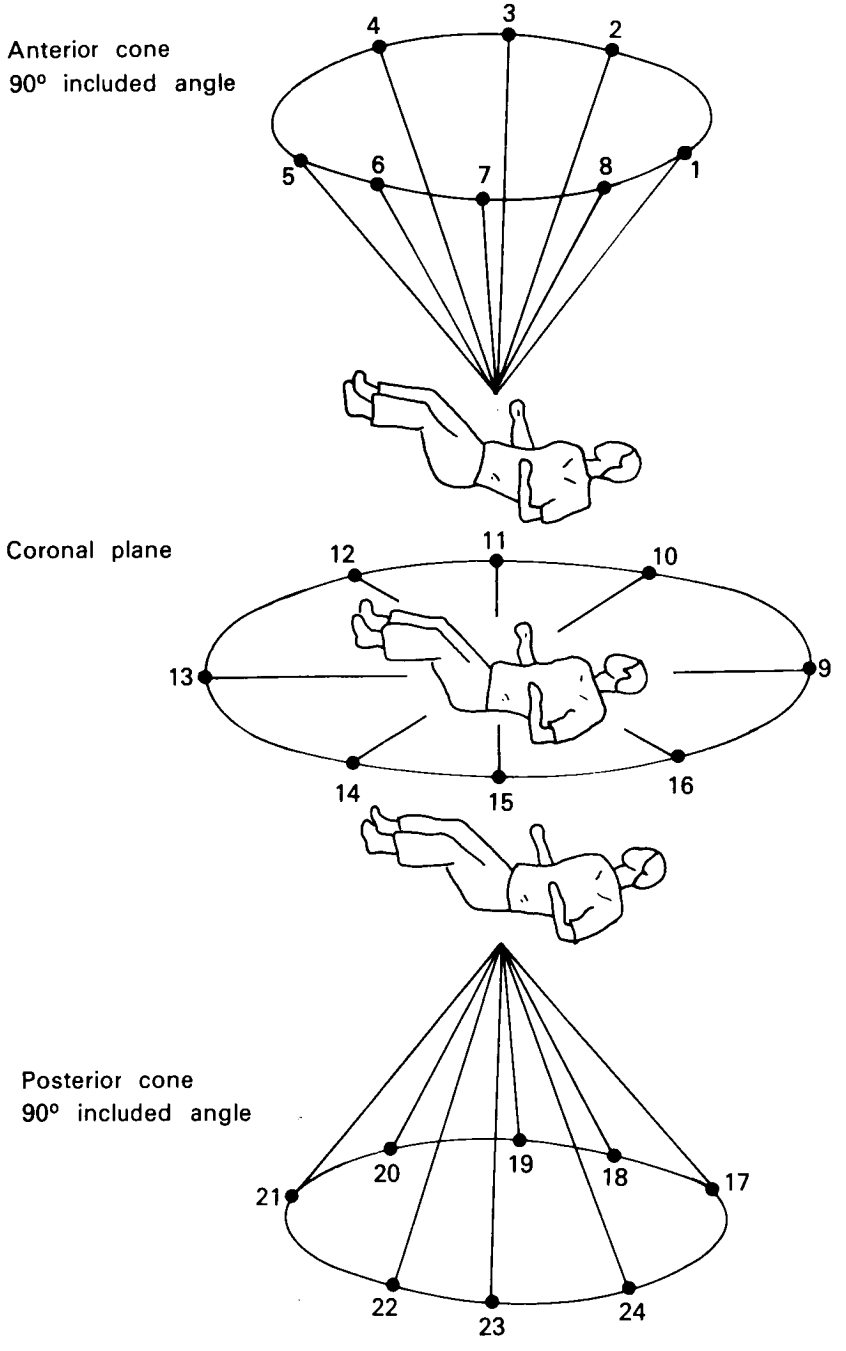
Impact exposure limits research has been concentrated on the cardinal axes, therefore, limits have not been developed for impact environments in other axes. Available data have been collected to evaluate acceptability of a narrow range of impact environments using body-support and restraint systems proposed or developed for specific aerospace systems. The most extensive work of this type was used to study impact effects resulting from descent velocities and crew module attitudes anticipated for Project Apollo landings. The scope of this work ranged from exploratory studies of the efficacy of methods to provide maximum body support and restraint to the evaluation of prototype spacecraft equipment. The effort was subdivided into several impact test programs conducted at different research facilities. The positions of the impact vector studied are described in Figure 13.

The initial series of impact tests was conducted on a vertical deceleration tower [7, 103]. In 32 tests to evaluate $\pm G_y$ impact vectors, there were no adverse subjective reactions to acceleration magnitudes to 22 g with velocity changes to 5.88 m/s. Subjects were restrained by lap belt, torso harness, and leg restraints and supported by a contoured pad filled with microspheres. This series was expanded to explore seven acceleration vector directions (positions 11, 15, 19, 20, 21, 22, and 23) and six acceleration-time histories; 20 volunteers were exposed to the impact profiles shown in Figure 14a. Peak accelerations ranged from 13.4 to 26.6 g with onsets from 426 to 1770 g/s; the power spectral density of each of these impact patterns is shown in "b" of Figure 14. Test subjects were restrained by shoulder straps and cross-chest straps converging at the sternum and a lap belt with crotch straps. The test seat included flat metal plates to support head, torso, and legs. No injuries were produced in this study, although some transient changes (abrupt rhythm changes and premature ventricular contractions) appeared in ECGs.

Sixty-one impact tests were conducted on a horizontal acceleration track with volunteer subjects to study the effects of $-G_z$ impact [40]. Subjects were restrained to a rigid couch by shoulder straps, cross-chest straps, lap belt, crotch straps,

and leg restraints. Impact magnitudes of 18.5 g were recorded on the accelerator sled with a velocity change of 5.94 m/s; onset rates ranged from 208 to 8140 g/s. Electrocardiograms of all subjects indicated transient sinus bradycardia for 2 s after impact. Bradycardia was observed in one subject for 30 min following impact.

Another series of 146 tests was conducted on a horizontal decelerator to supplement the above studies and to evaluate impact vector positions 1



Sled positions

Position no.	Roll	Pitch	Yaw
01	0	315	0
2	0	335	330
3	0	005	320
4	0	035	330
5	0	045	0
6	0	035	030
7	0	005	040
8	0	335	030
9	0	085	180
10	0	085	220
11	0	085	270
12	0	085	320
13	0	085	0
14	0	085	040
15	0	085	090
16	0	085	140
17	0	045	180
18	0	035	210
19	0	005	220
20	0	335	210
21	0	315	180
22	0	335	120
23	0	005	140
24	0	035	150

Note:
Deceleration force acts toward subject

FIGURE 13.—Deceleration force vector orientation for Apollo impact tests [9].

through 16, shown in Figure 13 [95]. Accelerations measured on the impact sled ranged from 6.0 to 26.3 g, onset rate varied from 250 to 2130 g/s, and the velocity of the sled at impact time ranged from 5.3 to 13.96 m/s. Acceleration magnitude and onset rate increased simultaneously. Restraint and support systems used in these experiments were similar to those used in the vertical deceleration tower [103]. No persistent or severe subjective complaints were found in 119 of the 146 tests conducted with volunteers. A forward-facing subject tipped back at 45° (position 5) sustained simultaneous compression and hyperflexion of the trunk which produced persistent soft tissue injury in the area of the 6th, 7th, and 8th thoracic vertebrae. Impact was 25 g at 960 g/s in 0.097 s. Blood and urine microscopic and chemical findings were within normal limits for all tests. Fifty-five of 144 ECGs showed significant bradycardia within 51 s after impact of more than 15 g. Incidents of bradycardia were associated with impacts with a $-G_z$ component.

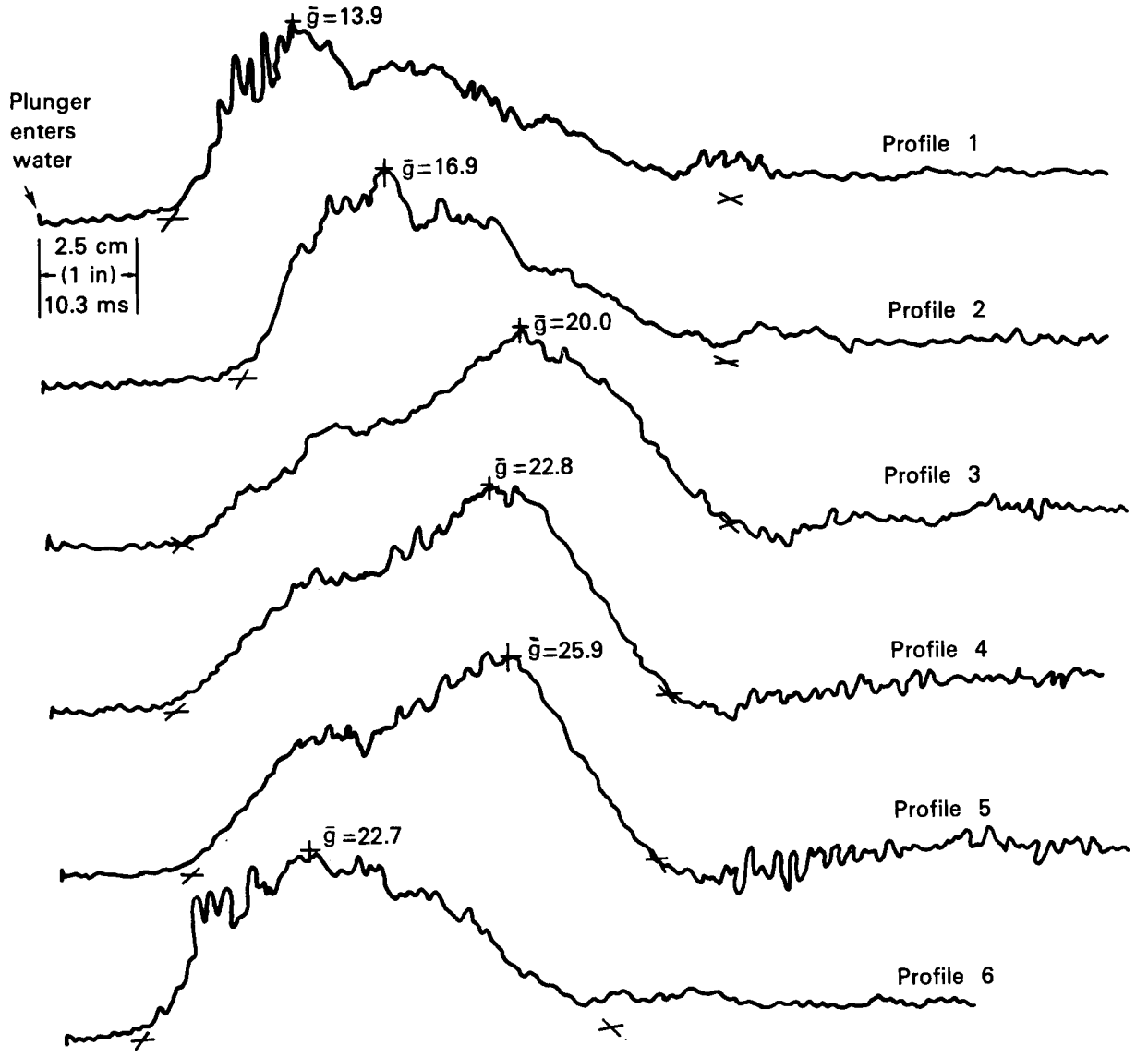


FIGURE 14a.—Vehicle acceleration profiles [103].

This series of impact experiments was later expanded to 288 tests to explore each of 24 positions of the impact vector [9]. Impact acceleration magnitude ranged from 5.5 to 30.7 g, rate of onset varied from 300 to 2500 g/s, and impact velocity ranged from 2.8 to 13.7 m/s. Significant findings of postimpact physical examination are summarized in Table 4.

Data are also available from a series of 11 (volunteer) impact tests conducted on the horizontal decelerator using a less restrictive body support and restraint system [79]. These tests were used to evaluate adequacy of an aircraft restraint harness configuration consisting of shoulder straps, lap belt, and inverted V crotch straps, and a noncontoured seat with a shallow, 5.08–cm deep head support. The configuration proved adequate for impact magnitudes to 14 g with velocity change of 10.9 m/s and onset rate of 1070 g/s.

Missile Impact

Injuries due to the impact of objects propelled by blast pressures, winds, ground or floor shock, and others are dependent upon a number of factors. Among them are mass, velocity, character, density, and impact angle of the projectile whether or not penetration occurs; the area and

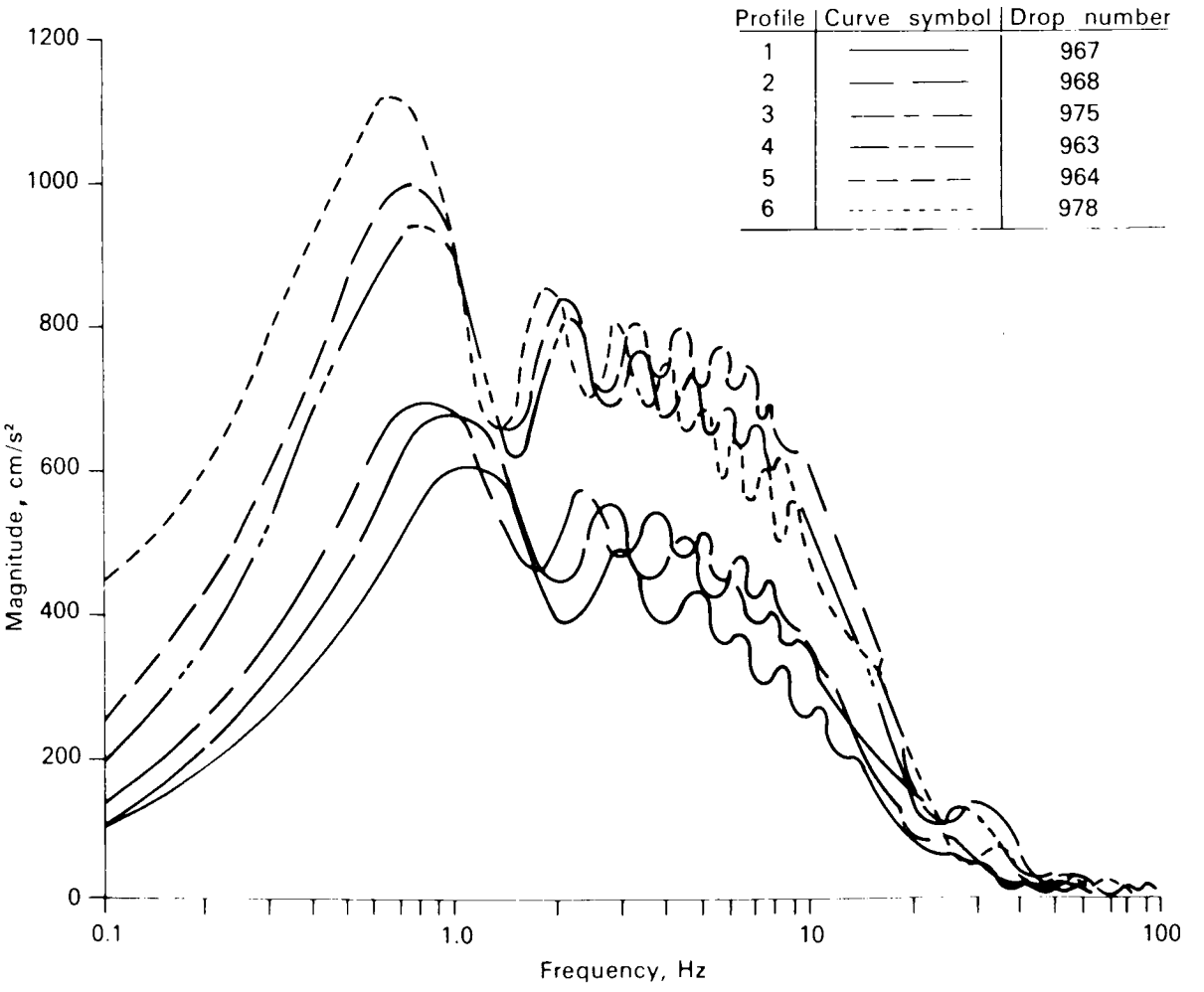


FIGURE 14b.—Power density spectra [103].

organ of the body involved; the amount and kind of clothing; and immunological status and general health condition of the injured individual [14, 105]. Studies of tissue damage by impact of small objects show that the energy of small objects striking a body surface overlying soft tissue is absorbed in the surrounding tissue and does not bring about motion of the whole body [21]. Tentative criteria for missile damage in humans are shown in Table 5.

Impact Protection

Impact protection of man or animal is dependent upon the manner in which impact stress is transmitted to the body and the degree of body support and restraint that have been provided. The method of fixation of the subject to the impacted structure is perhaps the most fundamental consideration. Seat structure and restraint reinforce the body to prevent injurious hyperflexion or hyperextension of anatomical joints and excursions of body organs [63]. Body support and restraint act to distribute impact loads over the body surface. Restraint systems constructed of webbing materials are usually designed to distribute impact loads into the skeletal system. Impact loads should generally be distributed uniformly over as wide an area as possible to avoid concentration of pressure. An exception to this rule would be where the body may act to attenuate the load being transmitted to vital parts, whereas direct coupling might be more injurious. Of many experimental approaches used to provide maximum load distribution, one was to immerse the body in fluid. Effectiveness of this technique to increase tolerance to long-duration acceleration has been demonstrated in centrifuge experiments.

Impact experiments with mice and dogs immersed in water and congealing gypsum have shown that tolerance may be increased up to six times higher than without immersion [63, 64, 65]. Covering the walls of the immersion vessel with porous rubber to attenuate high hydraulic pressure was a critical factor in animal survival [64].

Effects of several other methods of body support and restraint upon the probability of lethality have been demonstrated with guinea pigs [56, 57, 77]. In these experiments, the differences were explored between various degrees of support and restraint ranging from rigid, fully enclosing contoured shell, to a more conventional arrangement of flat seat pan and seat back with a webbing restraint configuration. In one series of experiments [77], guinea pigs were exposed to $+G_x$, $-G_x$, and $+G_z$ accelerations at impact velocities of 12.2, 18.3, and 24.4 m/s in two types of support and restraint systems (SARS). One support and restraint configuration, referred to as SARS IIa or the isovolumetric concept, consisted of a rigid, contoured support and a one-piece fabric apron and retention straps in the shoulder, upper chest, lower abdominal, and crotch regions. The fabric apron covered the ventral thoracic-abdominal area.

The second configuration, referred to as SARS IIIa, consisted of flat plates to provide back support and a seat pan and straps restraining the thoracic and abdominal-crotch areas. Head restraint used on both configurations was identical. The system using the thoracic-abdominal apron was markedly superior in $-G_x$ impacts, slightly superior in $-G_x$ impacts, and approximately equal in the $+G_z$ orientation. Major pathology associated with each of the support and restraint configurations is summarized in Table 6 in terms of occurrence percentage. The 50% probability of lethality values using average g ranged from 209 to 325 for $+G_x$, 287 to 350 for $-G_x$, and 103 to 135 for $+G_z$.

Seating and Other Devices

In many early studies of impact tolerance for spaceflight operations, molded couches of rigid plastic foam were used to support both animal and human subjects. Seats of varying degrees of contouring have been used in spacecraft applications to provide crew protection. Individually molded seats were used in Mercury, Gemini, and Voskhod spacecraft [4]. In Apollo spacecraft, simpler seat structures were used to enhance interchangeability of crew stations throughout long-duration flights [79]. These seat structures are supported within the spacecraft by impact-attenuating struts, shown in Figure 15, a and b. Various attenuation devices which have been studied range from simple, crushable honeycomb structures to more complex, hydraulically

damped spring systems and cyclic strain mechanisms [58, 99].

Impact protection to the crewman can be achieved to the greatest extent within the impact transmission pathway with devices such as externally mounted air bags or internally mounted impact-attenuating struts. Control of the entire pulse shape is essential to optimum protection, in addition to maintaining the most advantageous parameters in magnitude, duration, and mean rate of onset. Depending on elastic properties of the body being accelerated, a waveform can be chosen in which the ratio of the acceleration in the body being accelerated to the magnitude of the acceleration of the body imparting the acceleration will be equal to unity [28]. This can be accomplished by careful design of all acceleration transmission pathways in addition to impact-attenuation devices. Crushing of the vehicle structure provides some energy absorption and this characteristic can be enhanced by the vehicle

TABLE 4.—*Significant Postimpact Physical Exam Findings* [9]

Significant physical findings	Test position	Sled g
Harness burns (all first degree)	2	20.0
	7	23.0
Dazed and disoriented (lasting no longer than 2 min postimpact)	17	17.4
	17	18.9
	17	21.7
	17	25.8
	17	19.6
	19	30.0
	24	28.1
	24	24.6
	24	16.5
	9	9.8
	1	17.2
	21	19.0
Respiratory difficulty (lasting no longer than 1 min postimpact)	17	18.9
	23	19.5
	18	24.6
	18	23.2
	24	23.7
	24	16.5
Blood pressure difference (20 mm Hg at pre- and postrun physical exam)	19	30.0
Pulse difference (20 beats/min at pre- and postrun physical exam)	23	19.4
	17	19.6
	24	20.2
	12	19.5
Engorged retinal vessels	17	21.7
	3	9.2
Back and/or neck pain and decreased range of motion	17	25.8
	1	17.2
	5	25.1
	5	21.0

TABLE 5.—*Tentative Criteria for Indirect Blast Effects Involving Impact from Secondary Missiles* [106]

Missile, type	Critical organ/event	Related impact velocity (m/s)
Nonpenetrating 4.54 kg object	Cerebral concussion:	
	mostly "safe"	3.05
	threshold	4.58
	Skull fracture:	
	mostly "safe"	3.05
	threshold	4.58
	near 100%	7.02
Penetrating 10-g glass fragments	Skin laceration[1]:	
	threshold	15.3
	Serious wounds[1]:	
	threshold	30.5
	50%	54.9
	near 100%	91.5

[1] Represent impact velocities with unclothed skin. A serious wound arbitrarily defined as a laceration of the skin with missile penetration into tissues to 10 mm or more.

TABLE 6.—*Occurrence Percent of Major Pathology in Guinea Pigs at Cumulative Velocities*[1] [77]

Injury type	SARS IIIa			SARS IIa		
	$-G_x$	$+G_x$	$+G_z$	$-G_x$	$+G_x$	$+G_z$
Brain hemorrhage	42	61	30	42	91	22
Pulmonary hemorrhage	91	82	80	74	100	32
Cardiovascular pathology	33	52	48	19	0	0
Hepatic laceration	83	56	5	45	3	2
Gastrointestinal pathology	77	19	15	19	30	17
Paralysis	0	0	18	0	0	80
Total nonsurvivors	180			161		

[1] Entrance velocities, 12 to 24 m/s.

structure designer. Deformation of cushioning materials and restraint system can also be designed to minimize transmittal of energy at frequencies where particular segments of the human body, such as the head, are most sensitive; however, care must be taken to assure that these elements of the protective system do not, in fact, amplify accelerations transmitted to the body.

Control of impact vector direction can be used to take advantage of differences in impact tolerance levels for each body axis. Design of seat angles may also be critical in providing maximum tolerance [8].

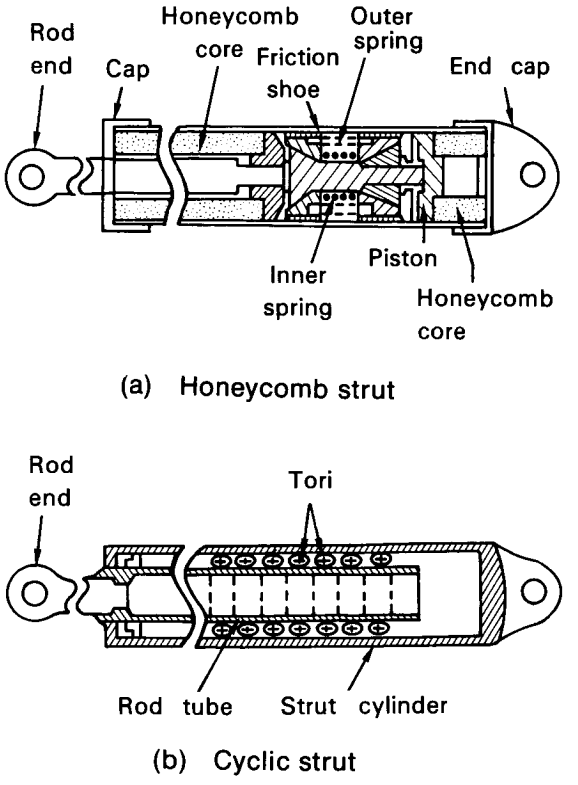


FIGURE 15.—Comparison of honeycomb and cyclic strain impact-attenuation systems for Apollo [98].

Mathematical models of both protection system and human body have greatly improved the designer's capability to select appropriate materials for crew seat cushioning and restraint systems, and impact-attenuation device performance characteristics [71, 72]. The same modeling techniques provided insight into effects of initial conditions of the crewman within his personal equipment. For example, these analytical techniques demonstrated the importance of eliminating slack or deadspace between crewman and his body-support and restraint system, and similarly provided design criteria for restraint-harness tensioning devices.

Other methods of crew protection include crew conditioning and use of pharmacological agents. Crew conditioning has been considered from several aspects. First, by assuring the best physical condition of the crewman through a sound program of preflight physical exercise. Second, by alterating the crewman's reaction to impact through crew training and exposure to mechanical stresses during simulated missions [28]. And finally, where long-duration missions may cause deconditioning of the musculoskeletal system, exercise and in the future, perhaps, use of chemotherapy to retard deconditioning are indicated.

Summary

The degree to which impact accelerations are an important factor in spaceflight environments depends primarily upon the technology of capsule landing deceleration and the weight permissible for the associated hardware: parachutes or deceleration rockets, inflatable air bags, or other impact-attenuation systems. Safe capsule landings on any type of terrestrial and extraterrestrial surface must be the goal of these hardware developments so that the restrictions imposed on most USSR and US space missions in the past can be relaxed. However, design for emergency situations such as crew escape during unforeseen failure on the launch pad will always require the most accurate information available on the limits of human tolerance and risk involved.

A considerable body of information has been available on human tolerance to impact and impact protection from aircraft escape, and aviation, as well as automotive crash research. However, both the USSR and US space programs had to define specific limits of human tolerance with higher accuracy and reliability than were previously known. Particular contributions in this area include: (a) exploration of impact tolerance for all impact directions; (b) definition of injury prob-

ability for low injury probabilities consistent with high reliability/safety requirements of space missions; and (c) development of mathematical models to predict injury probability for complex acceleration functions, and to calculate the crewman's biodynamic response when coupled to various support and restraint systems. These advances, as well as experience with new impact-attenuating crushable materials and structures, are of significance beyond the specific realm of space biotechnology.

The problem most specific to space medicine is the potential change of impact tolerance due to reduced bone mass and muscle stength caused by prolonged weightlessness and physical inactivity. Although valuable contributions to this area have been made through animal experimentation in the USSR and the US, considerably more research is required as space missions become extended over many weeks and months. Relationships between bone strength, bone mass, and muscle strength must be explored as a function of gravitational load, isotonic/isometric exercise, time pattern, and diet. For osteoporosis of disuse, appropriate time-scaling factors for bone dynamics as a function of gravitational exposure and activity time patterns must be established by relating animal experiments to human conditions. Changes in injury patterns due to these changes in the musculoskeletal system must be known and understood. Based on such studies, proper impact limit values, protection equipment, preventive measures such as exercise and possibly chemotherapy, and postflight care can be selected.

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Chapter 7

ANGULAR VELOCITIES, ANGULAR ACCELERATIONS, AND CORIOLIS ACCELERATIONS

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This chapter deals with the rotary motions generated by man and by machine that may be encountered in the exploration of space and the effects of such motions on the human organism. Under all conditions, active rotary motions will fall within the parameters of such movements executed by man under normal terrestrial conditions. These active rotations are characterized by short arcs, and the associated angular accelerations, although transient, may, in the case of head movements, far exceed the accelerations generated by conveyance or laboratory devices. It is also noteworthy that these active rotary motions produce their effects chiefly by stimulating sensory receptor systems with subsequent "amplification" in the central nervous system. The receptor systems in the semicircular canals deserve special attention, partly because these end organs are uniquely structured to respond to transient angular accelerations, and partly because they are gravity-independent.

Except in unprogramed situations, passive rotary motions to which man may be exposed are significant chiefly for the long duration of the angular velocities and not for the associated brief angular accelerations. In the generation of artificial gravity (by rotating part of a space vehicle or space station), spin-up or spin-down would rarely occur, and rotation at a constant angular velocity would be maintained for long periods. In this circumstance, active rotation of the head would generate Coriolis accelerations,[1] constituting abnormal patterns of vestibular stimulation that might elicit vestibular side effects. These side effects comprise reflex phenomena and widespread delayed epiphenomena (best known as motion sickness). Even in the weightless part, although head movements generate normal accelerative stimuli, the resulting sensory input encounters an abnormal integrative pattern (resulting from loss of stimulation of the otolithic receptors by gravity), and vestibular side effects may be elicited; thus, both vestibular organs may be involved by unnatural stimulatory conditions in space exploration.

Although all major sensory systems must be taken into account, their unfavorable influence, under conditions met in the exploration of space, are unequal. The organs of equilibrium, the semicircular canal and otolith organs, pose the essential problem. Much of the discussion which follows, therefore, will deal with the vestibular system, the mechanisms involved in the elicitation

[1] In this chapter Coriolis acceleration is defined as the "added acceleration" generated either by simultaneous exposure to angular velocities about two axes or to one linear and one angular velocity; it is left to the reader to determine from the context which one is applicable or if both are applicable.

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of side effects (especially motion sickness), and the operational problems engendered.[2]

MAN'S BIOLOGICALLY EFFECTIVE FORCE ENVIRONMENT

In this section, the concept of man's biologically effective force (BEF) environment is briefly developed in relation to life activities under terrestrial conditions and to the unique force environments in space exploration. The need for a common basis in discussing and comparing these forces is best exemplified in comparing "life" in a weightless spacecraft and life on Earth. The purpose here is not to attempt a comprehensive analysis and synthesis, which would involve a great undertaking and even then be incomplete, but to set forth major guidelines which point to further exploitation for practical or theoretical purposes.

Man's gravitoinertial force environment has its genesis in gravity due to a central field factor in the inertial forces generated by the motions of machine or man, or both in combination (Fig. 1). Under ordinary living conditions on Earth, gravitational force may be regarded as a constant and the only force of sufficient magnitude to affect total body weight significantly. It is the force to which man has become adapted throughout evolutionary development and to which he is accustomed through experience. The addition of mutually perpendicular lines to the vector representing gravitational upright forms the spatial frame of Earth reference. When man is exposed in conveyances and devices that generate accelerations or change his position with respect to the gravitational or gravitoinertial vertical, he is subjected to unnatural stimulatory conditions that may range far beyond physiologic limits. These accelerations generate an external force field that, along with gravity, comprises the total *external* force field.

The inertial forces generated by the active motions of the body or its parts may be regarded as "immanent" forces inasmuch as they do not contribute to the external force field, but are combined with it. These immanent forces are of small magnitude or short duration, deriving their significance partly because of being associated with motions that change the position of the body with regard to the other components in the force environment, and partly because these forces are sufficient to stimulate specialized sensory receptors that provide information about body statics and dynamics. Combined gravitational, inertial, and immanent accelerative forces constitute a complex, dynamic pattern that varies as a function of time.

Although the equivalence of gravitational and inertial mass is the unifying principle underlying the gravitoinertial force concept, this simplicity gives way to great complexity when taking into account the structural and functional characteristics of the body. Not only does the body lack uniformity, but also a state of mechanical equilibrium in all parts of the body is never reached.

The agravitoinertial forces are far more difficult to identify and measure in terms of a common unit than the accelerative forces. They assume great importance in a weightless environment, and a dichotomy may be drawn between agravitoinertial forces of mechanical and nonmechanical origin. With the latter, further distinctions are possible, ranging between forces so great at one extreme that absence of gravitational force is of no practical consequence, and the other extreme when its influence is felt. All these mechanical forces are generated by tensions and compressions and, with gravitoinertial forces, contribute to bodily deformations and stimulation of nonvestibular mechanoreceptors.

Weightlessness

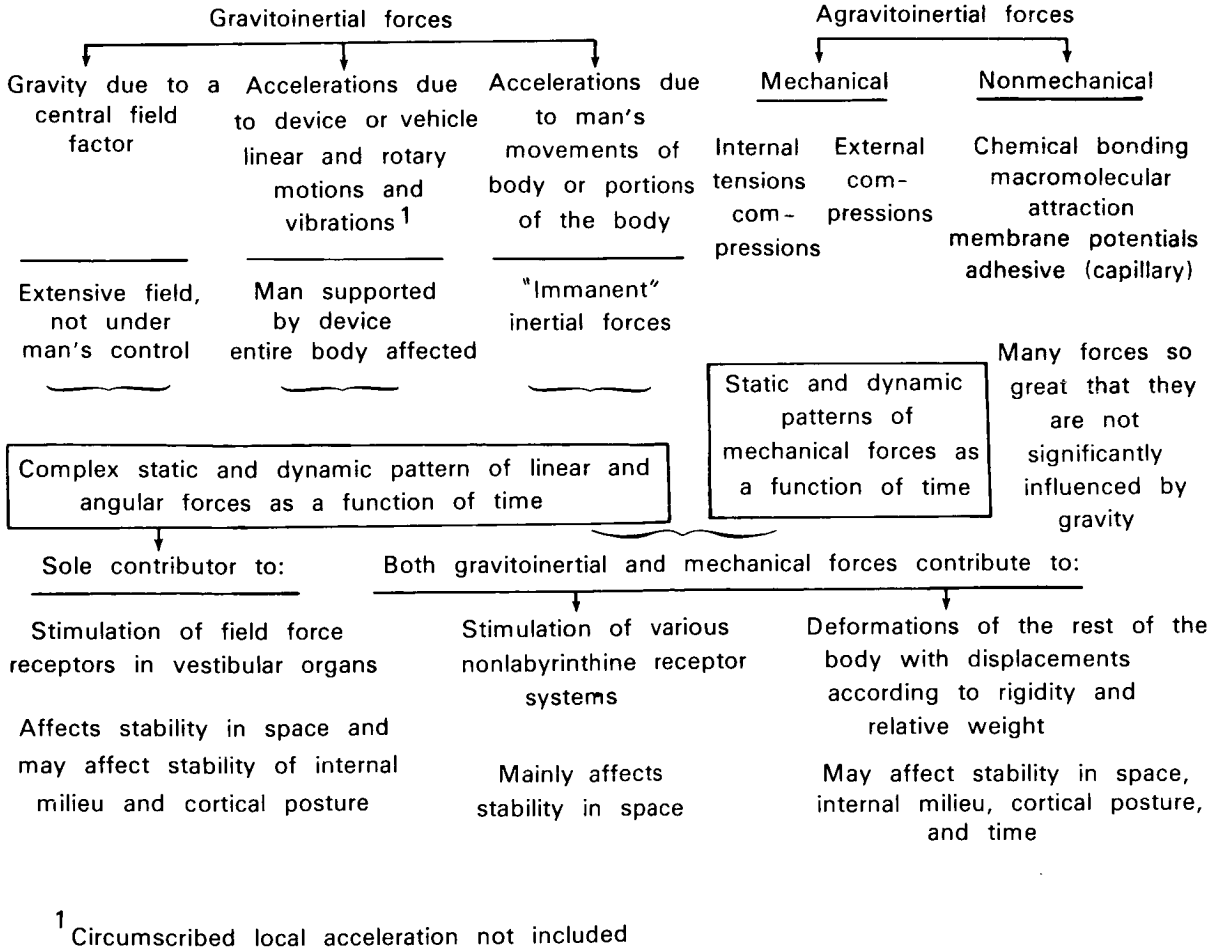
Under natural terrestrial conditions, the force of gravity due to a central field factor is only part of our BEF environment; hence, it is important to distinguish between weightlessness per se and man active in a weightless spacecraft. This difference, which may be very great, will be determined mainly by the role played by mechanical forces that are effective in countering the zero-gravity state.

[2] It is a pleasure to acknowledge my debt to Professor V. Polaev who provided an annotated bibliography covering key reports in the relevant Soviet literature.

Figure 2 illustrates an effort to analyze the BEF environment in a weightless spacecraft. Gravitoinertial forces are generated mainly by man's motions unless a device capable of generating accelerations is used. Immanent accelerations generated in the course of man's work and housekeeping activities contribute little to his "apparent weight" but are important since they stimulate sensory receptors (vestibular and nonvestibular mechanoreceptors) and thus contribute to the flow of information to the nervous system.

The preservation of man's well-being in a weightless spacecraft is heavily dependent upon agravitoinertial forces, which are of mechanical or nonmechanical origin. An analysis of the latter should be made in terms of their effectiveness at different organizational levels in the body. A table might be prepared indicating the forces operant at different levels; e.g. molecular, intracellular, cellular, and tissue levels. Cytochemical reactions involve forces (thermodynamic, bioelectric, and chemical) so great that they are gravity-independent. Agravitoinertial *mechanical* forces stimulate mechanoreceptors serving touch, pressure, and kinesthesis but cannot stimulate vestibular receptors.

The analysis is carried one step farther in Figure 3. Presumably, with the crew at rest and with head fixed, there would be physiologic deafferentation of the otolith apparatus, with consequent loss of its tonic discharge but retention of a spontaneous or resting discharge analogous to the difference between eyes open and closed. There would be no corresponding effect on the



[1] Circumscribed local acceleration not included

FIGURE 1.—Man's biological force environment under terrestrial conditions.

semicircular canals. Rotations of the head would provide stimulus to the canals the same as under terrestrial conditions, but the transient linear accelerations generated might or might not constitute an adequate stimulus to the otolith apparatus, and, if adequate, the information would be neither useful for orientation to the upright nor concordant with the canalicular input. Thus, among vestibular receptors and nonvestibular mechanoreceptors, the canals alone are stimulated essentially the same with natural movements of the head (body) under terrestrial and weightless conditions. The otolith organs encounter the unique stimulatory condition with the lifting of the stimulus due to nullification of gravity. Reference is made to reports that deal with the problem in a different manner or approach [32, 33, 51, 92, 122, 138].

Rotating Environment

In a slowly rotating room constrained to rotate about the Earth-vertical axis, a person carrying out various activities is subjected to complex changes in the gravitoinertial force environment. Not only must the forces acting at man's center of gravity be taken into account, but also the sep-

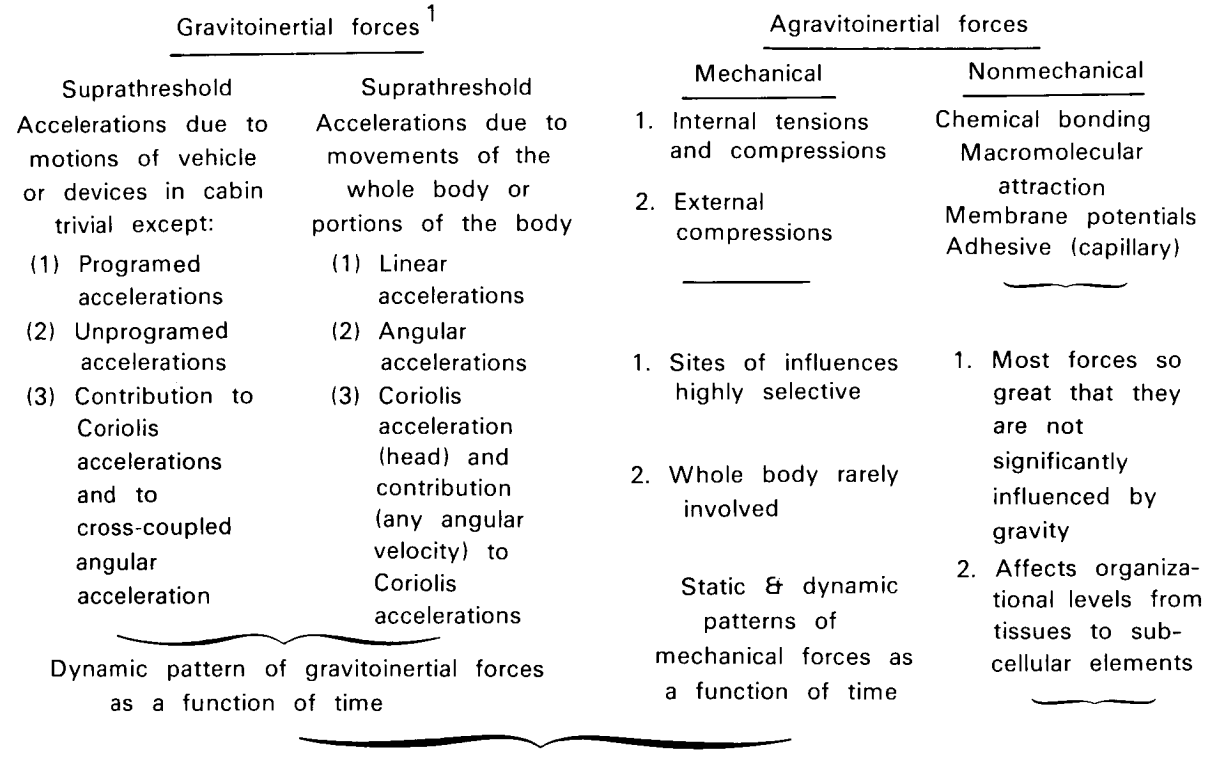


FIGURE 2.—Man's biological force environment in near-weightlessness. (Comparisons must be made with terrestrial conditions taking account of (1) body configurations and motions, and (2) the maintenance of homeostasis in terms of gravity-dependence.)

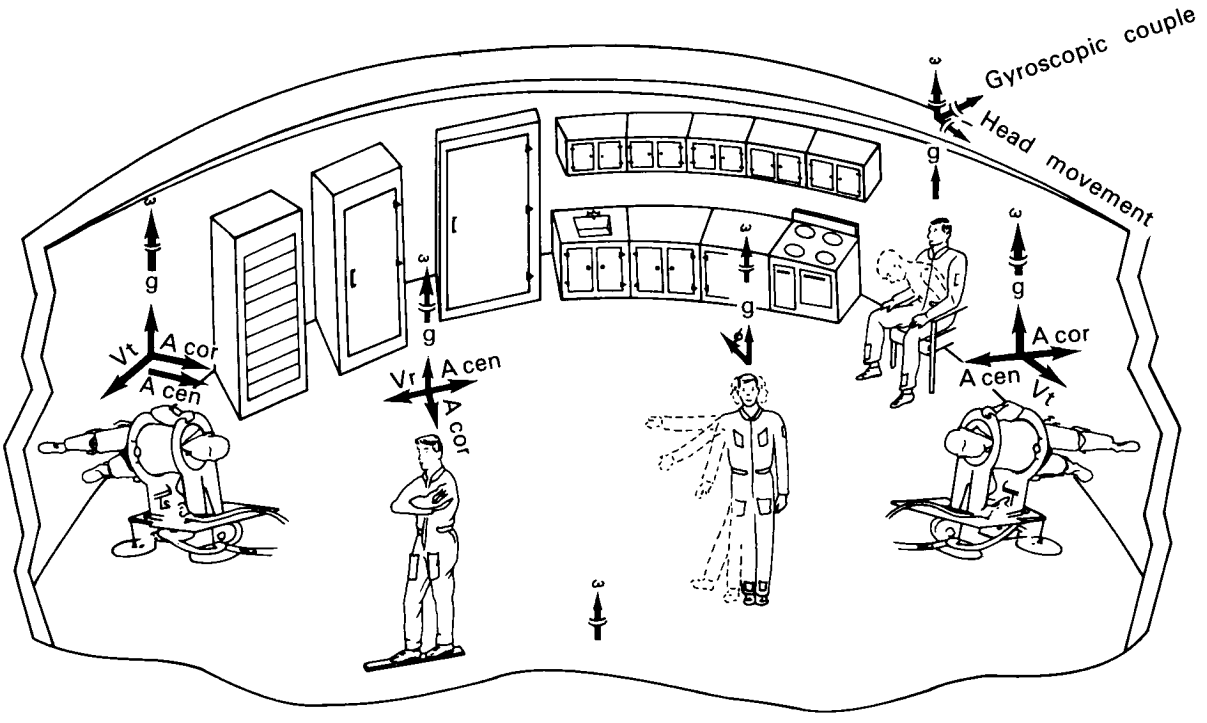
			Resting discharge						Physiological stimulus conditions						Artificial stimulus conditions		
		Genesis	Maint. neural 2nd neur	Maint. conh beyond 2nd n.	Modulated by oto. apparatus	Tonus	Affects R-L V. balance	Inc. susc. to CNS funct. dist.	Stimulus	Sensory	Mod. oto. output	Mod. by oto. output	Affects R-L vestib. balance	Inc. susc. to CNS dist.	Coriolis acc.	Angular acc.	Linear acc. & constant rotation within critical range
Canalicular system gravity-independent	Earth	Biochem. gravity-independent	Yes	Yes	Yes	Probably	Yes	?	Inertial angular & Coriolis acc.	Phasic	Yes	Yes	No	Yes	Abn. responses reflex phenom motion sickness	Response thresholds 0.04°/sec²	May constitute an adequate stimulus
	Spacecraft	Biochem. gravity-independent	Yes	Yes	Yes	Probably	Yes	?	Same	Phasic	Yes	Yes & may affect behavioral resp.	?	Yes	Abn. responses reflex phenom. motion sickness	Response thresholds may well be diff.	Should be differences (Quant.) at least imp. to investigate

				Physiological stimulus conditions				Artificial stimulus conditions	
		Presence	Genesis	Stimulus due to gravity: Proof	Stimulus due to gravity: Sensory input	Stimulus due to change in position of head in gravitational field: During change	Stimulus due to change in position of head in gravitational field: Head fixed in new position	Stimulus due to immanent inertial linear acc.	Response thresholds to stimulation	Suprathreshold levels of stimulation
Otolithic systems gravity-dependent	Earth	Inferred	Chem–el. act.	Ocular counterroll, oculogravic illusion A&E & percept. upright vary as function of g-loading	Tonic modulates reflex activity and canalicular influence	Dynamics not investigated in systematic fashion	Few systematic studies. Servation decreases with large departures from upright	Probably less imp. than canals for maintaining postural upright in man	Vary with departures from grav. upright or gravitoinertial upright	Establishment of gravitoinertial vertical other than in long body axis characterized by a "lag" and a "magnitude" effect (overcompensation at levels greater than 1.2 g units)
	Spacecraft	Demonstrated in parabolic flight	Gravity independent	? No A&E C-roll percept. upright A&E Mueller & Aubert phenomena	No input	Not possible		Mainly transients Should be measured Stimulus thresholds may be affected by loss of g loading Probably effective in stimulating oto. system	Has not been investicated carefully but there are reports of "increased sensitivity" Behavioral significance in terms of gravitoinertial upright necessarily different	Absence of the earth's standard of gravity will have effect of exaggerating influence of vectors not in accord with body or visual upright. Possible effects on orientation and susceptibility to motion sickness

FIGURE 3.—Certain differences between life on Earth and in weightless spacecraft with reference to the canalicular and otolithic systems.

arate consequences of head and limb motions with and without whole body motions.

Figure 4 illustrates the forces acting on the subject's mass when he is recumbent and seated. Centrifugal force derives from $r\omega^2$ where r = radius and ω = angular velocity. The angle ϕ represents the change in direction of the gravitoinertial upright from the gravitational upright. With the subject moving with or against the direction of rotation or toward or away from the center of rotation, Coriolis forces must be taken into account as well as the changes in centripetal force. The fundamental law relating the time rate of change of a vector, measured by an observer in space rotating with respect to the reference space, may be expressed mathematically by the vector equation:



g - Acceleration of gravity
A cen - Centripetal acceleration
A cor - Coriolis acceleration
Vt - Tangential velocity
Vr - Radial velocity
ω - Angular velocity of rotating room
ø - Angle between gravitoinertial and gravitational upright

FIGURE 4.—Responses to the force environment in a rotating room. Crewmen 1 and 2, in articulated molds supported by air-bearing devices, are "walking on the wall," simulating the orientation in a rotating spacecraft. Crewman 2, walking in the direction of rotation becomes somewhat heavier because his angular velocity, hence, centripetal acceleration, is increased and sums with the Coriolis accelerations generated. Crewman 1, walking opposite the direction of rotation becomes somewhat lighter because his centripetal accelerations are decreased and Coriolis accelerations must be subtracted. Crewman 3, walking toward the periphery of the room is exposed to increasing levels of centripetal acceleration and constant levels of Coriolis accelerations. Crewman 4, standing, is demonstrating two phenomena: first, as he moves his arm or leg sideways, a tendency to veer backward, the so-called "giant-hand" effect; second, as he makes (rotates) his head move in the plane of the room's rotation, Coriolis accelerations and illusions are not generated, a so-called "free movement;" third, the angle phi (ϕ) indicates the change in direction of the gravitational upright due to centripetal force. Crewman 5 is making a head movement out of the plane of rotation which does generate Coriolis accelerations producing characteristic illusions described. (Drawing courtesy of Dr. D. B. Cramer)

$$\left(\frac{d\bar{V}}{dt}\right)_r = \left(\frac{d\bar{V}}{dt}\right)_m + (\bar{\omega}rm \times \bar{V}) \qquad (1)$$

where

$(d\bar{V}/dt)_r$ = change in velocity vector with respect to the reference space,
$(d\bar{V}/dt)_m$ = change of velocity with respect to moving space,
$(\omega rm \times \bar{V})$ = change of velocity vector due to rotation of moving space.

To a subject in the rotating environment, this acceleration or force vector may manifest itself in two ways. First, it adds to the apparent weight of a body moving in the direction of rotation and subtracts from the apparent weight when it moves against the direction of rotation. Second, when a body moves toward the center of rotation, the linear Coriolis force is exerted in the direction of rotation at right angles to the body's motion; when moving away from the center of rotation, the force is opposite the direction of rotation. A motion parallel to the axis of rotation will generate no Coriolis acceleration. The value of Coriolis acceleration in g-units for a body moving perpendicularly to the axis of rotation in a spinning system may be determined by:

$$F\ (\text{Coriolis}) = 0.00651\ VN \qquad (2)$$

where

V = velocity of body relative to rotating vehicle in feet per second,
N = vehicle rate of rotation in revolutions per minute.

For any motion not exactly perpendicular to the axis of rotation, the component of the velocity that is perpendicular is used to determine the Coriolis force; hence, the value must be multiplied by the sine of the angle between the angular rotation rate vector and the velocity vector. Figure 5 illustrates the Coriolis force in g-units for various rates of movement perpendicular to the axis of rotation at different rates of the room's rotation. The combined Coriolis and centripetal forces influence ataxia exhibited by subjects. It is apparent from Figures 4 and 5 that a person walking against the direction of spin will experience a slight decrease of apparent weight and a slight increase when walking with the direction of rotation. Also, moving toward the center, the linear Coriolis force would be in the direction of spin, and walking toward the periphery, the direction would be reversed.

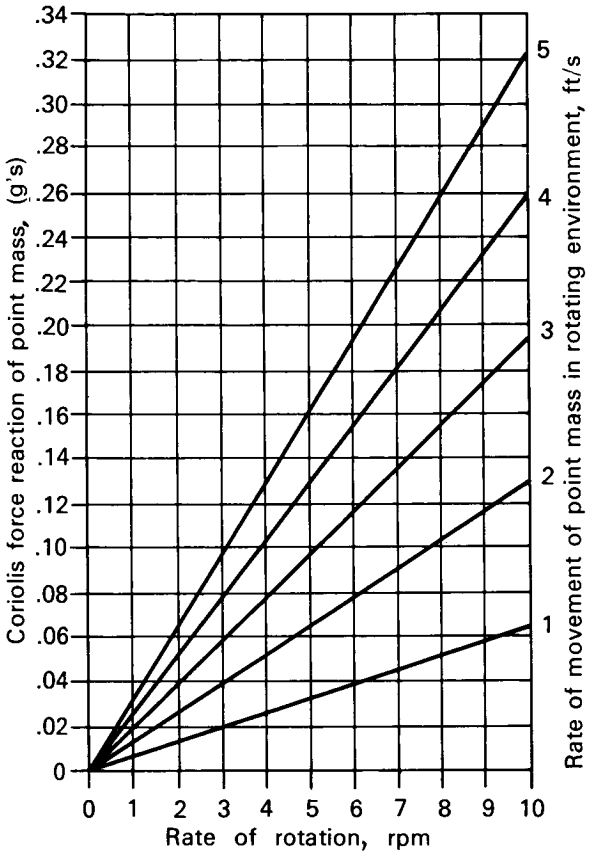


FIGURE 5.—Coriolis force reaction of a mass moving in a rotating environment. Force in pounds = Earth gravity weight × g units

The above analysis is oversimplified because the motions of limbs and head need not conform to motions of the center of gravity; moreover, the motion of the center of gravity itself is complex, although motions normal to the Earth horizontal would not generate a Coriolis acceleration.

Consideration must also be given to the angular Coriolis accelerations which constitute an abnormal stimulatory pattern where the semicircular canals are concerned. When angular Coriolis accelerations are above threshold, reflex vestibular disturbances result and may be followed by motion

sickness, making them of great practical importance in dealing with rotating environments. Angular Coriolis accelerations per se are independent of the distance from the center of rotation of the room and, indeed, of the level of G-loading within the ranges to be encountered in rotating environments.

Mathematical Analysis of Coriolis Accelerations

Stone and Letko [127][3] have developed equations for the effects of angular acceleration and angular velocity about two axes.

Definitions and Symbols

Nodding — a rotation of the head about the y-axis (Fig. 6).

Turning — a rotation ot the head about the z-axis (Fig. 6).

Rolling — a rotation of the head about the x-axis (Fig. 6).

α_{G_θ} angular nodding acceleration (component of angular acceleration about the y-axis)

α_{G_ψ} angular turning acceleration (component of angular acceleration about the z-axis)

α_{G_ϕ} angular rolling acceleration (component of angular acceleration about the x-axis)

$$\omega_{G_\theta} = \int \alpha_{G_\theta}\, dt$$

$$\omega_{G_\psi} = \int \alpha_{G_\psi}\, dt$$

$$\omega_{G_\phi} = \int \alpha_{G_\phi}\, dt$$

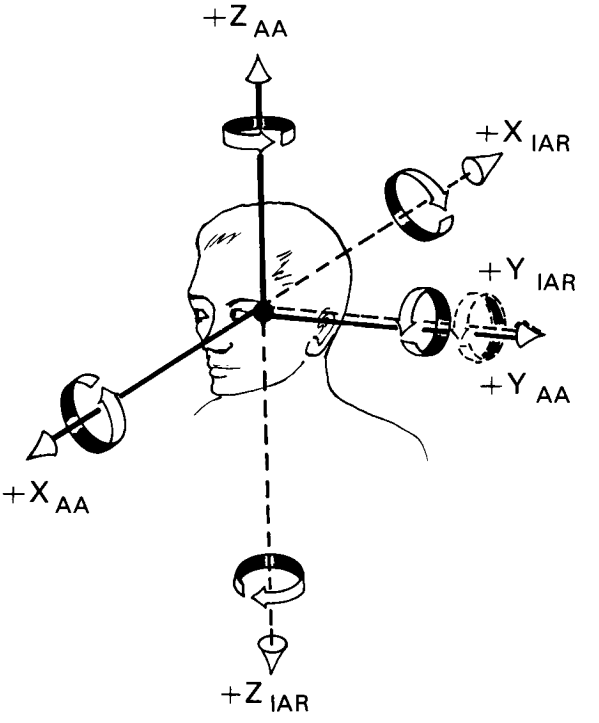


FIGURE 6.—Right-hand rule applied to the True reference system (angular accelerations) and the inertial (reaction) force system. Note that the two systems have opposite signs except in y axis—facing the page (True) and facing the left side of the body (inertial).

ω_{h_θ} nodding velocity—a fore and aft motion of the head at the neck or from the whole body [4]

ω_{h_ψ} turning velocity—a motion about the neck or long-body axis [4]

ω_{h_ϕ} rolling velocity—a sideways motion of the head or from the body [4]

[3] Their original publication has been reworked by Professor J. L. Patterson, Jr., with the help of Stone, and reproduced here with their kind permission.

[4] These are angular head motions which may be from motions at the neck and shoulders or from body bending, and similar.

ω_V vehicle rotational velocity

ω_{h_x} total angular velocity of head about rolling axis (x-axis)

ω_{h_y} total angular velocity of head about nodding axis (y-axis)

ω_{h_z} total angular velocity of head about turning axis (z-axis)

t time

θ_G $\iint \alpha_{G_\theta}\, dt^2$

$\psi_G =$ $\iint \alpha_{G_\psi}\, dt^2$

$\phi_G =$ $\iint \alpha_{G_\phi}\, dt^2$

θ_n nodding displacement of the head (about the y-axis)

ψ_n turning displacement of the head (about the z-axis)

ϕ_n rolling displacement of the head (about the x-axis)

ϕ_e, θ_e, ψ_e Euler angular displacement using this order of rotation. (Euler angles relate one set of axes to another set and are used in the classical method of this transformation.)

θ_{sc} backward tilt of semicircular canals from X_bY_b plane

ψ_{sc} rotation of semicircular canals from X_bY_b

X, Y, Z inertial space axes

$x_b, y_b, z_b,$ body axes

Subscripts:

lr, ll right and left lateral canals, respectively

pr, pl right and left posterior canals, respectively

ar, al right and left anterior canals, respectively

Head Axes Used by Stone and Letko

x is (+) facing forward out of the nose.
y is (+) extending out of the right ear.
z is (+) extending downward (caudad) from the head.

Note: These head axes are part of a rectangular coordinate system. The negative of each axis has the sense and direction opposite the positive.

Semicircular Canal Axes

Equations (21–26) and (27–32) relate to the axes of the semicircular canals themselves. Each acceleration vector in these equations represents an angular acceleration vector that is perpendicular to the plane of the canal in question. The angles in these equations represent the transformation of head axes into canal axes. A dot over a symbol indicates its first derivative with respect to time.

The equations for the *total angular velocities experienced by the head* are the sum of the various angular velocities acting:

$$\omega_{h_x} = \omega_{h_\phi} + w_V \cos\theta_e \cos\psi_e \quad (3)$$

$$\omega_{h_y} = \omega_{h_\theta} - w_V \cos\theta_e \sin\psi_e \quad (4)$$

$$\omega_{h_z} = \omega_{h_\psi} + w_V \sin\theta_e \quad (5)$$

where w_V, the angular or rotational velocity of the vehicle, is assumed to be constant.

The differentiation of Equations (3–5) with respect to time gives the *angular accelerations experienced by the moving head*, where $\dot{\omega}_{h_x}$, $\dot{\omega}_{h_y}$, and $\dot{\omega}_{h_z}$ are the angular accelerations of the head in inertial space (the accelerations which will stimulate the semicircular canals) and $\dot{\omega}_{h_\phi}$, $\dot{\omega}_{h_\theta}$, and $\dot{\omega}_{h_\psi}$ are the angular accelerations of the head in the rotating frame of reference.

$$\dot{\omega}_{h_x} = \dot{\omega}_{h_\phi} - w_V (\sin\theta_e \cos\psi_e \dot{\theta}_e + \cos\theta_e \sin\psi_e \dot{\psi}_e) \quad (6)$$

$$\dot{\omega}_{h_y} = \dot{\omega}_{h_\theta} - w_V (\cos\theta_e \cos\psi_e \dot{\psi}_e - \sin\theta_e \sin\psi_e \dot{\theta}_e \quad (7)$$

$$\dot{\omega}_{h_z} = \dot{\omega}_{h_\psi} + w_V \cos\theta_e \dot{\theta}_e \quad (8)$$

Applying the principles of classical mechanics, the rates of change of the Euler angles in Equations (6–8) may be calculated from the following:

$$\dot{\phi}_c = \left(\omega_{h_\phi} \cos\psi_e - \omega_{h_\theta} \sin\psi_e \frac{1}{\cos\theta_e}\right) \quad (9)$$

$$\dot{\theta}_e = (\omega_{h_\phi} \sin\psi_e + \omega_{h_\theta} \cos\psi_e) \quad (10)$$

$$\dot{\psi}_e = \omega_{h_\psi} - \tan\theta_e(\omega_{h_\phi} \cos\psi_e - \omega_{h_\theta} \sin\psi_e) \quad (11)$$

A substitution of Equations (9–11) into Equations (6–8) then gives the *general expressions for the total angular acceleration* that would be experienced *for any orientation of the head and for any head motion* when *in a vehicle rotating at constant angular velocity:*

$$\dot{\omega}_{h_x} = \dot{\omega}_{h_\phi} - w_V(\omega_{h_\theta} \sin\theta_e + \omega_{h_\psi} \cos\theta_e \sin\psi_e) \quad (12)$$

$$\dot{\omega}_{h_y} = \dot{\omega}_{h_\theta} - w_V(\omega_{h_\psi} \cos\theta_e \cos\psi_e - \omega_{h_\phi} \sin\theta_e) \quad (13)$$

$$\dot{\omega}_{h_z} = \dot{\omega}_{h_\psi} + w_V(\omega_{h_\theta} \cos\theta_e \cos\psi_e + \omega_{h_\phi} \cos\theta_e \sin\psi_e) \quad (14)$$

When the vehicle is not rotating ($w_V = 0$) the equations simplify to:

$$\dot{\omega}_{h_x} = \dot{\omega}_{h_\phi} \quad (15)$$

$$\dot{\omega}_{h_y} = \dot{\omega}_{h_\theta} \quad (16)$$

$$\dot{\omega}_{h_z} = \dot{\omega}_{h_\psi} \quad (17)$$

When Equations (15–17) are subtracted from Equations (12–14), a set of expressions results for the accelerations caused by the rotation of the vehicle. These accelerations are termed by Stone and Letko [127] the *cross-coupled angular accelerations* or Coriolis accelerations which are given by the Equations:

$$\alpha_{G_\theta} = -w_V(\omega_{h_\theta} \sin\theta_e + \omega_{h_\psi} \cos\theta_e \sin\psi_e) \quad (18)$$

$$\alpha_{G_\theta} = w_V(\omega_{h_\theta} \sin\theta_e - \omega_{h_\psi} \cos\theta_e \cos\psi_e) \quad (19)$$

$$\alpha_{G_\psi} = w_V(\omega_{h_\theta} \cos\theta_e \cos\psi_e + \omega_{h_\theta} \cos\theta_e \sin\psi_e) \quad (20)$$

A number of investigators concerned with the physics of stimulation of the semicircular canals have believed that the Coriolis accelerations are those which primarily cause the disturbing symptoms and signs during rotation of a vehicle. It should be noted that the instantaneous angular velocities (ω) in these equations are not necessarily associated with a condition of angular acceleration, but can be part of a constant angular velocity profile. Thus, Coriolis accelerations (α) can result from the cross-coupling effects of constant angular velocities about more than one axis—an extremely important principle.

Coriolis Acceleration

At the beginning of the last century, a French engineer and mathematician, G. G. de Coriolis, carried out a mathematical analysis of an apparent force generated when a body is moving in a linear path in a rotating frame. Such a situation obtains when a mass is moving on the surface of a rotating carousel or when a projectile is fired from a gun on the surface of the rotating earth. This has been discussed previously in the introductory section and will not be considered in detail here. The point should be emphasized, however, that there is increasing use in physics, engineering, and physiology, of the term "Coriolis" force or acceleration where there is rotation of a body about more than one axis simultaneously.

Effective Components of Coriolis Accelerations

The effective component of the Coriolis acceleration which applies to each of the six semicircular canals can be derived from Equations (18–20). These derivations, kindly provided by Stone (personal communication), are:

$$\Delta\dot{\omega}_{sc_{lr}} = \alpha_{G_\phi} \sin\theta_{sc} + \alpha_{G_\psi} \cos\theta_{sc} \quad (21)$$

$$\Delta\dot{\omega}_{sc_{ll}} = \alpha_{G_\phi} \sin\theta_{sc} + \alpha_{G_\psi} \cos\theta_{sc} \quad (22)$$

$$\Delta\dot{\omega}_{sc_{ar}} = \alpha_{G_\theta} \cos\psi_{sc} - \alpha_{G_\phi} \cos\theta_{sc} \sin\psi_{sc} + \alpha_{G_\psi} \sin\theta_{sc} \sin\psi_{sc} \quad (23)$$

$$\Delta\dot{\omega}_{sc_{al}} = \alpha_{G_\theta}\cos\psi_{sc} - \alpha_{G_\phi}\cos\theta_{sc}\sin\psi_{sc} + \alpha_{G_\psi}\sin\theta_{sc}\sin\psi_{sc} \quad (24)$$

$$\Delta\dot{\omega}_{sc_{pr}} = \alpha_{G_\phi}\cos\theta_{sc}\cos\psi_{sc} + \alpha_{G_\theta}\sin\psi_{sc} - \alpha_{G_\psi}\sin\theta_{sc}\cos\psi_{sc} \quad (25)$$

$$\Delta\dot{\omega}_{sc_{pl}} = \alpha_{G_\phi}\cos\theta_{sc}\cos\psi_{sc} - \alpha_{G_\theta}\sin\psi_{sc} - \alpha_{G_\psi}\sin\theta_{sc}\cos\psi_{sc} \quad (26)$$

Total Angular Acceleration Experienced by Each Semicircular Canal

The total angular acceleration experienced by each of the six semicircular canals is given by the following equations, which include the cross-coupled components of angular acceleration. It will assist visualization of these relationships if Figure 12 (p. 260, in the next section of this chapter) is consulted, which shows orientation of the semicircular canals within the cranium.

$$\dot{\omega}_{sc_{lr}} = \dot{\omega}_{h_x}\sin\theta_{sc} + \dot{\omega}_{h_z}\cos\theta_{sc} \quad (27)$$

$$\dot{\omega}_{sc_{ll}} = \dot{\omega}_{h_x}\sin\theta_{sc} + \dot{\omega}_{h_z}\cos\theta_{sc} \quad (28)$$

$$\dot{\omega}_{sc_{ar}} = \dot{\omega}_{h_y}\cos\psi_{sc} - \dot{\omega}_{h_x}\cos\theta_{sc}\sin\psi_{sc} + \dot{\omega}_{h_z}\sin\theta_{sc}\sin\psi_{sc} \quad (29)$$

$$\dot{\omega}_{sc_{al}} = \dot{\omega}_{h_y}\cos\psi_{sc} - \dot{\omega}_{h_x}\cos\theta_{sc}\sin\psi_{sc} + \dot{\omega}_{h_z}\sin\theta_{sc}\sin\psi_{sc} \quad (30)$$

$$\dot{\omega}_{sc_{pr}} = \dot{\omega}_{h_x}\cos\theta_{sc}\cos\psi_{sc} + \dot{\omega}_{h_y}\sin\psi_{sc} - \dot{\omega}_{h_z}\sin\theta_{sc}\cos\psi_{sc} \quad (31)$$

$$\dot{\omega}_{sc_{pl}} = \dot{\omega}_{h_x}\cos\theta_{sc}\cos\psi_{sc} - \dot{\omega}_{h_y}\sin\psi_{sc} - \dot{\omega}_{h_z}\sin\theta_{sc}\cos\psi_{sc} \quad (32)$$

Application of the Equations for Angular Accelerations

The equations presented enable calculation of instantaneous angular accelerations. Since inertial, viscous, and other damping properties provide the semicircular canal system with various delays, which can be expressed as time constants, the canals do not represent transducers whose output of nerve impulses at any moment is directly proportional to the instantaneous angular acceleration experienced by each canal. There may well be, and probably are, moments when the afferent nerve traffic from the cupula of a given canal is proportional to the instantaneous angular acceleration, or some instances where the momentary physical conditions combine to produce a response proportional to the instantaneous angular velocity. These moments would be exceptional, according to expectations.

Apparently, a continuous readout of the solutions to these equations is actually needed for the solution of a number of physiological problems. Accelerometers and computing circuits presently available make it technically feasible to provide continuous recording of angular velocity and angular acceleration in the axes of the accelerometers, together with the necessary transformations to render the data applicable to the plane of each semicircular canal. In this way, the antecedent history of the major variables could be studied in relation to the subjective and objective physiological phenomena. Anatomic differences among different subjects, it is true, will introduce some, usually small, error in the assumed positions of the semicircular canals within a given subject's head; yet it is probable that such on-line computation of these functions would quite likely make a major contribution toward understanding of the responses both of physical models and of biological systems, including man.

THE VESTIBULAR SYSTEM

The End Organs

The labyrinth of the human inner ear comprises the cochlea (organ of hearing), otolith organs, and semicircular canals—collectively termed the vestibular organs. These are paired end organs with similar histologic features, a common blood supply, a shared secondary lymph circulation, and with afferent and efferent nerve fibers comprising the acoustic nerve. These sensory organs are situated in hollowed-out channels in the petrous portion of the temporal bone (Fig. 7 [2]), and, within the bony labyrinth, the membranous labyrinth is surrounded by perilymph and filled with endolymph. Thus, the sensory receptor mechanisms are protected from the effects of superimposed body weight by the bony labyrinth and, by virtue of the contained fluids, receive additional protection from impact accelerations.

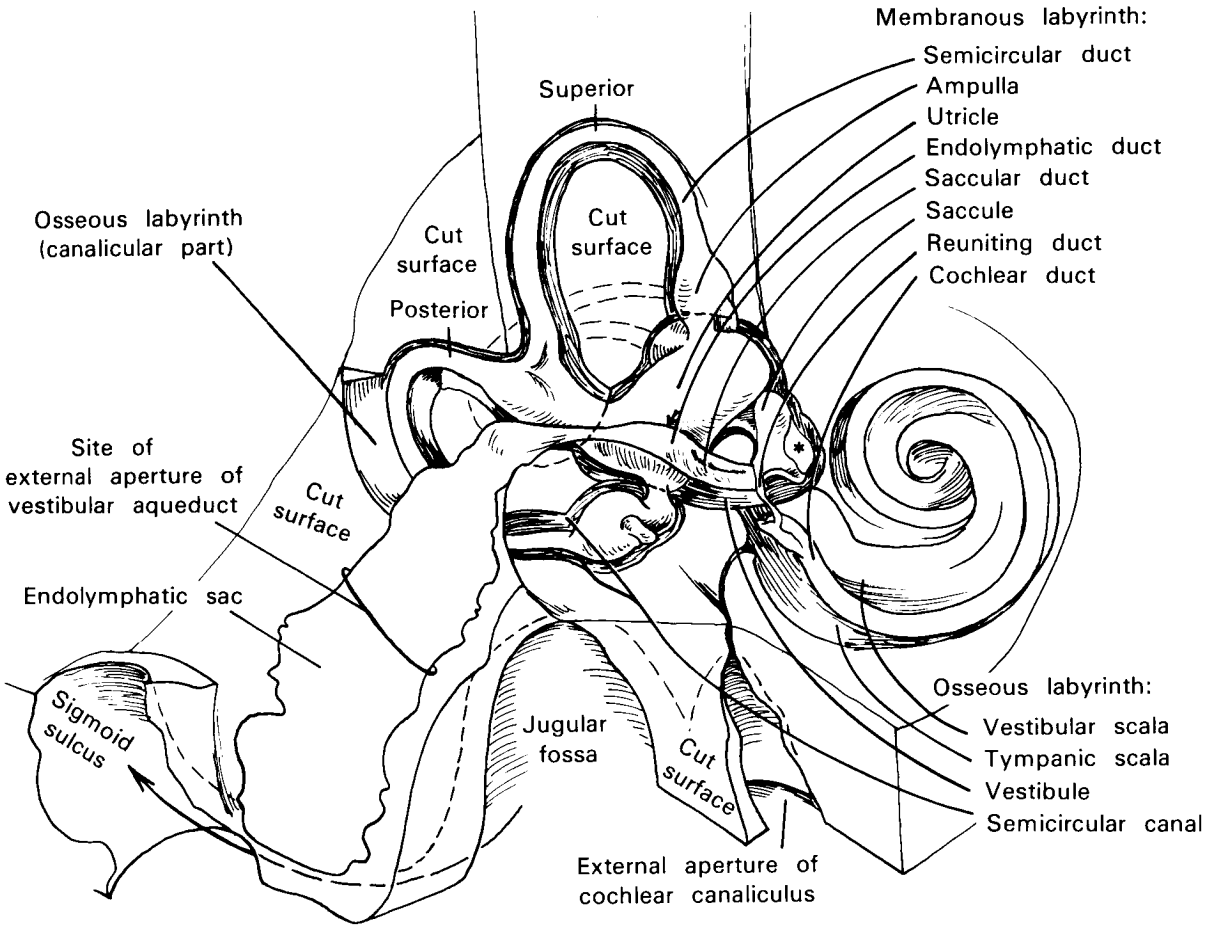


FIGURE 7.—Reconstruction of the membranous labyrinth and related anatomy. (From Ref. [2])

Otolith Organs

The four otolith organs appear as thickened portions on the inner walls of the paired utricle and saccule (Fig. 8) that are termed macular plates. A cross section of the saccular macula of a squirrel monkey and a sketch of the zonal structure are shown in Figure 9 [61]. The otolithic membrane contains otoconia (concretions of calcium carbonate crystals with a specific weight of about 2.71) which are embedded in a gelatinous material. It is noteworthy that this membrane comprises the only tissue within the bony labyrinth that differs considerably from the specific gravity of the lymph fluids. The hairlike projections of the sensory cells protrude into the cupular membrane on which the otolith membrane rests.

Figure 10 was drawn from electronmicrographs of the sensory epithelium of the utricular macula of the squirrel monkey [125]. Two types of hair cells, each with two types of cilia, are depicted. Each cell has 60 to 70 sterocilia and one kinocilium laid out in strict geometrical arrangement. In different regions of the macula, the kinocilia (which play the major role in the energy transfer) are polarized in different directions; hence, a shearing force in one plane will result in kinocilia moving in different directions with reference to the kinociliar pole. The result is mechanical deformation of the cilia which, in turn, causes chemical changes, resulting in the generation of bioelectricity (nerve action potentials). This apparatus may be termed the cilia-otolith mechanism.

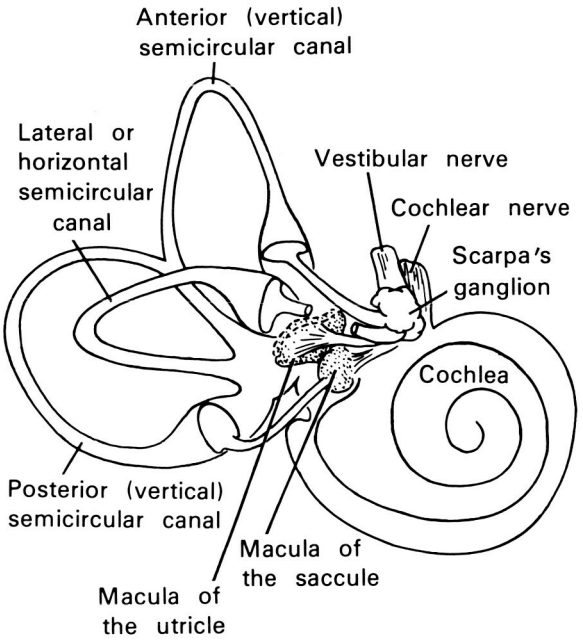
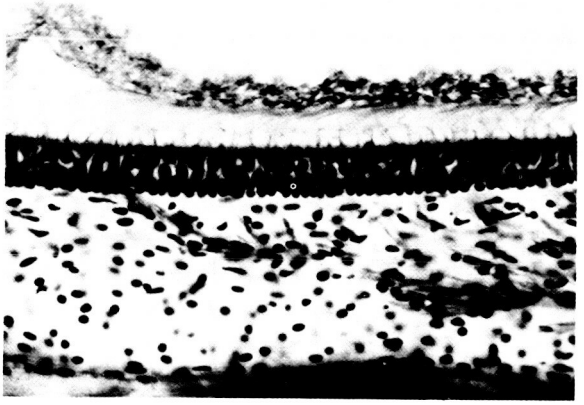


FIGURE 8.—Labyrinth of the left ear viewed from the medial aspect.

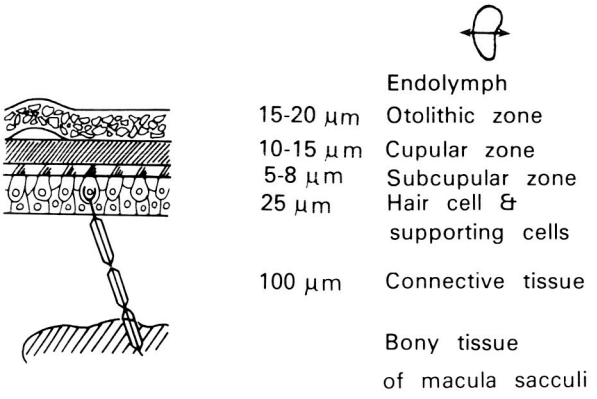
Semicircular Canals

The mechanoreceptors in the two vestibular organs are similar, but the gross structure of the semicircular canals bears little resemblance to that of the otolith organs (Fig. 7). The three canals in each human labyrinth are mutually perpendicular, and each so-called semicircular canal actually forms a complete circuit by virtue of its connections with the utricle, near which the duct expands into what is called the ampulla. A section through the ampulla of an exceptionally well-preserved human specimen[5] is shown in Figure 11. The crista is a transverse ridge of tissue covered with the sensory epithelium containing hair cells (similar to those in the maculae) whose cilia extend into the cupula. The kinocilia in the hair cells are uniformly polarized; in the horizontal canals they are toward the utricle (utricular pole) and in the vertical canals toward the opposite pole. The cupula, a meshwork (presumably of collagen fibers), extends to the roof of the ampulla (not shown in Fig. 11), completing a fluid-tight gate across the ampulla, hinged

[5] Kindly provided by Professor Makoto Igarashi, Department of Otolaryngology, Baylor University College of Medicine, Texas Medical Center, Houston.



a A view of macula sacculi from a squirrel monkey. Zonal structure is clearly seen.



b Schematic of the zonal structures in the squirrel monkey.

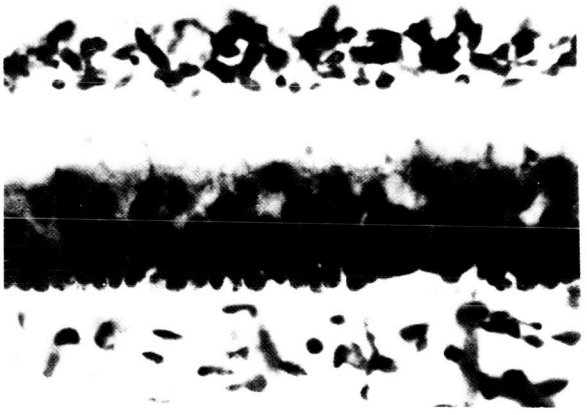


FIGURE 9.—Cross section of macula saccular of a squirrel monkey with zonal structure as inset. (Modified from Ref. [61])

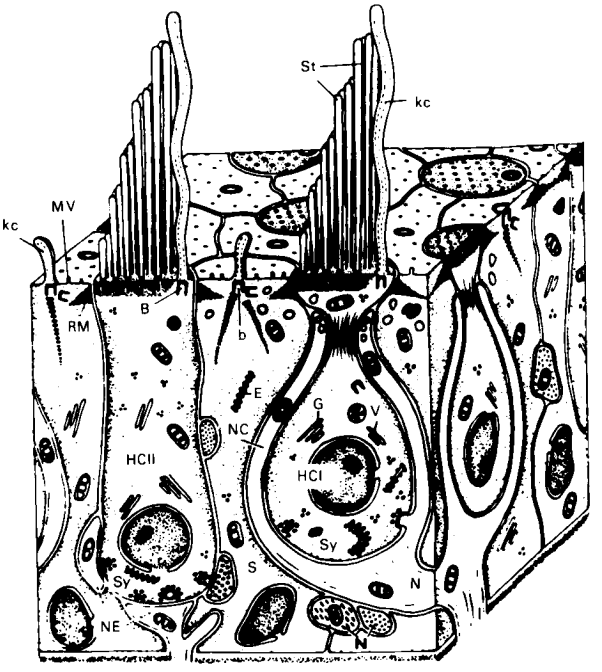


FIGURE 10.—Schematic of an area from a vestibular sensory epithelium with the two types of haircells (HCI and HCII), KC, Kinocilia; St. sterocilia. (From Ref. [125])

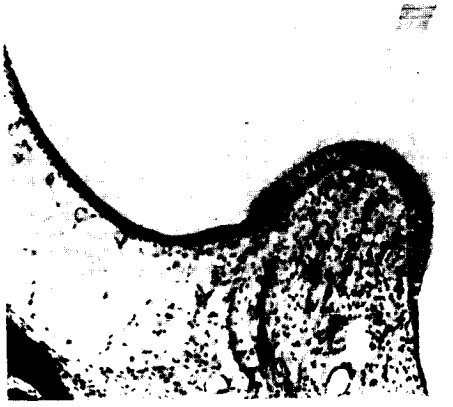


FIGURE 11.—Cross section of normal human ampulla (posterior semicircular canal) showing the crista with its sensory epithelium surmounted by the cupula.

at the crista, and free to move back and forth in response to movements of the endolymph. This apparatus constitutes the cupula-endolymph mechanism. On rotation of the head, the endolymph lags behind the movement of the bony canal, thus displacing the cupula in a direction counter to the rotary motion. The cupula-endolymph system, responding only to impulse angular accelerations in the plane of the canal, has been likened to a fluid-filled torus, with the cupula responding to movements of the endolymph in the manner of a spring-mass system with viscous damping.

Head motions, under natural conditions, generate a high angular acceleration with the onset of rotation, transient in character, followed by a very brief period of rotation approaching constant velocity, and ending with another transient acceleration of opposite sign. Although the acceleration and deceleration magnitude may be different, the time-integral of angular acceleration at the onset and offset is equal (area under the curves). Thus, it is thought that under most natural conditions the end organ responds as an integrating accelerometer.

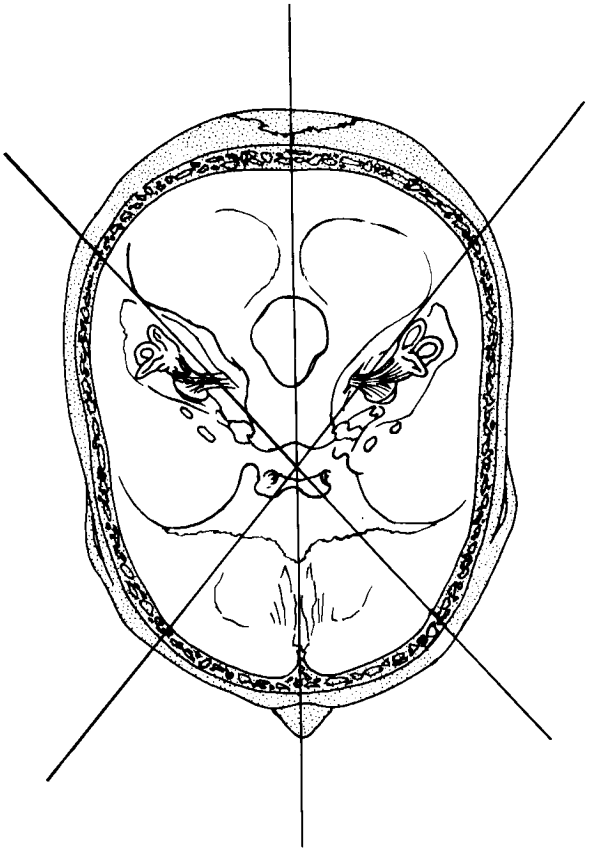


FIGURE 12.—Orientation of semicircular canals (enlarged) viewed in the skull from above.

Orientation of the six semicircular canals with reference to the head is shown in Figure 12. Although the three canals on one side lie approxi-

mately in mutually perpendicular planes, only the horizontal canals lie close to one of the coordinate planes of the skull, the superior and posterior canals deviating by 45° from the sagittal and frontal planes. Thus, rotary motions in the horizontal plane generating impulse angular accelerations would stimulate the horizontal pair of canals (although not maximally) with the subject's head upright; but, with head tilted forward about 25°, near-maximal stimulation would result. Rotation in the sagittal and frontal planes would generate angular accelerations in planes almost 45° from the planes of the vertical (superior and posterior) canals.

Functional Neurology

The reflex character of the vestibular system differs markedly from the predominantly sensory character of the auditory system; auditory pathways to the cortex have been almost fully delineated, whereas a corresponding vestibular pathway has not been identified. The vestibular system functions automatically, mainly through motor effector mechanisms, which accounts for it not being placed in the same category as somatic sensory systems and that the vestibular organs are termed special sense organs rather than organs of special sense. The great differences in structure and modes of stimulation of the two end organs indicate that they serve different functions by providing different information; yet, when we leave the periphery, their identity is lost when we use the combining term "vestibular." Added to this vagueness is the need to take into account the differences between vestibular influences under natural and unnatural stimulatory conditions. Under certain abnormal stimulatory conditions, it would seem that "preferential pathways" are open to vestibular activity. A very brief condensation of the neurology of the vestibular system based on anatomical, physiological, and behavioral studies follows. References are given to detailed reports on these important but exceedingly complex aspects of the vestibular system.

Anatomical Aspects

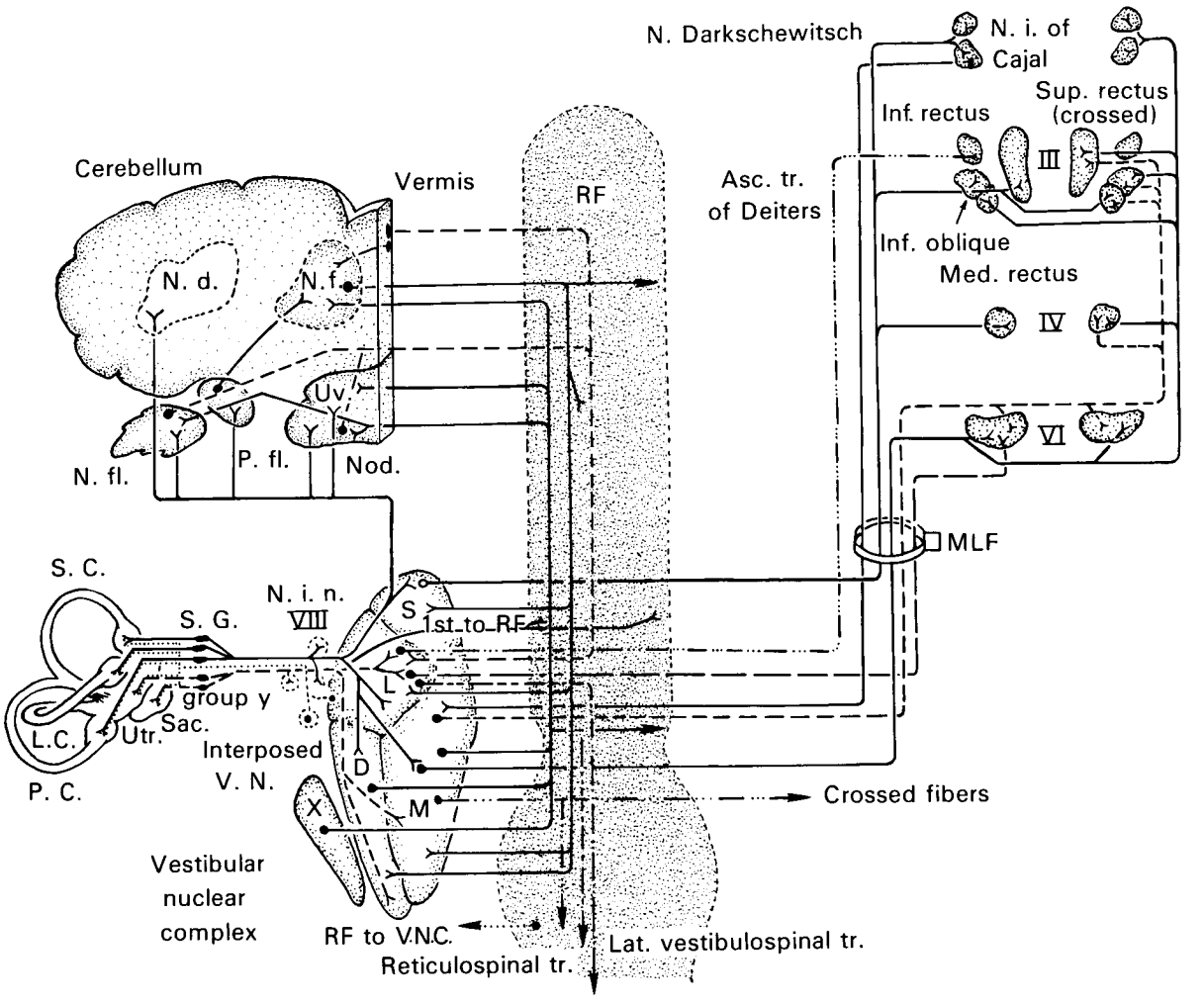
Morphological studies using classical techniques are definitive in nature, have important functional implications, and derive a great advantage from the high relevance to man of studies conducted on animals. Prior to the fourth edition (1952) of Rasmussen's *The Principal Nervous Pathways* [111], important contributions were made by Cajal, Lorente de No', Retzius, Burlet, Camis, and Vilstrup, among others. During the past 20 years, extensive morphologic studies have been carried out in a number of countries; the details may be found in the literature [14, 23, 112, 113, 133].

Figure 13 shows the main connections, revealed by classic anatomical techniques, comprising the reflex vestibular system. The vestibular nerve carries primary afferent fibers to the vestibular nuclear complex, cerebellum, and reticular formation and return efferent fibers to the mechanoreceptors in cristae and maculae. The vestibular nuclear complex (a term introduced by Brodal and associates [14]) comprises not only subdivisions within the confines of the four classical nuclei (superior, medial, lateral, and descending), but also small cell groups (known as *f*, *g*, *i*, *x*, *y*, *z*, *Sv*) and the interstitial nucleus of the vestibular nerve.

Cerebellar connections extend beyond the archicerebellum or classical vestibulocerebellum and include much of the vermis but not the hemispheres. Only a few fibers have been traced to the (pontine) reticular formation, but the absence of discrete nuclei may account for part of the sparsity. In general, sites of termination of primary fibers are sites of origin of secondary fibers that not only consolidate interrelations among the three major recipients of primary fibers but also ascend, descend, and cross the neuraxis.

The vestibular nerve. This nerve is the smaller division of the acoustic nerve coursing from the internal auditory meatus to the cerebellopontine angle where it enters the dorsolateral aspect of the brain stem, medial and somewhat ventral to the cochlear part of the VIIIth nerve.

Efferent vestibular system. Rasmussen, whose schema [111] did not show efferent fibers to the end organs, led the way in their discovery [112] and participated in defining their origin, course, and termination [123]. Efferent fibers arise in the lateral vestibular nucleus (Fig. 13) and, according to Rossi and Cortesina [121], in the nearby interposed vestibular nucleus. They leave



Abbreviations

III, IV, and VI: cranial motor nerve nuclei
D: descending vestibular nucleus
group y: small cell group
Interposed V. N.: Interposed nucleus of the vestibular nerve
L: lateral vestibular nucleus (Deiters')
L. C.: lateral semicircular canal
M.: medial vestibular nucleus
MLF: medial longitudinal fasciculus (ascending)
N. d.: dentate nucleus
N. f.: fastigial nucleus
Nod.: nodulus
Nin. VIII: interstitial nuclei (above and below afferents from cristae) of the vestibular nerve
N. i.: interstitial nucleus of Cajal
P. C.: posterior semicircular canal
P. fl.: paraflocculus
RF: reticular formation
S.: superior vestibular nucleus
Sac.: saccule
S. C.: superior semicircular canal
S. G.: Scarpa's (vestibular) ganglion
Utr.: utricle
U. V.: uvula
V. N. C.: vestibular nuclear complex
X.: small-celled group x

FIGURE 13.—Schema of the reflex vestibular system showing: (1) sites of origin and termination of first- and second-order neurons, (2) efferent fibers of the vestibular nerve, and (3) third- (or higher) order fastigial fibers. Note absence of pathways to the cerebral cortex.

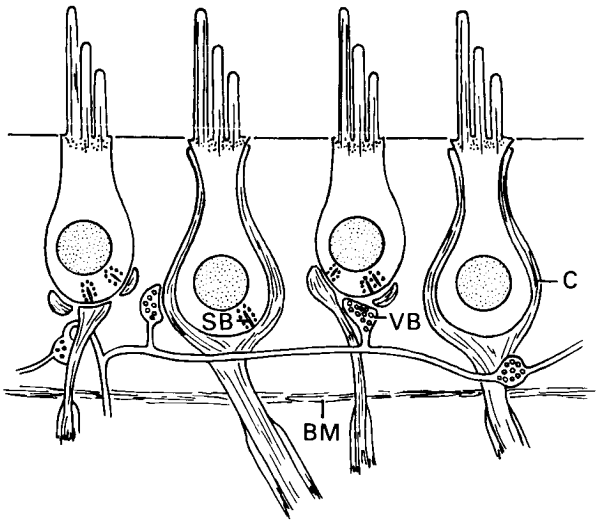


FIGURE 14.—Diagrammatic presentation of four hair cells, their nerve endings, and the relationships of vesiculated boutons (VB) to hair cells, chalice terminals (C), other boutons and nerve fibers in the chinchilla maculae. BM, basement membrane; SB, synaptic bar. It is believed the efferent nerves form a horizontal plexus as drawn.

the brain in company with the cochlear efferent fibers, reach the end organs in company with vestibular dendrites, and terminate on the second-type vesiculated boutons (Fig. 14) of all hair cells in cristae and maculae [123]. Anatomically, these efferent fibers complete a feedback loop, holding out the possibility that central influences of an inhibitory or regulatory nature can be brought to bear on the end organs.

Primary afferent fibers. Although primary vestibular fibers have been studied intensively, special mention should be made of the recent findings of Gacek [27], who traced their course from specific end organs to specific central terminations in the vestibular nuclei in the cat. He took into account fiber size at the end organ and, at central termination, cell size in the vestibular nuclei. Figure 13 indicates that primary canalicular neurons, after giving off short collaterals to the interstitial nucleus of the vestibular nerve, enter the brain stem where each axon divides into an ascending and a descending branch. The former terminates in the superior vestibular nucleus (and the cerebellum). The descending branches give off collaterals to the lateral, medial, and descending vestibular nuclei. Gacek was able to trace large and small fibers from the posterior canalicular cristae to large and small cells in the superior nucleus. (In higher vertebrates, the sensory epithelium of the horizontal canal was split off from the superior [vertical] canal; hence, the fibers from both are intermixed and impossible to trace as single bundles.) Primary utricular fibers, after dividing into ascending and descending branches, terminate, respectively, in the lateral and medial nuclei and in the medial and descending nuclei. Primary saccular fibers terminate mainly in the small-group *y* nucleus, with some fibers terminating in the lateral and descending nuclei. In summary, afferents from cristae and maculae are differentially distributed to sites in the vestibular nuclear complex; only canalicular fibers terminate in the interstitial nucleus of the vestibular nerve and in the superior nucleus.

Primary afferents have been traced to the flocculonodular node and ventral part of the uvula comprising the archicerebellum and to the ventral and dorsal paraflocculus and to the lateral dentate nucleus. First-order neurons do not reach the fastigial nucleus, contrary to former belief. Primary vestibular fibers to the cerebellum end as a particular type of mossy fiber, not only in the flocculonodular lobe comprising what Brodal [13] termed the classical vestibulocerebellum, but also the ventral and dorsal paraflocculus. Only a few primary fibers have been traced to the reticular formation, which is shown in Figure 13.

Interconnections between cerebellum and vestibular nuclear complex. In general, it is difficult (using classical anatomical procedures) to trace pathways in the vestibular system beyond second-order neurons, but an important exception is in the fastigial nucleus of the cerebellum, which is not a receiving site for primary vestibular fibers. The role of the fastigial nucleus as a relay station for cerebellovestibular fibers would also appear to serve as a major center in the vestibular system. The fastigial nucleus receives fibers from the vermis, paramedian lobule (both sides), dorsal paraflocculus, crus II, and vestibular nuclei. The fastigial nucleus sends fibers to reticular formation, all vestibular nuclei, mainly ipsilaterally, and especially to the lateral vestibular nucleus.

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Vestibulocerebellar fibers, mainly from the descending nucleus but also from the medial nucleus and group x, project, chiefly ipsilaterally, to end as mossy fibers in the flocculonodular lobe, ventral part of the uvula, and the fastigial nucleus.

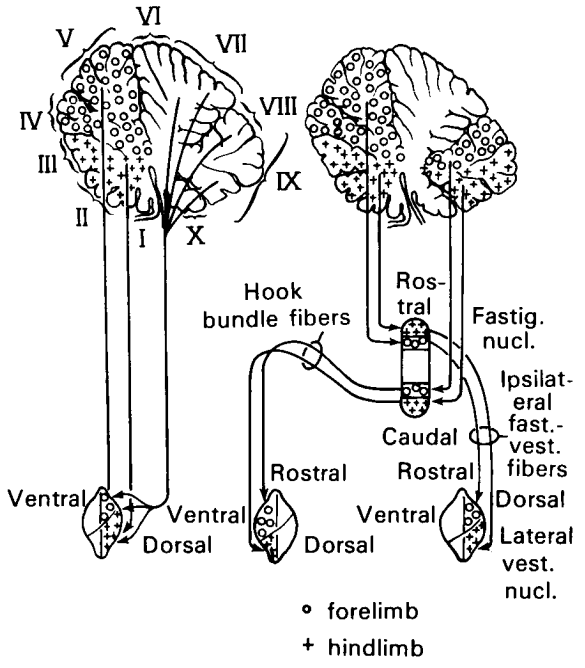


FIGURE 15.—Diagram illustrating major features in the projections from the cerebellar cortex onto the nucleus of Deiters (to the left) and (to the right) in the projections from the cerebellar cortex onto the fastigial nucleus and from this to the lateral vestibular nuclei. Note that the direct cerebellovestibular fibers and projection from the rostral part of the fastigial nucleus end in the dorsal half of the ipsilateral lateral vestibular nucleus, while fibers from the caudal part of the fastigial nucleus via the hook bundle supply the ventral half of the contralateral lateral vestibular nucleus. Within each of these projections there is a somatotopic localization. (From Ref. [13])

With regard to cerebellovestibular fibers, distinction is made between second-order fibers and fibers from the fastigial nucleus. Second-order fibers, which originate in the archicerebellum and in vermal cortices (mainly anterior lobe), project chiefly to the lateral nucleus. Fibers from the fastigial nucleus project to the reticular formation and to all vestibular nuclei; those fibers projecting to the lateral nucleus (which show a somatotopical arrangement) have been intensively studied by Brodal and his group [14]. Figure 15 shows the perseveration of an orderly arrangement from vermal cortices via fastigial nucleus to ipsilateral and contralateral Deiters' nuclei [14]. The ipsilateral system (involving forelimb and hindlimb) projecting to rostral and caudal parts of the lateral nucleus originate, respectively, in rostral and caudal parts of the anterior vermis with their relay stations in the rostral part of the fastigial nucleus. The contralateral system is analogous, except that it projects to the ventral half of the lateral vestibular nucleus and crosses the neuraxis in the hook bundle via a relay station in the caudal part of the fastigial nucleus.

Ascending projections. In continuing studies demonstrating a high degree of differential distribution of primary fibers to sites in the vestibular nuclear complex, Gacek [28] traced the ascending pathways from these sites to their termination. Five major pathways are shown in Figure 13; all except the ascending tract of Deiters comprise the (ascending) medial longitudinal fasciculus (MLF). Two pathways in the MLF may be activated by primary canalicular neurons constituting the ascending and descending branches. The former, arising in the superior vestibular nucleus, ascends ipsilaterally, giving off fibers to N IV and N III (some crossing to the nucleus of the medial rectus), and terminating in the interstitial nucleus of Cajal and the nucleus of Darkschewitsch. The continuation of the descending branch (of the primary canalicular fibers) arising in the medial vestibular nucleus after giving off fibers to N VI bilaterally, ascends contralaterally, giving off fibers to N IV and N III (nucleus of the superior rectus and inferior oblique) and terminates in the interstitial nucleus of Cajal and Darkschewitsch's nucleus.

Three pathways may be activated by primary macular fibers constituting the ascending and descending branches. The former splits in the lateral vestibular nucleus, one part coursing outside the MLF (as the ascending tract of Deiters) to terminate in the nucleus of the inferior rectus in N III, the other terminating ipsilaterally in N VI. Continuation of the descending branch (of the primary canalicular fibers) arising chiefly in the medial vestibular nucleus gives off fibers ipsilaterally to N VI, then crosses the midline,

giving off fibers to N VI, N IV, inferior oblique, medial rectus in the oculomotor nuclear complex, and nuclei of the superior rectus.

A direct cerebellar projection to (contralateral) N IV and N III and ipsilateral fibers in the reticular formation are not shown in Figure 13; these might comprise the independent vestibuloocular pathway readily demonstrated in physiologic studies.

Descending pathways. The three major descending pathways comprise the lateral and medial vestibulospinal tracts and the reticulospinal tract (Fig. 13). The lateral vestibulospinal tract arises in the somatotopically arranged part of the lateral vestibular nucleus and projects the length of the cord, preserving its somatotopical arrangement. Nyberg-Hansen [104] has described the terminations in great detail, based on Rexed's subdividions of the spinal gray matter, pointing out that fibers in the vestibulospinal tract influence the entire cord by modulating stretch reflexes and muscular tone. The medial tract (Fig. 13), arising chiefly in the medial vestibular nucleus, descends bilaterally in the (descending) MLF and terminates in the upper half of the cord without evidence of a somatotopical arrangement.

In summary, the anatomic organization of the reflex vestibular system, while not extensive (few third-order pathways have been traced outside the cerebellum) is complex. The complexities are evident in the high degree of differentiation from hair cells to sites of terminations of primary and secondary fibers, and in their interconnections both within the vestibular system and between vestibular and nonvestibular systems. Brodal [13] stated, "Much remains to be investigated. The anatomical data available at present indicate functional differentiations between cell groups and parts of nuclei which go beyond what has so far been clarified in physiological studies."

Physiological Aspects

Only a few experiments had been conducted until recently, using electrical stimulation in normal unanesthetized animals. The use of abnormal stimuli, in addition to anesthesia or decerebration, raises the question whether the response is normal or if a vestibular side effect is involved. Depending on the animal used, there is the question of relevance for man. All these considerations are increasingly being taken into account; consider the use of human subjects, techniques that minimize departure from physiologic conditions, and testing at organizational levels characterized by similarity among species. Some examples have in common that vestibular activity involves pathways not yet identified, using classical anatomic procedures. These may involve vestibular projections beyond the reflex system, interactions between vestibular and nonvestibular systems, and the intrinsic organization of the vestibular system.

Projections beyond the reflex vestibular system. Razumeyev and Shipov [116] devote Chapter IX of their monograph to "connections of the labyrinth with the cerebral cortex." This excellent summary of the authors' studies (and of other investigators) gives details, as well as representative reports [1, 65, 88, 91, 93, 124, 130].

Studies have been conducted with human and animal subjects; accelerative, thermal, and electrical stimuli; and responses have been measured in electroencephalograms, electrocorticograms, or in recordings of single neuron activity in many parts of the brain.

It was established early that stimulation of the vestibular nerve in the lightly anesthetized cat elicited short-latency responses (around 0.6 ms) in parts of contralateral suprasylvian and ectosylvian gyri, that depended on the functional integrity of the nonacoustic labyrinth. Stimulation of the flocculonodular lobe elicits short-latency responses bilaterally, but removal of the cerebellum does not influence responses from the labyrinth.

Responses in the cat elicited by angular and "alternate" linear accelerations, studied in great detail by Razumeyev and Shipov [116], revealed differences, but, in general, the changes reflected the intensity of stimulation and were characterized by desynchronization in the electrocorticogram over wide (diffuse) areas. Short-latency responses elicited at the onset of acceleration yielded to long-latency response on deceleration and reached the brain by nonspecific pathways in the reticular formation.

Changes in the activity of single neurons in cortical and subcortical regions as the result of linear accelerative stimuli fell into four classes based on impulse frequency: (1) increase, (2) decrease, (3) phasic (with acceleration), and (4) no change. Convergence of vestibular and nonvestibular afferent "signals" were reviewed, categorized, and summarized by Razumeyev and Shipov [116] as:

> Electrophysiological experiments which have been performed to date show that the so-called specific cortical convergence of visual, vestibular, auditory and also, in all probability, somatic afferentation takes place almost exclusively in the anterior portions of the ecto- and suprasylvian gyri; i.e., in the portions of the cortex defined as cortical projection fields of the vestibular analyzer. Therefore, the assumption of Gorgiladze and Smirnov (1967), which states that the "vestibular cortical field is the coordination center which integrates afferent impulses from various sense organs and creates images of spatial relationships between the individual and surrounding objects of the visible world," appears to be correct.

Vestibular connections with the visceral nervous system have been described. Some of the early findings reported by Akert and Gernandt [1] may have to be amended where vestibulovagal connections are inferred. In a subsequent report, Tang and Gernandt [130] demonstrated the vestibular influences above, not below the point where the recurrent laryngeal parts company with the vagus. These authors reported that vestibular stimulation in cats elicited responses in recordings from the phrenic and recurrent laryngeal nerves. The responses were associated with increases in rate and depth of respiration and blood pressure. In a study to be reported, Tang [129] raises the possibility of artifacts vitiating many experiments involving electrical stimulation of the vestibular nerve.

Vestibular-nonvestibular connections. Electrophysiological studies have helped greatly in demonstrating connections between vestibular and nonvestibular systems; recent studies contribute much to knowledge of this aspect of vestibular neurology [25, 109, 116, 134]. Pompeiano [109] points out that in deep sleep, activity of second-order neurons in the vestibular nuclei increases phasically due to extralabyrinthine inputs; this results in rapid eye movement (REM) sleep. Wilson [134] has demonstrated that impulses from peripheral nerves ascending the spinal cord facilitate cells in the lateral vestibular nucleus that are sites of origin of the lateral vestibular spinal tract. Frederickson and Schwarz [25] investigated cells in the vestibular nucleus of unanesthetized cats by means of single-unit analysis. Ninety-nine percent of the units were responsive to labyrinthine stimulation and 80% to joint movement. There were no reponses to muscle pressure, optic, or acoustic stimuli, and cerebellectomy did not grossly alter joint influence.

Intrinsic organization of the vestibular system. Morphologists are among the first to point out that much work (including the use of electron microscopy) remains before anatomical observations suffice as a basis for functional interpretations. Among many examples, two must suffice for illustration.

The vestibuloocular reflex arc has long been of great interest. Fluur [24] found that selective stimulation of the nerve from individual semicircular canals in cats yielded two types of responses: Type I characterized by spontaneous activity in the extraocular muscles and conjugate deviation of the eyes; and Type II characterized by absence of spontaneous activity and of nonconjugate movements during stimulation. The differences in types of responses were considered in the light of differences in end organ receptors, the functional state either of the extraocular muscles and their proprioceptive mechanisms or the brain stem, and technical factors. Type I responses to selective stimulation of the nerve to the left lateral canal resulted in conjugate eye movement to the right, with activation and reciprocal inhibition of the appropriate muscles; similar stimulation in the left anterior canal caused upward deviation; of the left inferior, down deviation; and of both left vertical canals, counterclockwise rotary deviation. While stimulation of the horizontal canal caused deviation in that plane, stimulation of either vertical canal caused movement in the sagittal plane. In brief, impulses from a single canal must carry messages

not only to the extraocular nuclei, but also to their functional subdivisions. Gacek [28] raised the question—whether one of the two (canalicular) pathways might be inhibitory and the other facilitory, thus making unidirectional eye movements possible.

Cortical, cerebellar, and reticular influences on vestibular activity have generally been regarded as inhibitory, but these broad generalizations must be modified in the light of recent studies [25, 52, 62, 109, 116, 134]. An illustration is a model that Ito [62] has proposed, based on motoneurons in combination with certain receptors and muscles that would form a simple control system with a negative feedback loop (Fig. 16). With the insertion of the cerebellum in this control system, a more complex performance is possible (Fig. 17, part A, left). Ito reported that, insertion of the cerebellar nuclei between the cerebellar cortex and the brain stem may modify the ability of this unit in two respects: (1) integration of excitatory inputs with the inhibitory Purkinje cell signals is performed at the cerebellar nuclei, allowing the brain stem centers to carry out more integration with other signals (Fig. 17, part B, center); (2) a reverberating circuit may be formed between the cerebellar nucleus neurons and those originating in certain cerebellar afferents (Fig. 17, part C, right). Anatomical evidence suggests a reverberating connection between the descending vestibular nucleus and fastigial nucleus, between the paramedian reticular formation and fastigial nucleus, and between the pontine nucleus and the intracerebellar lateral nucleus. According to Ito, these connections would favor maintenance of a certain standard of activity in the cerebellum-brainstem system, which would provide the bias around which the dynamic characteristics of the system may be optimum.

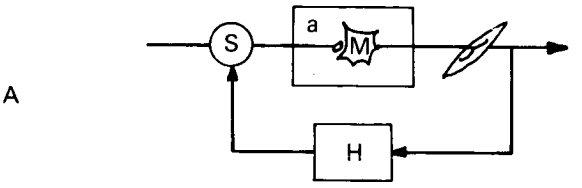


FIGURE 16.—Block diagram illustrating development of the motor control system. M: motoneuron. S: sensory part of the system. H: feedback loop.

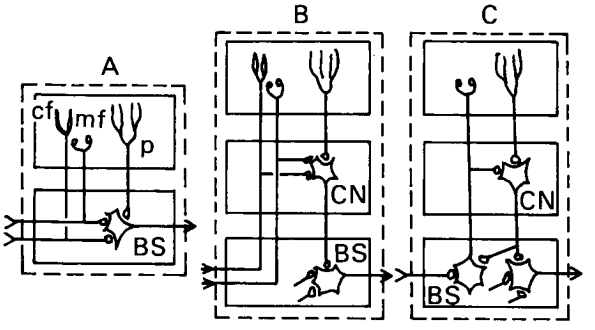


FIGURE 17.—Diagrammatic illustration of variation in cerebellar corticosubcortical connections. BS: brain stem, CN: cerebellar nuclei, cf: climbing fiber, mf: mossy fiber, P:Purkinje cell. See text.

Behavioral Aspects

Vestibular responses (normal and abnormal) elicited in healthy persons have important neurologic implications. Indeed, our point of departure might well have been reversed (discussing behavioral aspects first rather than anatomical) since behavioral phenomena demand explanation while the anatomical do not. Thus, under natural living conditions today, man's nervous system may contain redundant or vestigal elements. Under unnatural conditions (motion environments), we must seek explanations for phenomena that only recently have become part of our lives. In addition to the distinction between behavioral phenomena elicited under natural and unnatural stimulus conditions, the latter (vestibular side effects) may be categorized according to the immediacy and nature of the response. Immediate reflex responses may be divided into those that represent perturbations of normal responses, e.g., nystagmus, and those that do not, e.g., perception of the oculogravic illusion. Delayed responses comprise epiphenomena, best known as motion sickness. Vestibular side effects will be discussed in subsequent sections; it will suffice here to point out a few examples that illustrate neurologic aspects not mentioned in the preceding section.

Perception of rotation. Under favorable conditions, when subjects are passively exposed for 10 s to angular acceleration about the vertical axis, thresholds for the perception of rotation

are in range 0.17°/s² [17], and on "sudden stop" after constant rotation at 1 rpm, the perception is "immediate" in behavioral terms. Persons with bilateral loss of vestibular (canalicular) function do not perceive rotation at the highest angular accelerations achieved in the laboratory. These findings suggest that vestibular impulses reach cortical levels when a normal type stimulus many magnitudes lower in intensity is used, rather than that generated during normal head movements.

Perception of the oculogravic illusion. This illusion is readily perceived when a person is exposed to change in direction of the gravito-inertial vertical on a certrifuge; it is not readily perceived by subjects with bilateral loss of vestibular function, especially when exposed during water immersion [45]. This influence on perception of the visual upright must involve integration of otolithic and optic neural activity.

Pseudo-Coriolis illusion. Recent studies by Brandt and colleagues [12] demonstrated pseudo-Coriolis effects, so termed—a visually induced perception of self-rotation and a pseudo-Coriolis illusion. The Coriolis (or oculogyral) illusion is readily perceived under favorable circumstances in a room rotating at constant velocity if a person rotates his head out of the plane of the room's rotation. The pseudo-oculogyral illusion can be elicited by substituting rotation of the visual environment (a striped drum) for rotation of the "room." Rotation of the head is essential, thus implicating the vestibular organs, although the head movements generate normal accelerative stimuli. After abolition of the visual stimulus, abnormal effects can be elicited for as long as 30 s. The sites of interaction between the normal vestibular inputs and abnormal visual inputs are probably in the medial and lateral vestibular complex and adjacent reticular formation, which was demonstrated by single fiber recordings in rabbits. Some fibers responded not only to accelerative but also to optokinetic stimuli. (In this connection it is important to recall that subjects who have never perceived light may, nevertheless, be highly susceptible to motion sickness when exposed to Coriolis accelerations [38].)

Motion sickness. Motion sickness (discussed in the next section) represents a constellation of delayed epiphenomena, precipitated by repetitive vestibular sensory inputs that are either abnormal or (if normal) encounter an abnormal integrative pattern. The immediate origin of cardinal symptoms is in nonvestibular systems; hence, first-order responses (at least) must reach cell groups via preferential pathways (presumably in the brain stem reticular formation) not used under natural stimulus conditions.

In summary, the vestibular system under artificial stimulus conditions readily evokes responses that range from near-normal (the oculogravic illusion) to the absurd (motion sickness). Preferential pathways and unusual interactions with nonvestibular systems deserve study for scientific reasons and for practical benefits.

Input-Output Relations

The schema in Figure 18 represents an attempt to fit important elements concerned with vestibular input-output relations into a conceptual framework.

In Block I are the types and combinations of natural and artificial accelerative stimuli that reach the semicircular canals and otolith organs. The important contribution to artificial stimulus patterns made by man's motions, especially those involving rotation of the head, deserves emphasis. In the footnotes at the bottom of the schematic are: (1) categories of activation of the vestibular system, some of which are not accelerative in nature, e.g., disease process; and (2) typical activity patterns.

Block II indicates the transducer functions of the end organs. Although a feature common to both end organs is the conversion of the accelerative stimuli to electrical energy, thus altering the temporal and spatial patterning constituting the propogated discharge, the well-known differences between the two end organs must be taken into account.

The cupula-endolymph mechanism in the six semicircular canals responds to impulse and Coriolis accelerations and, for practical purposes, is gravity-independent. Under nearly all natural conditions, the canals are stimulated only by the motions of man that involve rotations of the head. Under artificial conditions, of course, the canals respond to the same types of accelerations generated by a machine. In the absence of head

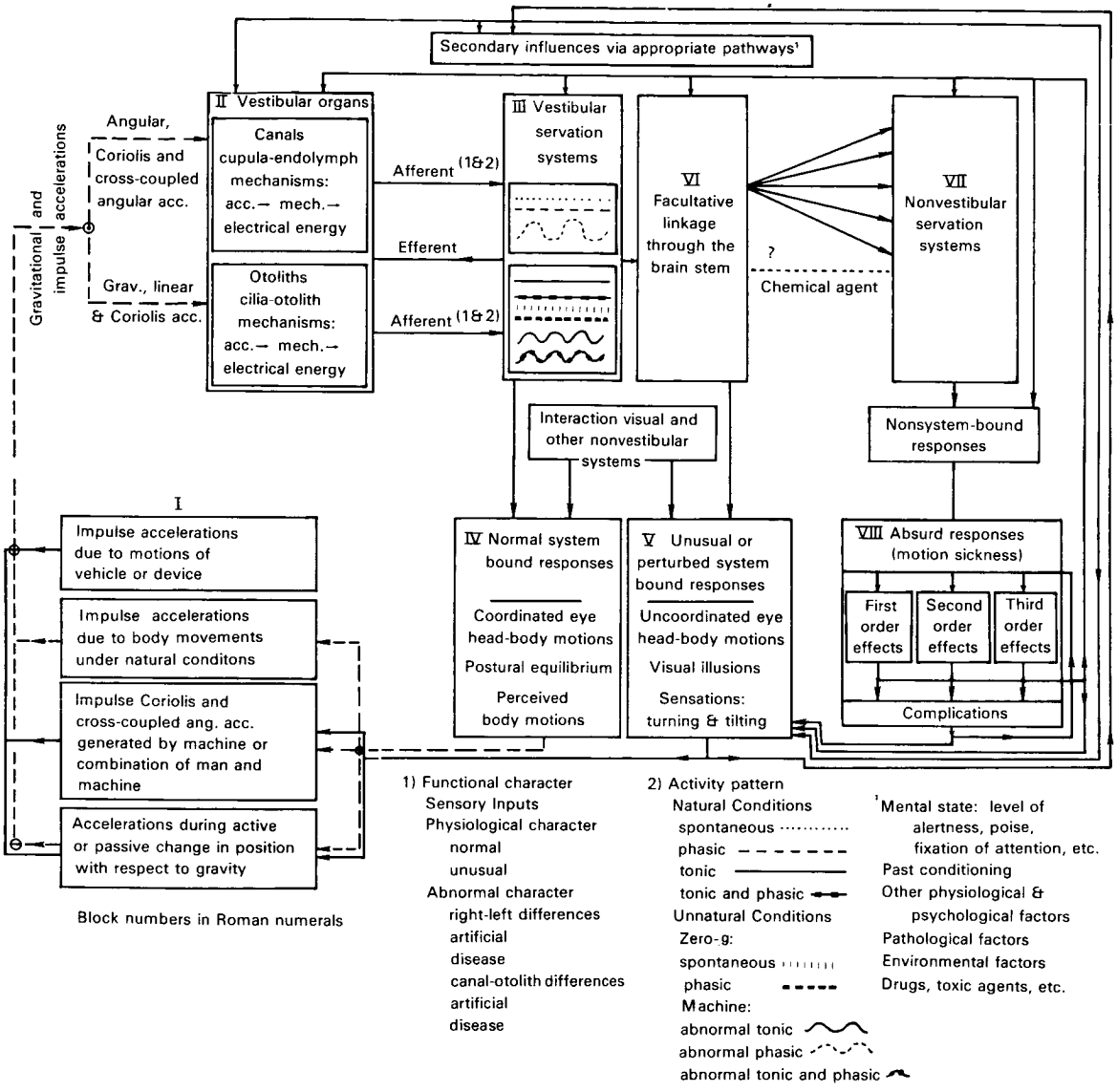


FIGURE 18.—Conceptual framework showing important elements and their interactions underlying system-bound vestibular disturbances and nonsystem-bound disturbances (motion sickness).

motions (active or passive) there is no accelerative canalicular stimulus, but a resting discharge, presumably of chemical origin, is present. Its precise origin and role, however, have not been determined.

The cilia-otolith mechanism in the four otolith organs is activated by gravity and by impulse linear and Coriolis accelerations directed so as to cause a shearing displacement between the otolithic membrane supporting the hair cells. The result is mechanical deformation of the cilia (kinocilia) which, in turn, results in chemical changes affecting the generation of bioelectricity (nerve action potentials).

Block III are the vestibular servation system and its two components (canalicular and otolithic), which have reciprocal modulating influences, and the vestibular efferent fibers ensuring a return flow of impulses to the end organs, thus closing one loop. An effort has been made to indicate typical normal and abnormal canalicular and otolith activity patterns and some opportunities for interaction with nonvestibular systems, notably vision.

Natural Terrestrial Stimulus Conditions

Typical responses to which the vestibular organs contribute under natural terrestrial conditions are shown in Block IV(A) (Fig. 18), and the entire chain of events involves Blocks I through IV(A).

Astonishingly little is known concerning the normal function of the vestibular system in man under natural conditions. The canals and otoliths serve mainly as "participants" in motor functions, and it is exceedingly difficult to elucidate these contributory roles. The reason is that "natural activities" greatly limit the investigator, both in terms of stimulus manipulation and measurement and in the use of specific indications (responses) of canal or otolith stimulation that are available for measurement. Thus, the investigator must resort to unnatural stimulation of canals, otoliths, or both, which elicits abnormal responses that can be measured. In doing this he elicits the same responses experienced by susceptible persons in conveyances of different kinds which generate abnormal patterns of accelerations, with the important difference, however, that in the laboratory, the stimuli are under the experimenter's control.

A classical experimental approach to this question involves the use of human or animal subjects with bilateral loss of canalicular and otolithic functions. Experiments on animals alone, however, will never suffice; the findings are not directly applicable to man. The identification of human subjects with bilateral loss of labyrinthine function (L–D subjects) has been accomplished by screening groups of deaf persons, but experimentation on subjects identified in this way is complicated by the great differences between persons who hear and those who do not. Moreover, in all such subjects there is not only the need to make sure that pathologic changes are quiescent and adaptive changes are complete following any loss of function, but there is also the need to take into account the unmeasurable factor of "compensatory adjustment."

Despite these limitations, the best information has been derived from a comparison in performance of persons with and without vestibular defects. Under present-day ordinary living conditions, severe losses of vestibular function have gone undetected. This is dramatically illustrated by the rare persons with loss of vestibular function early in life but whose hearing had been retained [49]. Two such persons, discovered fortuitously, revealed that neither they, their families, nor their physicians were aware of the loss. Despite the loss of function being readily revealed, this takes little away from the fact that they met not only the ordinary demands of present-day living, but also were above the average in proficiency in a variety of sports. When apprised of their loss, it was brought out that they had experienced difficulties under circumstances where visual cues were inadequate and, possibly, in eye-head-body coordination when visual cues were inadequate.

A comparison between normal and L–D subjects under natural stimulus conditions reveals not only performance decrements but also the important observation that the stimulus to the otolith organs due to gravity generates a tonic discharge over and above the resting discharge. Performance decrement is readily demonstrated using tests for postural equilibrium [26].

When the head is "fixed" in the gravitational field, there is no question that the otolith organs are stimulated, indicated not only by the persistence of ocular counterrolling [98] and the oculogravic illusion [19], but also by these responses varying with hypogravity and supragravity g-loadings [97]. Whether the effective stimulus is due to a constant weight (or pressure) or to slight unavoidable changes in position of the macular plates with respect to gravity (even though the head is presumably fixed) is not clear. In either event the stimulus gives rise to a tonic sensory input over and above the resting discharge, and the significance of this finding for exposures in subgravity and weightlessness is obvious, although Yuganov [140] has brought out evidence that weightlessness may act as a specific stimulus to the maculae.

Nashner [103] has published the results of a sophisticated study on postural sway under near-normal conditions. Based on available information, he developed a general postural control model that, in turn, was used in devising a series of experiments dealing with postural sway resulting from rotation about the ankle. The experimental findings were combined with the general model to develop specific models for the sensory-motor interfaces. Three normal subjects and one L-D subject participated. The latter, age 20, had compensated "to the extent possible" following bilateral transection of the VIIIth nerve, 2 years prior to testing. Four types of tests were conducted:

(1) Reflex response gains. In normal subjects the average gain of the stretch reflex response induced by small rotations was about one-third that necessary for postural stability. In the L-D subject with eyes open the gains were larger than in the normals but below those necessary for postural stability; with eyes closed the average gain increased markedly, and, for extensor muscles, resulted in "rigid" postural stability.

(2) Induced sway: thresholds for perception with eyes open. Threshold values in terms of response time and body angle are shown in Figure 19 [103].

(3) Continuous recording of postural response and body angle motion. With eyes open the "control strategy" is the same for the L-D subject and normal controls, but in making corrections for transient disturbances (higher center commands) performance was better for the normals than the L-D subjects. With eyes closed the strategy remains the same for normal subjects (periods of reflex stability and transient disturbances), but changes for the L-D subject in that reflex stability gives way to continuous oscillation.

(4) Frequency spectra of body angle

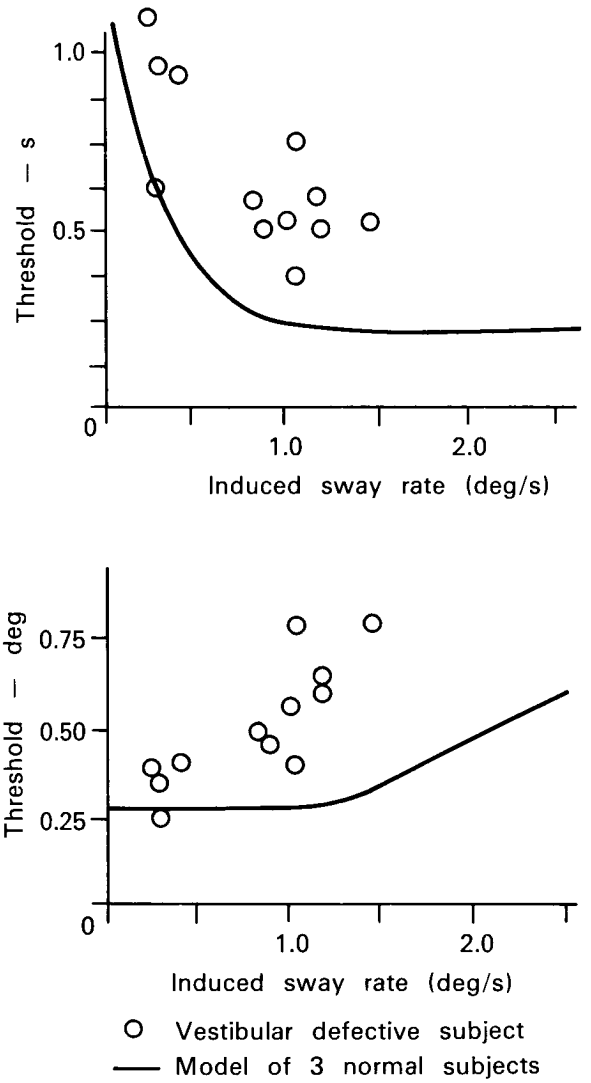


FIGURE 19. – Response threshold to induced sway in terms of response time and body angle; note increase when vestibular cues absent. (From Ref. [103])

motions. Comparative values are shown in Figures 20 A and B [103].

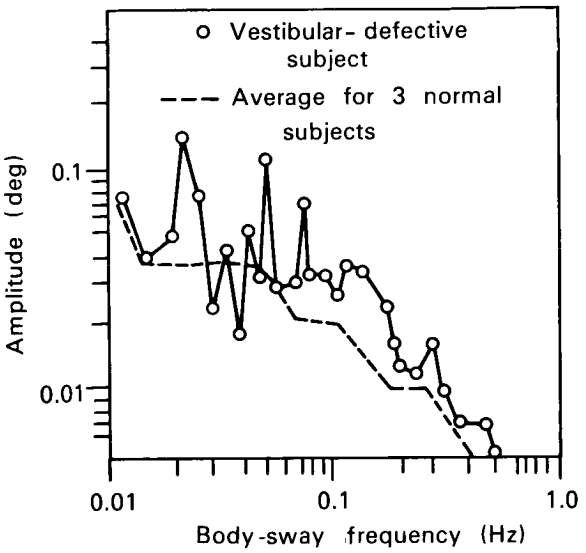


FIGURE 20A.—Body-sway frequency compared in vestibular-defective and normal subjects: Fourier coefficients of body-sway motion for vestibular-defective subject standing on a rigid, flat surface with eyes open. (From Ref. [103])

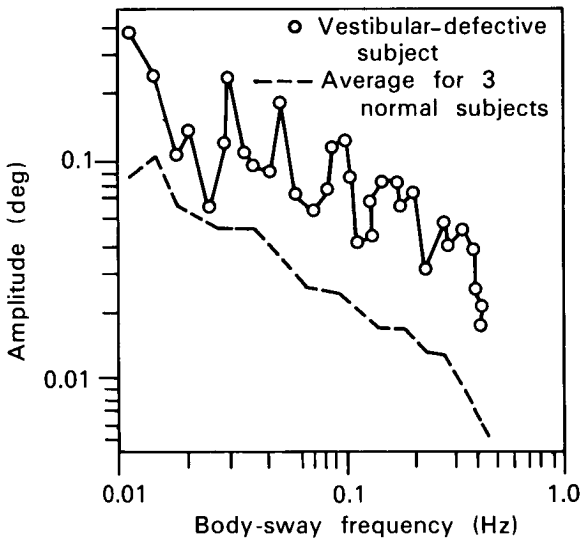


FIGURE 20B.—Body-sway frequency compared in vestibular-defective and normal subjects: Fourier coefficient of body-sway motion for vestibular-defective subject standing on a rigid, flat surface with eyes closed. (From Ref. [103])

In summary, the normal subject regulates posture with a combination of high-frequency (canal and somatosensory receptors) stabilization and low-frequency (otolith and optic receptors) stabilization; with eyes closed he still has otoliths functioning. The L-D subject with eyes closed is without low-frequency stabilization, resulting in a "rigid" stability.

Unnatural Stimulus Conditions

The vestibular responses under abnormal stimulus conditions fall mainly into two categories: system-bound and nonsystem-bound. The main chain of events in system-bound responses involves Blocks I, II, III, IV(B), and V of Figure 18.

Reflex phenomena. Some, but not all system-bound responses reflect instability of the vestibular system, which will be referred to as reflex vestibular disturbances (RVD). Typical manifestations in normal persons include nystagmus, the oculogyral illusion, past-pointing, and postural disequilibrium. Systematic studies of reflex manifestations reveal characteristics of the various responses which may be observed or inferred and, in general, have in common: (1) short latencies, (2) maximal response to the initial stimulus, (3) no perseveration of responses unless explicable by continuation of stimulation, and (4) response decline with acquisition of adaptation effects.

A large, important body of information deals with the input-output relations of the semicircular canals, otolith organs, and their interactions. The literature dealing with eye motions [59, 90, 117] has reached the level of a subspecialty with the introduction of nystagmography. Reference may also be made to modeling of the vestibular system [21, 33, 36, 51, 53, 57, 60, 71, 92, 114, 139]; in this chapter, much of a practical nature will be mentioned.

Delayed epiphenomena. Nonsystem-bound responses (Blocks I–III and VI–VII of Fig. 18) constitute an epiphenomenon elicited by certain repetitive accelerative stimuli that not only disturb the vestibular system, but allow vestibular influences (by means of a facultative or temporary linkage) to stimulate cells or cell groups outside the system. These responses include the symptoms of motion sickness and are superimposed on any reflex manifestations also present. Inasmuch as they are not elicited in response to physiologic stimuli and serve no useful purpose, they may be properly characterized as absurd manifestations.

Little is known concerning the facultative linkage (Block V). That "irradiating" vestibular activity is demonstrably open to modulating influences points to the use of common pathways in the brain stem reticular formation; mild symptoms of motion sickness have disappeared under the influence of experimenter-directed tasks which may have preempted neural pathways used by irradiating vestibular activity. The vestibular facultative linkage is made unusual but not unique by the readiness with which vestibular activity may get "out of bounds" and elicit the widespread responses which include typical symptoms of motion sickness. The occasional long delay between onset of stimulation and appearance of motion sickness suggests that a chemical linkage may also be involved [37].

Certain secondary etiological influences are categorized in Figure 18 (right lower corner). Some of these influences, e.g., eyes open or closed, are always present, tending to increase or decrease susceptibility to motion sickness. Also, it may be assumed that any factor tending either to evoke or inhibit a response characteristic of motion sickness will affect the susceptibility accordingly.

Although typical symptoms of motion sickness are well-known, a list of first-order responses (let alone the precise sites of origin) has not been compiled (Block VII). At least some first-order responses also act as a stimulus, and so on, until the disturbances involve the organism as a whole.

The cardinal symptoms useful in making a clinical diagnosis include cold sweating, pallor, drowsiness, increased salivation, and the nausea syndrome. Release of the antidiuretic hormone and urinary excretion of 17-hydroxycorticosteroids and catecholamines are among the many biochemical changes that may be manifested [20, 63]. It is apparent that there are great gaps in our knowledge of mechanisms underlying the symptomatology of motion sickness. The starting point in conducting studies, it seems, would not be the full constellation of symptoms and syndromes but rather the first-order responses. Although there is general agreement on what constitutes frank motion sickness, this agreement dwindles with the reduction in number and kinds of responses. It is possible, for example, to elicit either sweating (probably a first-order response) or drowsiness (undoubtedly a second or higher order response) as the only definite overt symptom.

Typical manifestations of motion sickness are: (1) delay in appearance of symptoms (cumulation) after onset of stressful stimuli, (2) gradual or rapid increase in severity of symptoms, (3) modulation by secondary influences, (4) perseveration after sudden cessation of stimuli, and (5) response decline indicating adaptation.

Recovery during continual exposure to stress is complicated. First, the nonvestibular systems (Block VI) must be freed from vestibular influences (Block III) by adaptation taking place in the vestibular system. The point in time at which this occurs is difficult or impossible to determine because it is not immediately reflected by the disappearance of symptoms. Symptoms perseverate until restoration takes place (spontaneously) through homeostatic mechanisms. The time of engagement and disengagement between the vestibular and nonvestibular systems is best determined when a subject is exposed to severe stress for only a short period.

Another important omission in Figure 18 relates to mechanisms underlying adaptation in the vestibular system (with the possible exception of the role of vestibular efferent activity). In general terms, it would appear that individuals differ greatly in the ability to cope with abnormal vestibular inputs. Part of this difference may be attributable to differences in susceptibility and part to differences in the rate at which they can adapt to the abnormal inputs. The need to adjust must be triggered by a recognizable difference between the incoming stimulus pattern and the central patterning into which it must integrate. The fact that motion sickness may be prevented by incremental exposure to otherwise intolerable angular velocities in a slowly rotating room implies that this "recognizable difference" may be smaller than that necessary to elicit symptoms. An additional implication is that adaptation achieved by small increments in stressful accelerations must involve the vestibular system proper (Block III), and not the nonvestibular systems (Block VI) where first-order responses characteristic of motion sickness have their

immediate origin. Money [102] and Reason [118] have reviewed the literature on motion sickness.

GROUND-BASED STUDIES IN PREPARATION FOR SPACE MISSIONS

In this section of the chapter there are five parts: Functional Tests, Provocative Tests, Adaptive Capacity Tests, Simulation Studies in Parabolic Flight and Rotating Environments, and Antimotion Sickness Drug Therapy. Only simulation studies will be discussed in detail, partly because some of the material is not readily accessible elsewhere, but mainly because they comprise the most important studies in preparation for space missions.

Functional Tests

The tests described here should be regarded as possibly supplementing, and not taking the place of, a comprehensive clinical otolaryngological examination [7, 59, 68, 90], although there is evidence that function test scores within the normal range have no value in predicting individual differences in susceptibility to reflex vestibular disturbances and motion sickness [68]. They are valuable nevertheless for making comparative measurements, the crewman serving as his own control. The reliability of most vestibular tests is not high compared with vision or hearing tests; hence, there is need or desirability for repeated measurements on the crew serving as experimental subjects. Functional tests should be used not only in the selection of the crew but also in the selection of subjects for vestibular experimentation.

Semicircular Canals

Nearly all clinical test batteries include tests for spontaneous and positional nystagmus and a modified Hallpike test; hence, those tests will not be described here.

The threshold caloric test [89] is fairly reliable and may be useful; the vestibular disturbance is brief and recovery quick. Irrigating temperatures just below body temperature usually suffice, but if not, stepwise decreases are made until a response is obtained. If irrigating temperatures below 35° C are required to elicit a response, some abnormality should be suspected.

Rotating devices provide not only a physiological type stimulus (albeit abnormal) but also may be instrumented to include preprograming (Fig. 21). The most sensitive indicator is the oculogyral illusion, but "sensations" and nystagmus are used more routinely.

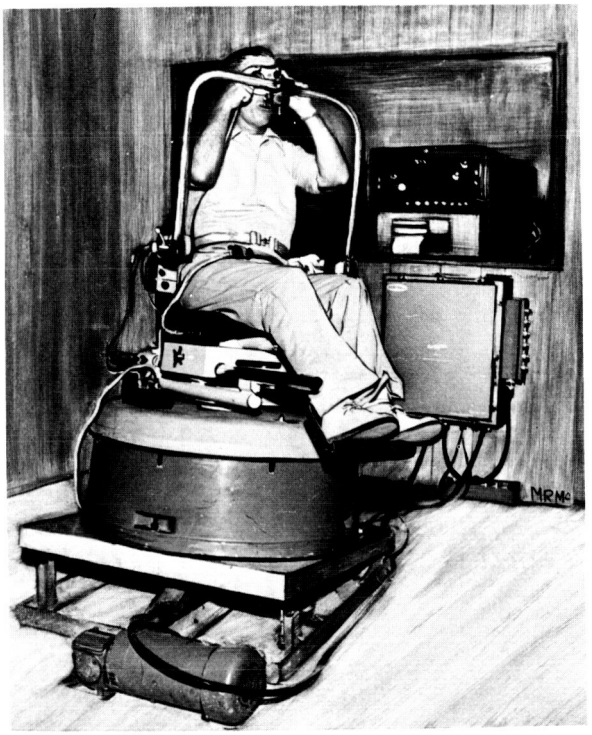


FIGURE 21.—Subject manipulating a dim line of light in darkness, using a goggle device with recording equipment. The target does not furnish a visual cue for space localization but does provide a good indicator. The readout is automatic.

The oculogyral illusion is a form of apparent motion in the direction of angular acceleration; its genesis is in the behavior of the cupula-endolymph mechanism. In measuring "thresholds," favorable conditions include a dimly lighted three-dimensional target viewed in darkness and fixed with respect to the subject, or a goggle device that greatly simplifies the method. The goggle device (Fig. 22), described elsewhere in detail [100], is essentially a collimated line of light in an otherwise dark field. This "line" can be rotated about its center by means of a knurled

knob. A digital readout of "line" position is easily seen and is accurate within ±0.25°. Normal thresholds of perception are in the range of 0.1 to 0.2°/s².

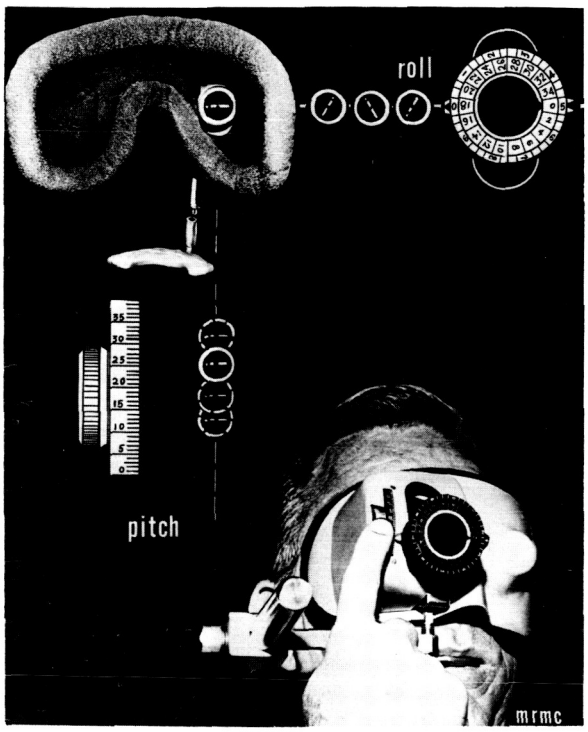


FIGURE 22.—Goggle device without automatic readout; pitch or roll, or both, may be measured. Note the dental appliance (individually fitted) that aids in maintaining the device in a fixed position with reference to the head.

Tests of Otolith Function

Ocular counterrolling has the advantage of not disturbing the vestibular system; hence, it qualifies as a test conducted under near-normal stimulus conditions. Ocular torsion may be defined as the involuntary conjugate rolling movement of the eyes around their lines of sight in the direction opposite the leftward- or rightward-tilted position of the head (and body) with respect to the gravitational upright. The measurements are made by comparing the position of a metal frame, to which the subject is thoroughly secured (head secured by individually fitted dental appliance), and the relative position of the uncovered eye from colored photographs made in the upright and tilt positions. The roll is measured in degrees of arc.

The values obtained with different degrees of rightward and leftward tilt describe curves that can be examined for left-right symmetry. The "index" (one-half the sum of the maximal left and right roll) values obtained in a group of 550 presumably normal persons and 10 L-D subjects are shown in Figure 23 [94]. The rare instances when values fall below 120 seconds of arc are unexplained.

A variety of other tests is available but none is recommended as a substitute for ocular counterrolling. The elicitation of nystagmus in a device that rotates a person about an axis other than the Earth-vertical is receiving attention. Figure 24 shows the type of nystagmus elicited when a normal subject is rotated at constant velocity about an Earth-horizontal axis [44]. During rotation in a clockwise direction, the subject displays a right-beating nystagmus that is diminished as he rotates through the right-ear-down position and is augmented as he rotates through the left-ear-down position. During counterclockwise rotation, he displays a left-beating nystagmus that is diminished as he rotates through the left-ear-down position and enhanced as he rotates through the right-ear-down position. Both a directional bias and a cyclic modulation about the bias level are manifested, indicating that two etiologic factors are operant [126].

Test of Combined Canalicular and Otolithic Function

The postural equilibrium test battery. These tests have a limitation in the sense that many systems in addition to the vestibular reflexes are challenged, but a great advantage is that they test natural behavioral mechanisms.

A useful test battery, described elsewhere in detail [26], comprising six individual items, requires the subject to stand or walk in the stringent position of body erect, arms folded against chest. The test items that constitute this battery are:

1. Sharpened Romberg (SR): standing on the floor in strict tandem heel-to-toe position with eyes closed, arms folded against chest, and body erect for 60 s.
2. Walk Eyes Open (Walk E/O): walking heel-to-toe with feet in strictly tandem posi-

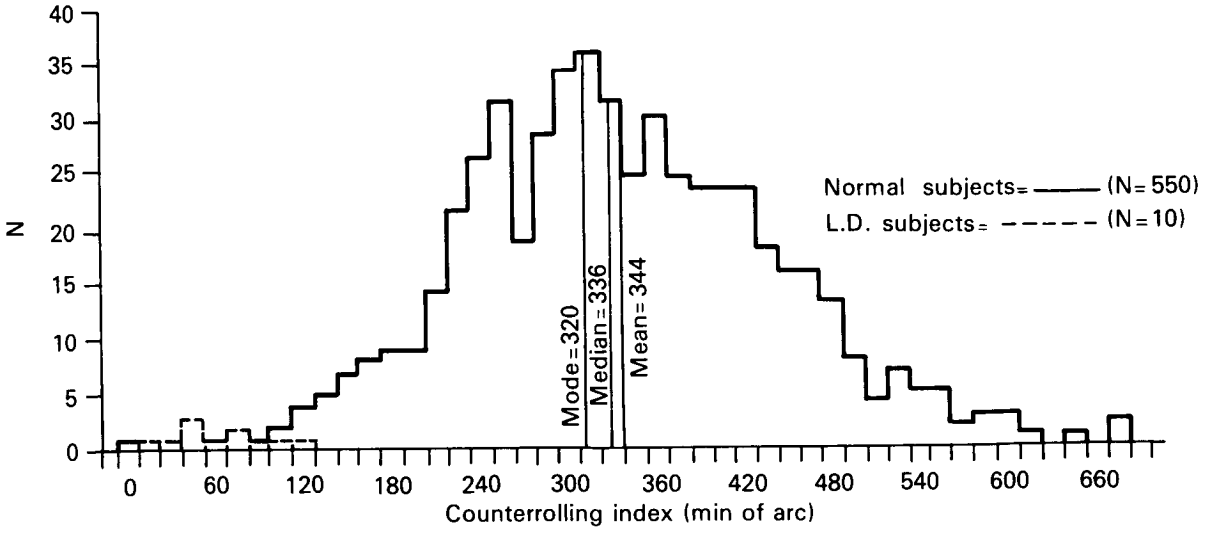


FIGURE 23.—Distribution of counterrolling index among normal and labyrinthine-defective subjects. (From Ref. [94])

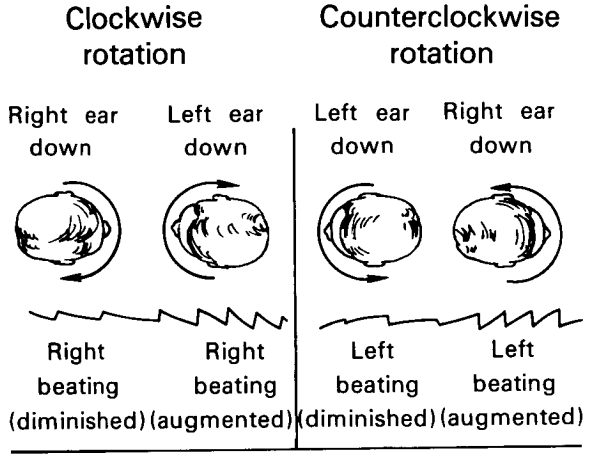


FIGURE 24.—Normal nystagmic responses (drawings) to rotation about an Earth-horizontal axis. Note directional bias and cyclic modulation.

tion and arms folded against chest while in a body-erect position on a 3/4-inch-wide by 8-foot-long rail.

3. Stand Eye Open (Stand E/O): standing heel-to-toe with feet in a strictly tandem position and arms folded against the chest while in a body-erect position on the 3/4-inch-wide rail for a period of 60 s.

4. Stand Eyes Closed (Stand E/C): standing, as for the Stand E/O test, on a 2¼-inch-wide by 30-inch-long rail for a period of 60 s.

5. Stand One Leg Eyes Closed (SOLEC-R and SOLEC-L): standing stationary on the floor on each leg for 30 s while arms are folded against chest and body in erect position.

6. WOFEC: walking on the floor eyes closed in the stringent position of arms folded against chest, body erect, and feet aligned tandemly heel-to-toe.

All subjects are tested while wearing shoes on a hard floor without rugs. The men wear hard-soled shoes and the women wear hard-soled "flats."

The scores and percentile equivalents measured on the normal subjects are shown in Table 1.

Comparative scores (normalized in percentile equivalents) for the other tests are in Table 2. A diagnosis of "frank ataxia" can be made if the walk-on-floor-eyes-closed (WOFEC) score is less than perfect and scores on the other tests are below the 6th percentile. The typical normal range requires a perfect WOFEC and scores about the 40th percentile in the other tests. A test comprising only the "floor" tests is quite satisfactory for screening purposes. In general, improvement in scores suggests normality, and its absence, abnormality.

TABLE 1.—*The WOFEC Test Scores of Normal Men and Women; Means, Standard Deviations, and Percentile Equivalents* [26]

N = 287 Normal men Ages 17–61 (Mean age = 24.5; S. D. = 8.73)		N = 100 Normal women Ages 18–65 (Mean age = 33.2; S. D. = 11.72)	
WOFEC score	Percentile equivalent	WOFEC score	Percentile equivalent
30	100th–5th	30	100th–12th
29	4th	29	11th
27–28	3rd	28	10th
23–26	2nd	27	9th
≤ 22	1st	26	8th
		24	6th
		23	5th
		22	3rd
		19–21	2nd
		≤ 18	1st
Mean: 29.7 S. D.: 1.65		Mean: 29.3 S. D.: 2.60	

Provocative Tests

Provocative tests of many types are widely used [5, 30, 31, 40, 64, 83, 86, 95, 101, 106, 108, 128], serve the important purpose of evaluating susceptibility to reflex vestibular disturbances and to motion sickness, and measure ability to cope with such disturbances either with or without the aid of countermeasures, including the use of drugs. Factors of etiologic significance in addition to the motion environment may be introduced, to simulate more completely the anticipated operational conditions or to explore their role in affecting an individual's susceptibility to novel circumstances. The distinctions between provocative and simulation tests involve primarily duration and, secondarily, specificity in terms of the global exposure conditions; thus, the predictive value of provocative tests is less than that of simulation tests. The validity of the findings, similar to functional tests, is compromised if the person tested is either suffering from active disease involving the vestibular systems, or, indeed, has not compensated completely following permanent injury that is no longer active.

In conducting and interpreting the results of provocative tests, difficulties are encountered and precautions must be taken, which are not unrelated. The origins of the difficulties are: (1) the individual differences in susceptibility with regard to a given test; (2) intra-individual differences in susceptibility, when exposed in different gravitoinertial force environments; (3) preternaturally high susceptibility if insufficient time has not elapsed between exposures; (4) that adaptation occurs as an inevitable consequence of every test, with much individual variation in the rate of acquisition and loss of adaptation; and (5) the difficulty in expressing the results in absolute values. The use of normalized scores and standardization of techniques would provide great advantages.

Advantages of provocative tests include: (1) the low "cost" in terms of time and equipment that

TABLE 2.—*A Comparison of Scores of Normal Men with the L–D Men on the Ataxia Test Battery; Means, Standard Deviations, Mean Differences, and Validity Coefficients* [26]

Chron. age and ataxia tests	Normal men (N = 287)		L–D men (N = 22)		Mean differences	Validity coefficients (r pt. bis)
	mean	S.D.	mean	S.D.		
Age.	24.5	8.73	27.5	8.11	3.0	.089
WOFEC	29.7	1.65	14.1	7.82	15.6	.838
SR	224.8	35.65	19.3	14.13	205.5	.837
SOLEC-R	125.9	35.75	15.9	5.57	110.5	.647
SOLEC-L	126.2	35.03	14.2	5.85	112.0	.634
Walk E/O	12.6	2.48	7.0	2.51	5.6	.502
Stand E/C	88.8	55.08	9.2	3.21	79.6	.360
Stand E/O	35.3	29.64	8.6	2.17	26.7	.234

makes a "test battery" feasible; (2) individual testing; and (3) their use in studying vestibular mechanisms and in evaluating countermeasures.

A number of provocative tests are in use, but brevity dictates limiting descriptions to a few representative tests relevant to spaceflight operations.

Standardized tests have been devised for determining susceptibility to vestibular side effects (usually motion sickness) in the Naval Aerospace Medical Research Laboratory, Pensacola, Fla., slow rotation room (SRR), with eyes open or in a rotating chair device with eyes closed. The stressful accelerations are generated by having the subject actively rotate his head (and body) out of the plane of the room's rotation. The head movements (front, back, left, and right) are limited by "stops," usually through arcs of 90°. Eight head movements, "over" and "return," in the four quadrants are randomized, and a taped recording sets the cadence.

Figure 25 shows the stress profile (Provocative Incremental Test Schedule) used in a slow rotation room in comparing susceptibility to motion sickness with eyes open and eyes closed [106]. The end point was a motion sickness score of

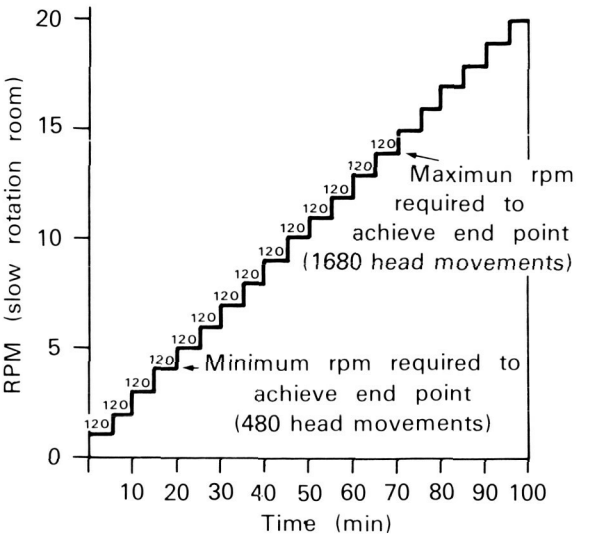


FIGURE 25.—Stress profile used in testing motion sickness susceptibility of 24 subjects. 120= number of head movements made in 4 quadrants at each step increase in velocity of the room. End point was 12 units on a scale used in grading severity of motion sickness.

FIGURE 26.—Off-vertical rotating chair device with recording equipment. Chair may be used upright for stimulating semicircular canals and in off-vertical (at constant angular velocity) for stimulating otolith organs. Instrumentation permits fairly complete programing.

C-4

TABLE 3.—*Diagnostic Categorization of Different Levels of Severity of Acute Motion Sickness* [96]

Category	Pathognomonic 16 points	Major 8 points	Minor 4 points	Minimal 2 points	AQS [1] 1 point
Nausea syndrome	Nausea III [2] retching or vomiting	Nausea II	Nausea I	Epigastric discomfort	Epigastric awareness
Skin		Pallor III	Pallor II	Pallor I	Flushing/subjective warmth ≥ II
Cold sweating		III	II	I	
Increased salivation		III	II	I	
Drowsiness		III	II	I	
Pain					Persistent headache ≥ II
Central nervous system					Persistent dizziness Eyes closed ≥ II Eyes open III

Levels of severity identified by total points scored

Frank sickness	Severe malaise	Moderate malaise A	Moderate malaise B	Slight malaise
(FS ≥ 16 points	(M III) 8–15 points	(M IIA) 5–7 points	(M IIB) 3–4 points	(M I) 1–2 points

[1] AQS—Additional qualifying symptoms.
[2] III—severe or marked, II—moderate, I—slight.

approximately 12 points (Table 3) [96]. Using the (terminal) rpm reached as the "normalized" score has the advantage of comparing susceptibility within and between subjects.

The Coriolis Sickness Susceptibility Index. This test represents a modification of the test just described, using a rotating chair instead of a room, and the subject is rotated with eyes closed [95]. A noteworthy feature of this test is the method of scoring, which yields a single value, the "index," enabling the investigator to make comparisons within and among subjects.

Off-Vertical Rotation Test. In contrast with the two tests just described, which initially "disturb" the canalicular system, exposure to rotating linear acceleration vectors or to rotation (at constant velocity) other than in the gravitational or gravitoinertial upright, initially disturbs the otolithic system. The device, shown in Figure 26, consists of a rotating chair [40] mounted on a platform that can be tilted either by a hand crank or by an electric motor, and the degree of tilt read from a large protractor. With each revolution of the off-vertical rotation (OVR) device the subject continually changes position with regard to the gravitational upright. Thus, receptors in the paired maculae of the utricles and saccules and nonvestibular proprioceptors are continually exposed to an unusual stimulus pattern. (This chair-device serves different purposes, including use in the upright mode.) In provocative testing, both the angle of tilt and the rpm are manipulated in different ways. At a predetermined angle of tilt, the rotation, programed on a time axis, involves periods of acceleration at 0.5°/s² for 30 s, followed by periods of constant velocity for 6 min, until either the end point is reached or 6 min completed at 25 rpm, the cut-off point. In effect, this program represents unit increases of 2.5 rpm every 6.5 min after the initial step. The end point can be expressed in terms of elapsed time at terminal velocity, as total elapsed time at terminal velocity, or as total elapsed time, which serves as an index of susceptibility to motion sickness. The findings in a group of healthy men, the great majority attached to a naval air station, are shown in Figure 27 [40]. All but 12 men reached the predetermined end point (M IIA) (Table 3) at a 10° tilt

[40]; all but five of the remainder reached it only when the angle of tilt was increased to 20°. Thus, the scores ranked 95 subjects in terms of their susceptibility to this unusual gravitoinertial force environment and demonstrated that five were highly insusceptible.

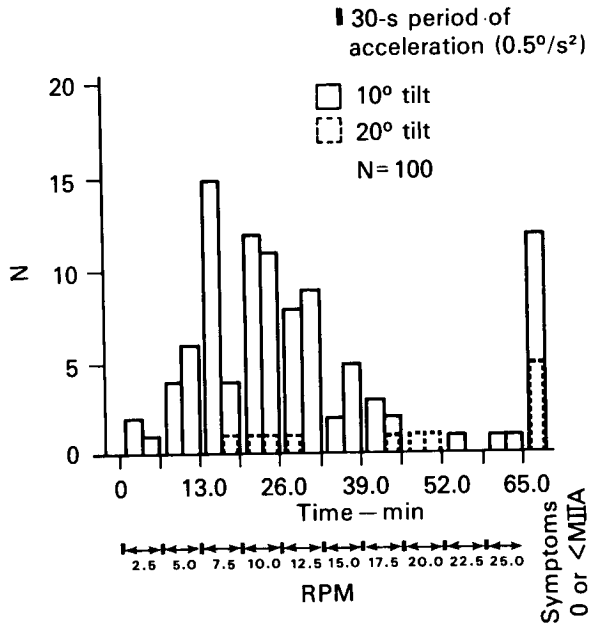


FIGURE 27.—Motion sickness susceptibility index in subjects exposed to off-vertical rotation according to programed stress indicated on abscissa. (From Ref. [40])

Figures 28 and 29 are plots comparing susceptibility to motion sickness with scores obtained in testing, respectively, the function of the semicircular canals and otolith organs [40]. Although it appears that significant relationships were not found between functional test scores and susceptibility to motion sickness, it is worth adding that, when extreme values are compared, susceptibility was lower in subjects with high rather than low values for the counterrolling index.

Adaptive Capacity Tests

The relevant Soviet literature should be consulted for a detailed knowledge of their tests and procedures along with validating studies dealing with the important subject of vestibular training and adaptation [10, 58, 66, 107, 110, 142].

Khilov [66], in reviewing this material, began

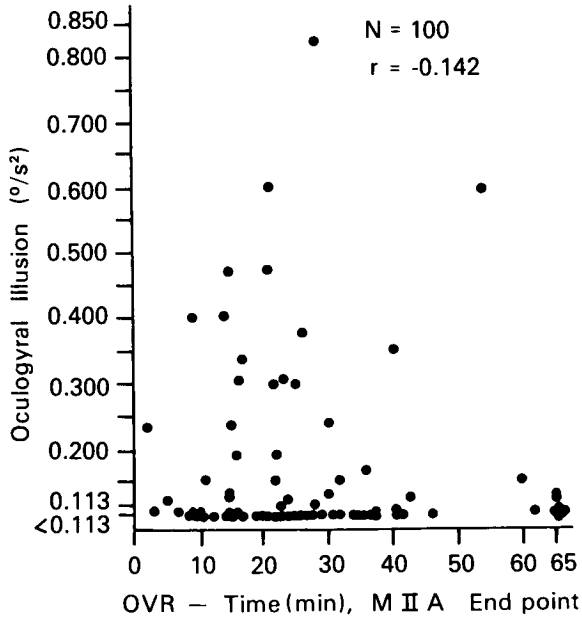


FIGURE 28.—Comparison of motion sickness susceptibility with scores on test of semicircular canal function (the oculogyral illusion). (From Ref. [40])

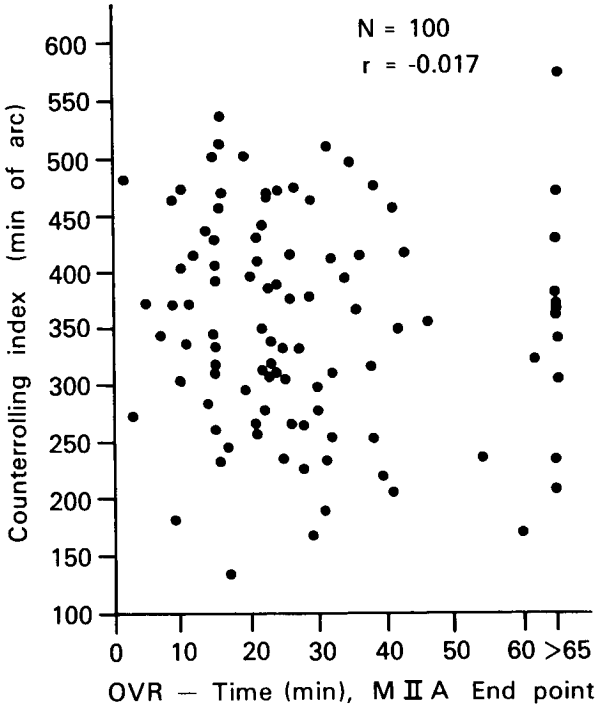


FIGURE 29.—Comparison of motion sickness susceptibility with scores on test of otolith function (counterrolling index). (From Ref. [40])

with the well-known tests used in the early days of aviation in the USSR, then described successive additions to the test battery. These additions were required to meet the need of not only selecting flyers with normal vestibular function but also to discriminate among those with normal function regarding their "sensitivity" to sensory inputs, the genesis of which are in successive increases in magnitude and complexity of the force environments in aircraft and spacecraft, including weightlessness. No less than seven such additions have been made, and validation of these additional test items has been carried out.

Khilov referred to one of his earlier articles expressing the opinion that otologists were ignoring the function of the otolith apparatus which, in flight, is subjected to greater stimulation than the semicircular canals.

With regard to otolith function, Khilov described a test based on the interaction between canals and otoliths (proposed by Voyachek in 1914). With trunk "inclined downward" the subject is rotated in a Bárány chair. After cessation of rotation "when primarily the frontal canals are responding" to the acceleration, the subject returns to the upright, "which is an adequate stimulus to the utricle altering the response of the canals. Persons in whom the duration of rotary nystagmus is reduced and in whom the reaction of falling is intensified with the simultaneous manifestation of autonomic reflexes, are not admitted to flight school."

Khilov rightly emphasized the point that persons with normal function of the canals and otoliths manifest great differences in sensitivity (motion sickness) and other innate or behavioral responses when exposed in different gravitoinertial force environments. This sensitivity may be overt or latent, and if so, it may be brought out by decreasing cortical inhibition through the use of chloral hydrate. The force environments associated with space were separately considered, although there is overlap with flights in aircraft.

In connection with space flight, he discussed the problems of repeated exposure to sustained high-level linear accelerations which can be simulated on a human centrifuge, the transition into weightlessness which can be simulated in parabolic flight, Coriolis accelerations which also are a possibility and readily simulated, and made recommendations on conducting a training program.

The importance of distinguishing between basic susceptibility to motion sickness and the role of adaptation has been explored at the Naval Aerospace Medical Research Laboratory in Pensacola, Fla. On a given occasion, a person's susceptibility to motion sickness is determined by: (1) the ease with which the vestibular system is disturbed in a particular motion environment, thus providing the opportunity for the escape of neuronal activity beyond its normal bounds; and (2) thresholds (presumably in the brain stem reticular formation) permitting the escape of this neuronal activity along certain preferential pathways (not normally used) to sites where first-order symptoms of motion sickness originate. If this person is exposed to an incremental adaptation schedule, additional information is gained regarding adaptation to the motion environment, but the level of susceptibility measured now comprises the two factors determining susceptibility just mentioned, minus the amount of adaptation acquired. These factors can be separated to some extent by using a modification of the stress profile mentioned previously, termed an incremental adaptation schedule (IAS).

Two "standard" stress profiles have been used. One required the execution of 120 head movements at each 1-rpm increase in rotation (clockwise or counterclockwise) between 0 and 6 rpm, and, after a single-step gradual return to zero velocity, the execution of 120 head movements either immediately after the return ("no delay") or after delay periods varying from 1 to 24 hours. The other standard stress profile differed by the addition of a second incremental adaptation schedule (IAS) in which the direction of rotation was reversed either immediately after return to zero velocity or after delay periods measured in hours. The terms "initial IAS" and "reverse IAS" are used because the initial direction of rotation was semirandom.

After each discrete head movement the subject signalled ("yes" or "no") whether he detected a "sensation" of movement, an apparent movement (visual illusion), or a tendency to be deflected from the plane in which the movement was carried out. The severity of motion sickness symptoms was given numerical scores according to the diagnostic criteria described in Table 3.

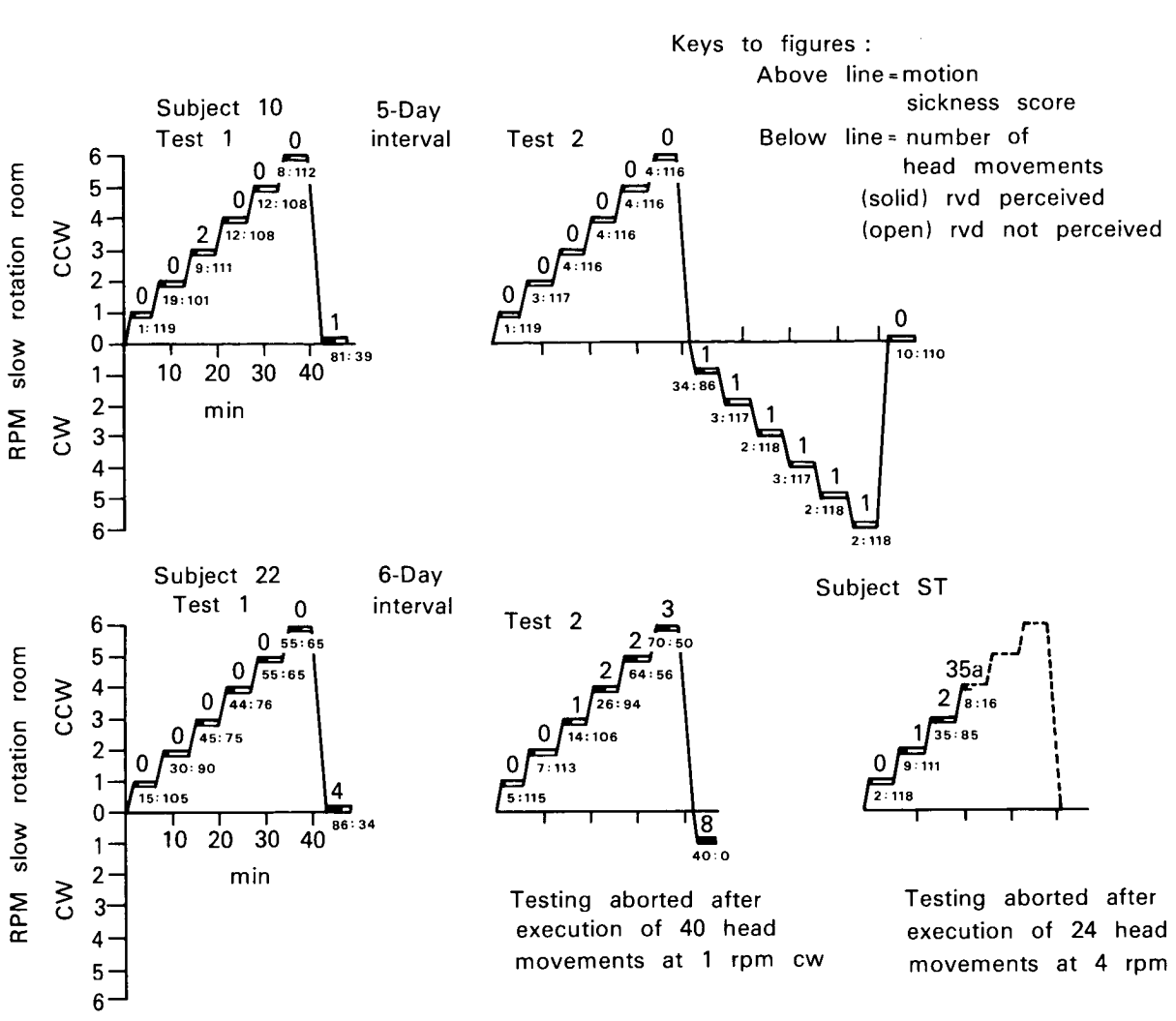


FIGURE 30.—Stress profiles, motion sickness scores, and occurrence of reflex vestibular disturbances in three normal young subjects: first and second numbers below line indicate, respectively, number of head movements when (one or more) reflex disturbances "perceived" and "not perceived." Subject 10 was virtually symptom-free (of motion sickness) despite a high occurrence of RVDs after return to zero velocity (Test 1) and during step 1 after reversal of direction in Test 2. Subject 22 experienced a high occurrence of RVDs but relatively low susceptibility to motion sickness in both tests. Subject ST demonstrated a relatively low incidence of RVDs but high susceptibility to motion sickness. For implications see text.

Figure 30 shows the measurements obtained in three young healthy subjects. On the two occasions Subject 10 was tested he was virtually free from symptoms of motion sickness. During the initial IAS in Test 1, the low susceptibility might be attributed mainly to the low level of instability in the vestibular system indicated by the low incidence of reflex vestibular disturbances (RVD). During the execution of head movements after return to zero velocity, however, a high level of vestibular instability is shown without elicitation of significant symptoms. In other words, insusceptibility involved the maintenance of both high stability in the vestibular system, and, even when the system was disturbed (after return to zero velocity), a high threshold preventing vestibular activity reaching sites of origin of motion sickness symptoms.

In the second test the incidence of RVD during the initial IAS was lower than in the first test, probably reflecting some retention of adaptation effects. On reversing the direction of rotation, the incidence of RVD rose sharply (at 1 rpm), but the subject again remained virtually immune to motion sickness.

Subject 22 was tested on two occasions. In Test 1 he did not manifest symptoms of motion sickness during the IAS, although the incidence of RVD's was high. During the challenge after return to zero velocity, very mild symptoms of motion sickness were experienced along with a substantial increase in the incidence of RVDs. The high incidence of positive responses (implying loss of stability in the vestibular system) was associated with a high threshold for spread of vestibular activity. In Test 2, during the initial IAS very mild symptoms of motion sickness were experienced, and rapid incremental increase in the incidence of RVD. On reversal of rotation, after 40 head movements testing was aborted due to nausea, and the RVD incidence was 100%. Despite the abort during reversal (indicating the acquisition of direction-specific adaptation effects during the IAS) the findings are in accord with those in Test 1.

The measurements obtained in exposing subject ST (Figure 30) to the stressful accelerations indicate typically normal findings during the execution of 120 head movements during the first three incremental steps, then an abort after 24 head movements at 4 rpm. The number of positive responses denoting instability of the vestibular system gave little or no clue to the impending abort. The time for acquisition of adaptation was brief, hence the high susceptibility, presumably, was the consequence of a low threshold permitting the escape of vestibular activity beyond its normal bounds.

In summary, a single test may reveal a great range of individual differences in adaptive capacity, and a succession of exposures can be used to reveal both the acquisition and the retention of adaptation, as described next in this section.

Simulation Studies

Some problems posed in attempting to predict susceptibility to vestibular side effects under the novel conditions in a rotating space base are pointed out in Figure 31. A slow rotation room (SRR), which can be used to simulate the angular velocity, is a completely enclosed space and provides for prolonged exposures and sudden transitions between the rotating and nonrotating states. The SRR fails to simulate space-base conditions in such notable aspects as weightlessness, subgravity levels, man's orientation when upright with regard to the axis of rotation, and the Coriolis forces while walking and handling objects. Stated differently, the SRR provides a useful simulation device for the important study of effects of Coriolis accelerations[6], except for the fractional subgravity levels and man's orientation with respect to the axis of rotation. The SRR is useful in demonstrating the qualitative aspects of the vestibular organs' role in postural equilibrium and in walking, but here, nonvestibular factors also play an important role. The necessary use of small rotating devices poses limitations in terms of visual references, length of exposure, and postural equilibrium.

Parabolic flight offers the opportunity to study the effects of weightlessness and fractional subgravity levels for brief periods. Orbital flights prior to the establishment of a space base offer not only the opportunity to use small or even fairly large rotating devices for validation of ground-based experimental findings, but they also offer the advantages of prolonged exposure to study adaptation effects.

Parabolic Flight

Studies involving parabolic flight have been conducted in the USSR and the US [68, 69, 72, 78, 80, 96, 141]. Insofar as the studies have used similar methods, the findings are not only concordant but also agree with findings on astronauts [9] and cosmonauts [66] in orbital flight.

Studies dealing with susceptibility to motion sickness in the weightless phase of parabolic

[6] There is general agreement in using the term Coriolis acceleration to define the "added acceleration" generated by one angular and one linear velocity. When the "added acceleration" is generated by two angular velocities acting on a mass simultaneously, some investigators (for clarity) have substituted for Coriolis acceleration such terms as "cross-coupled angular accelerations" or "angular Coriolis accelerations."

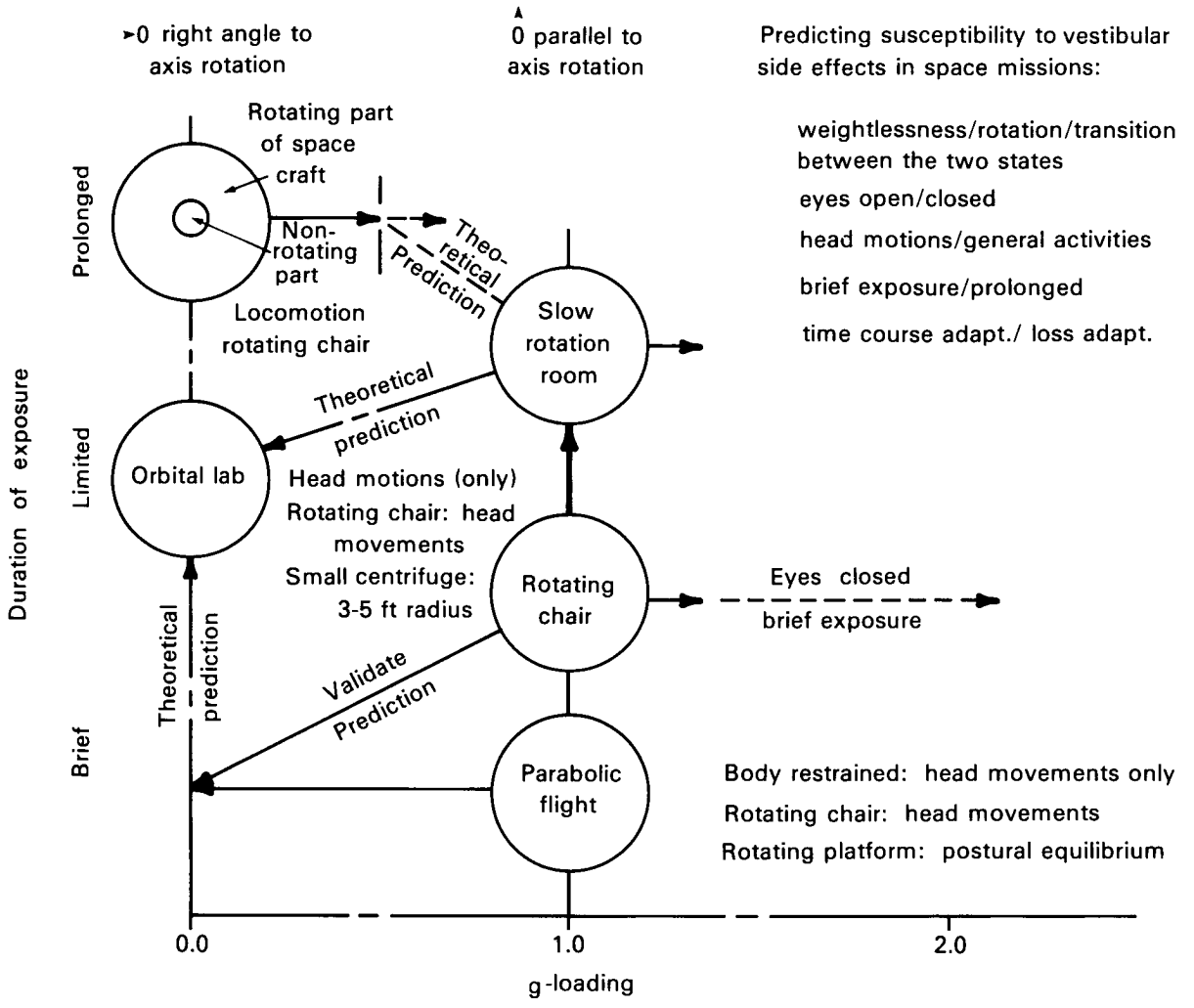


FIGURE 31.—Problems in predicting vestibular side effects in rotating space base.

flight have been mainly of two types. In one, the subjects were restrained in their seats and required to make standardized head motions during the weightless phase only. The findings in one experiment [96] are summarized in Figure 32 and demonstrate that, among the 12 subjects tested in this manner, six were asymptomatic. Five of the remaining six experienced symptoms only when making head motions; the last subject demonstrated increased susceptibility when making head motions compared to the head restraint (control) condition.

The second kind of experiment involved a rotating chair device, and the subjects were required to make standardized head motions similar to those used in the SRR but with eyes blindfolded. Each subject served as his own control; comparisons were made between susceptibility under terrestrial conditions and during parabolic flight, using similar periods of rotation and nonrotation. The findings on 74 subjects are shown in Figure 33 [96]. Susceptibility in weightlessness compared with ground-based conditions is ranked on the Y-axis, the topmost subject experiencing the greatest increase in susceptibility in weightlessness compared with terrestrial conditions. This ranking was made possible by the use of "equivalent head movements" (EHM), a universal scoring procedure described elsewhere in detail [95]. Scores on subjects tested on

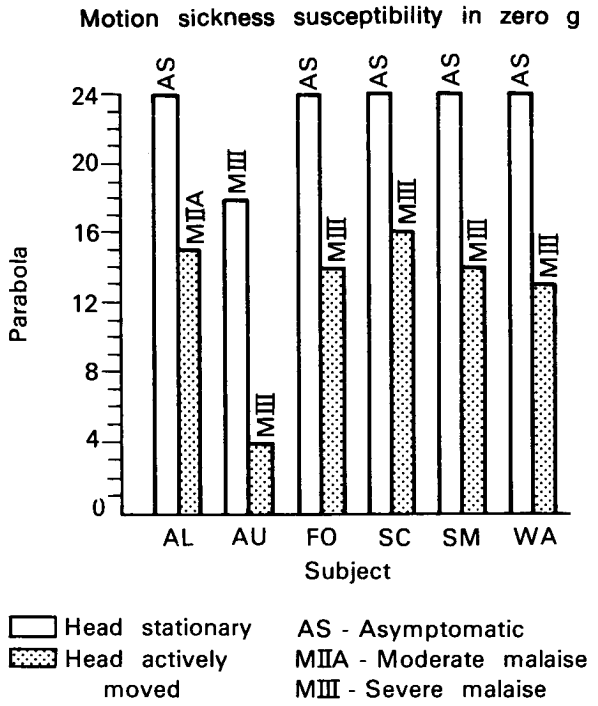


FIGURE 32. — Among six susceptible subjects, effects of active head movements relative to the restrained condition upon sickness susceptibility measured in terms of the number of parabolas required to provoke severe malaise. (From Ref. [96])

more than one occasion are given in chronological order, and the open circles indicate that the moderate malaise IIA (Table 3) end point was not reached [46]. The data indicate that more subjects have decreased than increased susceptibility in weightlessness and that in these subjects, the end point frequently was not reached. Susceptibility under ground-based conditions proved to be a poor indicator of susceptibility aloft.

The effects of preadaptation to the stressful accelerations generated by standardized head movements during rotation have been evaluated in 10 subjects.

Preadaptation to terminal velocities of either 7 or 10 rpm was accomplished by the use of so-called incremental adaptation schedules in a slow rotation room, the subject's eyes remaining open. In every instance the preadaptation was beneficial, often to a striking degree. Thus, in one subject, prior to adaptation, susceptibility was far greater in weightlessness than under terrestrial conditions, but after adaptation the subject was symptom-free in weightlessness. Moreover, whereas prior to adaptation the subject was susceptible to motion sickness in parabolic flight even when not rotating, after the adaptation he was symptom-free. In varying degrees, this transfer effect (from rotating room to nonrotating conditions in weightlessness) has been demonstrated in other subjects.

Rotating Environment

A great number of experiments has been carried out with normal subjects exposed to continual rotation at varying angular velocities and for periods up to 25 days. Many of these investigations were concerned with the overall response pattern [3, 18, 22, 29, 42, 50, 56, 64, 70, 74, 76, 79, 84, 132], while others were directed toward more specific goals: response thresholds [34], effects of varying body position [55, 82, 85] and of concomitant accelerations [77], transfer effects (between horizontal and vertical positions) [47], effects on hearing [137] and on sleep [6, 35, 105], cardiovascular effects [131], and the release of stress hormones [20, 63].

A person is not subjected to stressful stimuli in a rotating environment unless he rotates his head outside the plane of the room's rotation; hence, the situation differs from that in ships and planes where a person cannot avoid stressful accelerations generated by motions of the vehicle. On the other hand, it is difficult to carry out tasks without generating stressful accelerations. Moreover, if stressful head movements are avoided, adaptation effects are not acquired. Generally speaking, it is found that, for a given level of bodily activity, the two important factors governing the appearance of symptoms are susceptibility of the unprotected subject and the angular velocity of the room. With regard to angular velocity, even subjects highly susceptible to vestibular side effects are not handicapped on sudden exposure to 1 rpm, but above this level, countermeasures must be taken to prevent elicitation of symptoms.

The prevention of side effects, especially motion sickness, involves avoiding or at least minimizing nonvestibular etiological factors, thus reducing the problem to the prevention of that

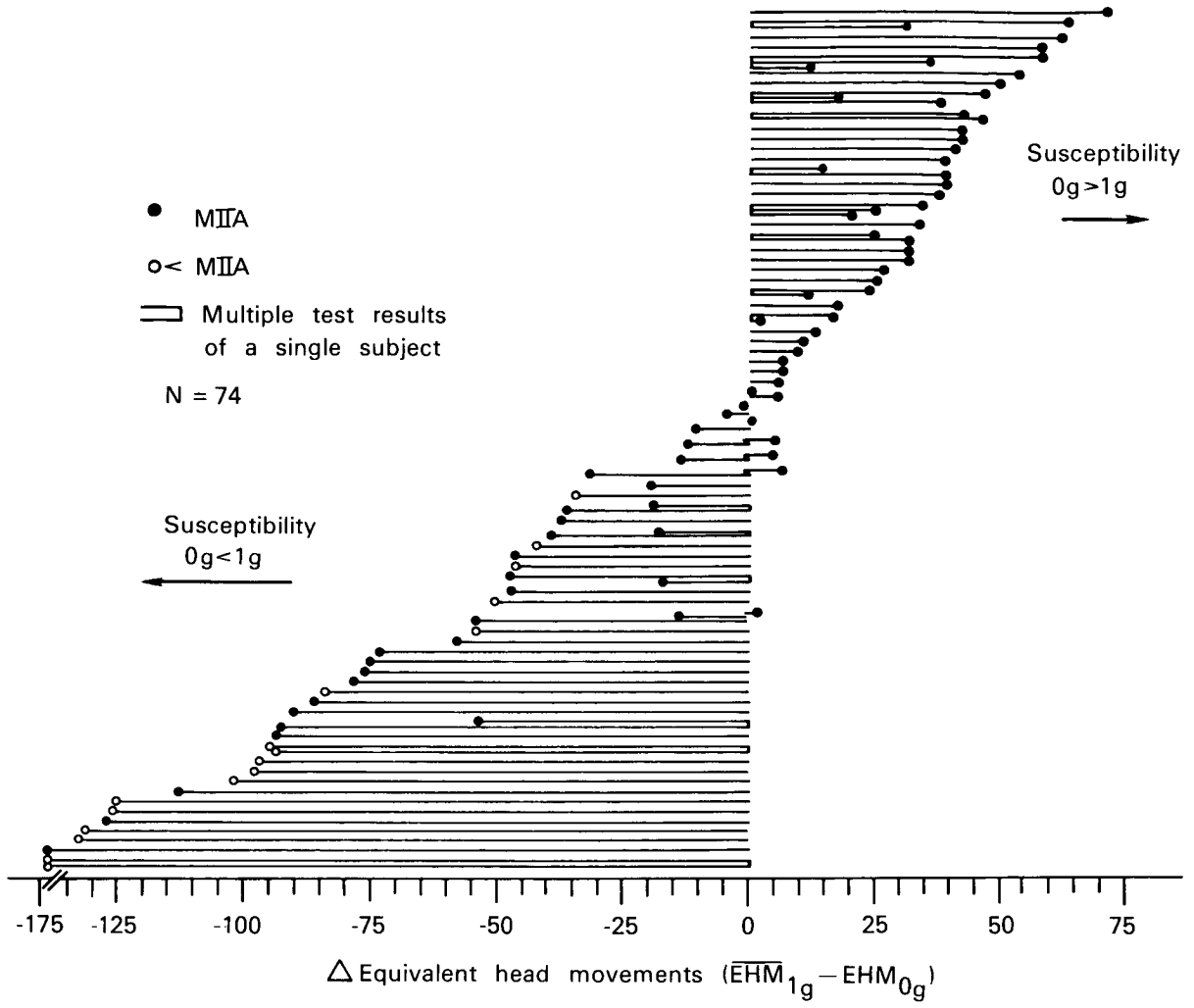


FIGURE 33.—Changes in susceptibility to motion sickness in 74 subjects on transition into the weightless phase of parabolic flight compared with similar stimulus conditions (standardized head movements during rotation) on Earth. The same end point was used but the stress was varied in intensity (rpm) and duration (indicated by number of head movements). "Equivalent head movements" implies these two stress factors were equaled (see text). Only a few subjects (scores near 0) experienced no change in susceptibility aloft, a majority were less susceptible (− scores), and a minority (+ scores) were more susceptible aloft than on the ground.

which might be termed vestibular sickness. Minimizing nonvestibular factors involves selection of typically normal spacemen (i.e. those whose responses to provocative tests are physiologic in character) and avoiding intrinsic and extrinsic factors known to lower susceptibility to motion sickness. Dealing with vestibular sickness eventually gets down to the selective process (discussed under **Adaptive Capacity Tests**), the use of incremental adaptation schedules and, possibly, antimotion sickness drugs.

With regard to adaptation schedules, three attempts to prevent motion sickness by step increases to a terminal velocity of 10 rpm at the Pensacola SRR [8] were unsuccessful; two involved three incremental steps during approximately 3 days, and the third a series of 40 incremental steps during 40 hours. In the next attempt [43], overt symptoms (with the probable exception of drowsiness) of motion sickness on exposure to otherwise intolerable stressful accelerations were prevented solely by means of

nine stepwise increases in rotational speeds during 25 days to a terminal velocity of 10 rpm. This experiment demonstrated the possibility of achieving (virtually) symptom-free adaptation to a rotation velocity of 10 rpm, but the time required was too "costly" for operational use, even for a terminal velocity of 4 rpm.

An attempt was then made to effect asymptomatic incremental adaptation in an experiment with three subjects required to execute experimenter-paced head-body movements [41]. The actual time spent making 1000 head movements was slightly more than half an hour. In Figure 34 [41] is shown the stress profile, the number of head movements made at each step (each up-down counting as one movement), and the level of symptoms experienced by the subjects. One subject, TA, was quite susceptible, becoming very drowsy at 2 rpm, experiencing epigastric discomfort at 5 rpm, and minimizing or refraining from making head motions at the higher rpm. The two remaining subjects experienced mild symptoms at terminal velocity, which became more severe on cessation of rotation. TA resorted to the use of an antimotion sickness drug. Noteworthy features were: (1) inability of TA to keep up with the schedule, (2) appearance of symptoms resulting from inadequate adaptation in the remaining two subjects, and (3) increase in symptoms experienced by all subjects on cessation of rotation.

The findings shown in Figure 35 [41] are from a similar test, except that more head movements were made at the higher angular velocities. Symptoms of motion sickness were trivial except in subject RO who experienced very mild symptoms at 8 and 9 rpm and on cessation of rotation. Except for ataxia, which was aggravated by head movements, complaints were minimal on cessation of rotation.

These findings confirmed the inferences drawn from the earlier studies and demonstrated that the time required to effect adaptation can be greatly shortened through control over head movements as well as over angular velocity and by setting up an adaptation schedule. The prob-

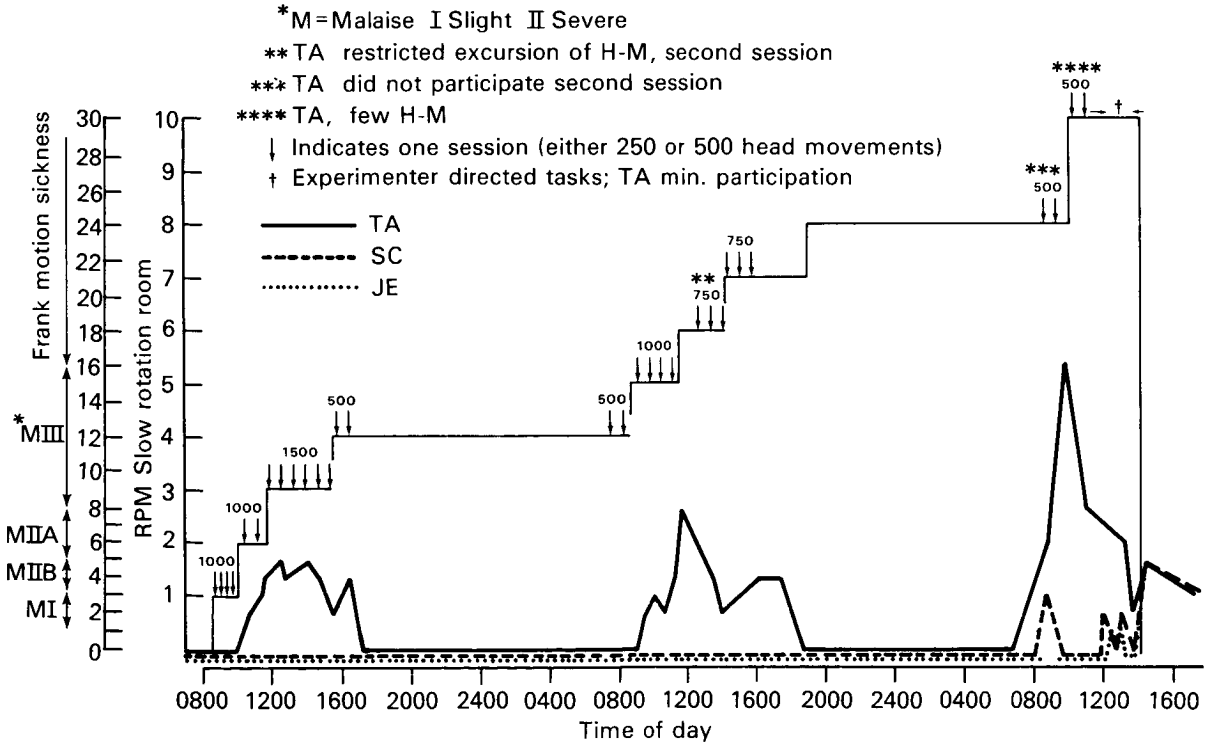


FIGURE 34.—Stress profile in the slow rotation room and manifestations of motion sickness in three healthy subjects exposed to rotation for more than 2 days. (From Ref. [41])

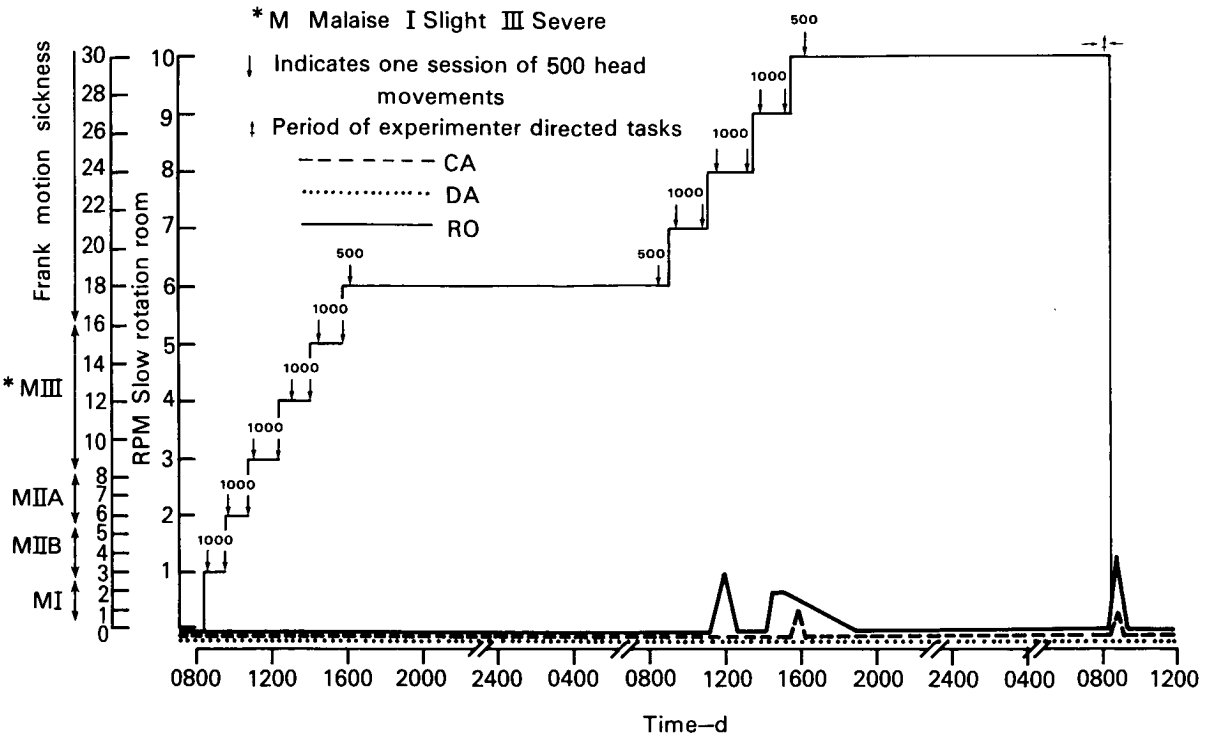


FIGURE 35.—Stress profile in the SRR and manifestations of motion sickness in three healthy subjects exposed to rotation for about 2 days. The large number of head motions accounts for the rapid adaptation. (From Ref. [41])

lems encountered were greater at relatively high compared with relatively low velocities, and that, except in one instance, problems were not experienced if the unit increase was 1 rpm.

A series of experiments was carried out in the SRR to determine if there were differences in susceptibility to vestibular side effects dependent upon man's orientation to the axis of rotation and if the acquisition of adaptation effects acquired in one orientation mode transferred to the other. A unique feature of this experiment was the provision for subjects to walk on the "wall" of the circular SRR and carry out their tasks while horizontal with respect to the Earth-vertical [47]. This was made possible by the use of air-bearing supports and custom-fitted articulated fiber glass molds. Four subjects participated in two different experiments involving adaptation to the stimulus conditions with the room rotating at 4 rpm for a period of either 4 or 5 days. One pair of subjects, initially in the horizontal mode, was changed to the vertical mode near the middle of the perrotation period when symptoms of motion sickness had disappeared; in the second experiment they began in the vertical mode. The order was reversed for the second pair. When in the horizontal mode, the subjects spent approximately 6 h/d in the airbearing device, 6 to 10 min upright, and the remainder of the time recumbent on a bunk. The findings, summarized in Figure 36, indicate no significant difference in susceptibility in the two modes and that transfer of adaptation is excellent. On cessation of rotation only mild symptoms of motion sickness were manifested. A byproduct of the experiment was the demonstration of important differences between motion sickness and postural disequilibrium during adaptation to the rotating environment and subsequent return to the stationary one. In the start-horizontal mode, adaptation ensuring freedom from symptoms of motion sickness on change to the vertical mode did not prevent ataxia. In the start-vertical mode, the adaptation resulted in greatly decreased ataxia; this adaptation perseverated throughout the finish-horizontal mode and as long as 36 h

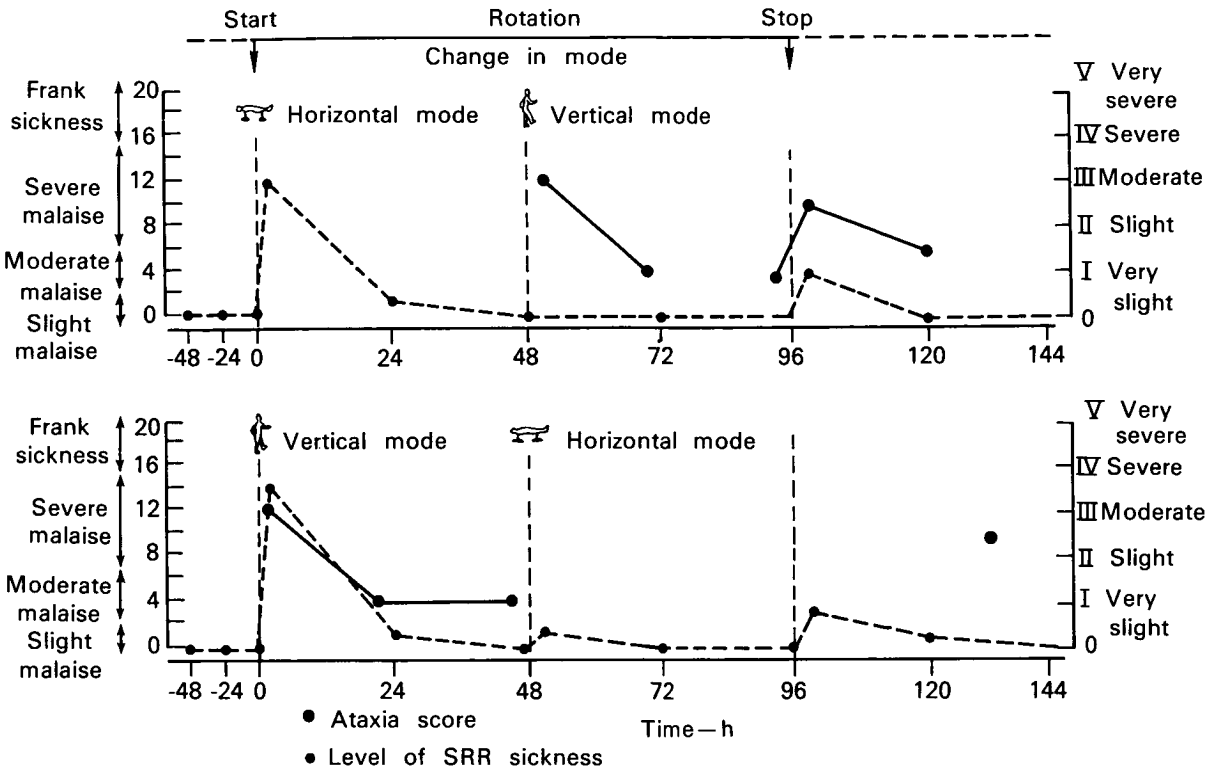


FIGURE 36.—Approximate mean changes in level of symptoms of motion sickness and in postural disequilibrium in four young healthy subjects exposed to continual rotation at 4 rpm.

after. This implied that the dynamic processes underlying postural homeostasis involved muscular activities largely rendered static when subjects were in the horizontal mode.

In the light of the experiment just described, earlier studies involving prolonged exposure in the SRR were reviewed, particularly from the standpoint of manifestations of motion sickness on cessation of rotation. An experiment in which four subjects were exposed at 10 rpm over a period of 12 d was notable in this regard [50]. Despite the severe symptoms that were experienced, especially in the first half of the perrotation period, manifestations of motion sickness on cessation of rotation were trivial or absent.

Rapid transitions between a rotating and a nonrotating environment. It has long been observed that normal persons with mild symptoms resulting from exposure to stressful accelerations in an SRR might experience an aggravation of motion sickness on cessation of rotation. In consequence, it appeared that sudden transitions between the weightless (nonrotating) and rotating parts of a space station posed the most serious aspect of generating artificial gravity. A series of studies demonstrated that: (1) persons remaining symptom-free during exposure to an incremental adaptation schedule (counterclockwise rotation) experienced motion sickness when the direction of rotation was reversed [37]; (2) head movements executed on return to zero velocity, after achieving symptom-free adaptation in an incremental fashion, would elicit symptoms of motion sickness [119]; and (3) adaptation to rotation in one direction transferred to rotation in the other direction [120].

The findings in an experiment to be reported [120] can be briefly summarized with the aid of Figure 37. Three subjects participated, and the adaptation schedule was the same for all subjects; the procedure was essentially the same as that described above in connection with Figure 30. On Day 1, while rotating counterclockwise, subjects executed 40 head movement sequences at 2 rpm, 50 at 3 rpm, 70 at 4 rpm, 90 at 5 rpm, and 110 at 6 rpm. The subjects, while rotating, were

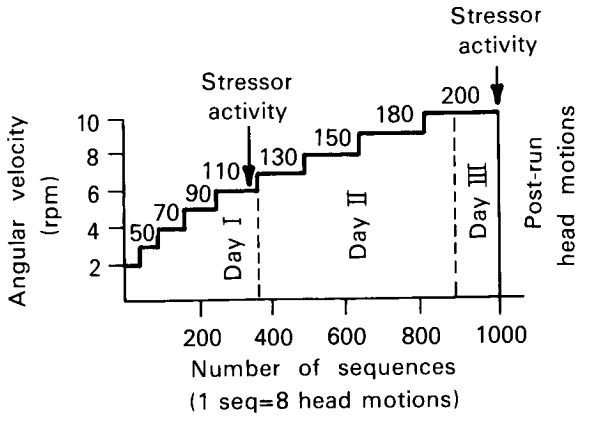


FIGURE 37.—Stimulus profile for a 3-day adaptaion schedule on the slow rotation room.

then transferred to carrying out highly stressful generalized activities in an attempt to evoke motion sickness, and their performance indicated that the head motions had produced a substantial degree of protection with respect to both reflex vestibular disturbances and motion sickness. On Day 2 the subjects executed 130 head movement sequences at 7 rpm, 150 at 8 rpm, 180 at 9 rpm, and 80 at 10 rpm. The subjects were again transferred to generalized activities, and their performance was similar to that on Day 1. On the morning of Day 3 after 120 head movement sequences at 10 rpm, the room was brought to a stop, and the subjects executed the same head motions as during rotation. There were no symptoms of motion sickness, and all reflex effects quickly disappeared.

The findings shown in Figure 38 were obtained on the same three subjects when they executed an incremental adaptation test before and after

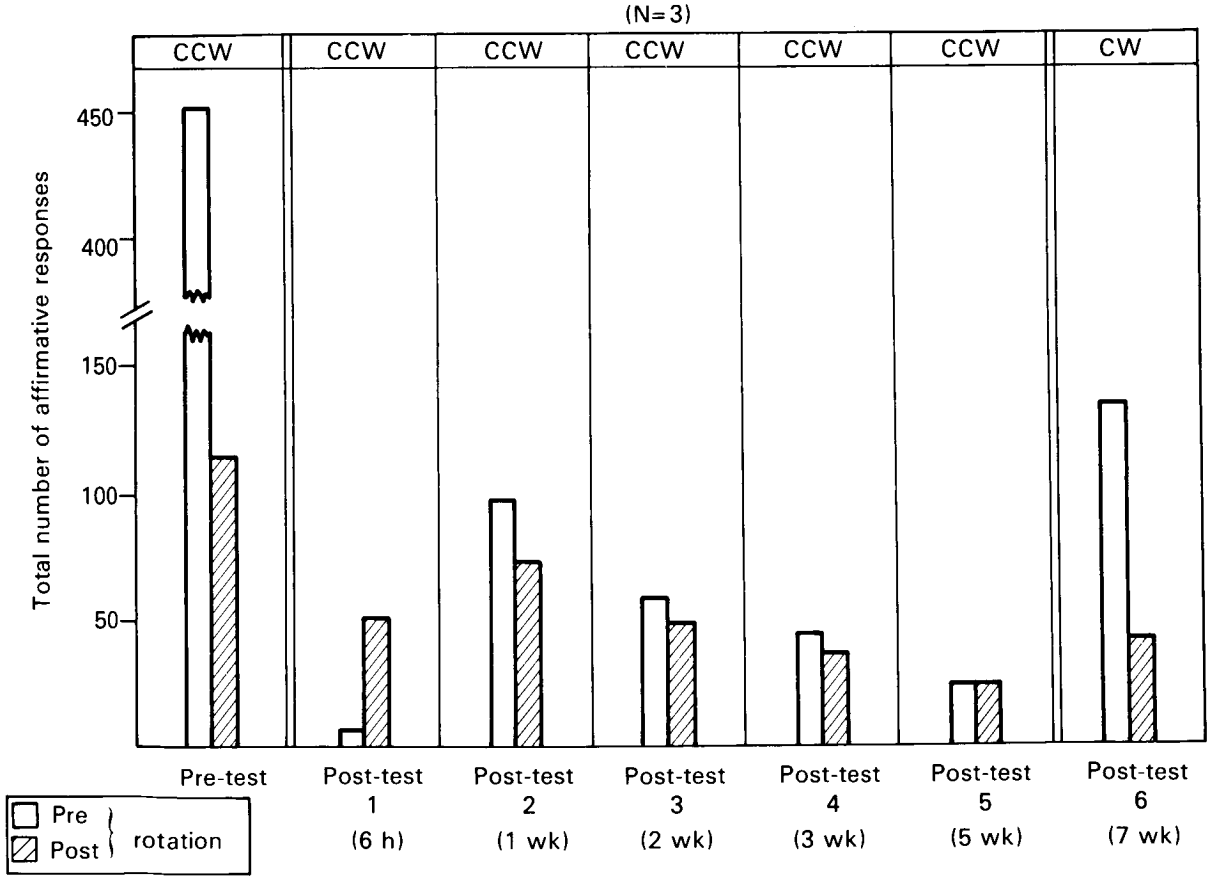


FIGURE 38.—Pre- and post-tests associated with a 3-day adaptation schedule for three subjects in the slow rotation room.

participating in the 3-day experiment just described. This test is also identical with the incremental adaptation test described in connection with Figure 30. The noteworthy findings are: (1) the small number of affirmative responses 6 hours after the 3-day experiment ended, (2) weekly exposures led to increasingly better performance, and (3) when the subjects were rotated in the opposite direction (clockwise), their performance was far better than on the first preexperimental test, indicating transfer of adaptation effects acquired during counterclockwise rotation. The findings support the conclusion that sudden transfers between the rotating and nonrotating environments are not only feasible in the SRR, but also the adaptation effects may not decay rapidly and with weekly practice may not only be retained but improved.

In a recent series of experiments [39], it was demonstrated that during exposure to an incremental adaptation schedule, normal persons simultaneously acquired both short-term (direction-specific) adaptation effects and long-term nondirection specific effects. The short-term effects disappeared spontaneously. This was demonstrated by requiring the subjects to remain seated or recumbent with head fixed for delay periods (measured in hours) after exposure to standardized incremental adaptation schedules. Figure 39 shows that the rate of decay (22 subjects) is exponential, revealed by the decline in susceptibility to motion sickness when head movements were executed at zero velocity.

With the spontaneous disappearance of direction-specific (short-term) adaptation effects, long-term adaptation effects are revealed that are nondirection-specific or nearly so. This important aspect was not investigated systematically but is illustrated by the findings in four subjects (Fig. 40). Measurements on subject 11 during his first four tests are shown in Figure 40, Part a. Prior to the one-step reversal in Test 4, the only other exposure in a reverse direction had been 20 days earlier in Test 2. The absence of symptoms during the execution of head movements at 6 rpm (CW) and especially after return to zero velocity suggests that subject 11 was completely insusceptible, with small likelihood that this insusceptibility was due solely to adaptation acquired during the reverse incremental adaptation schedule (IAS) in Test 2.

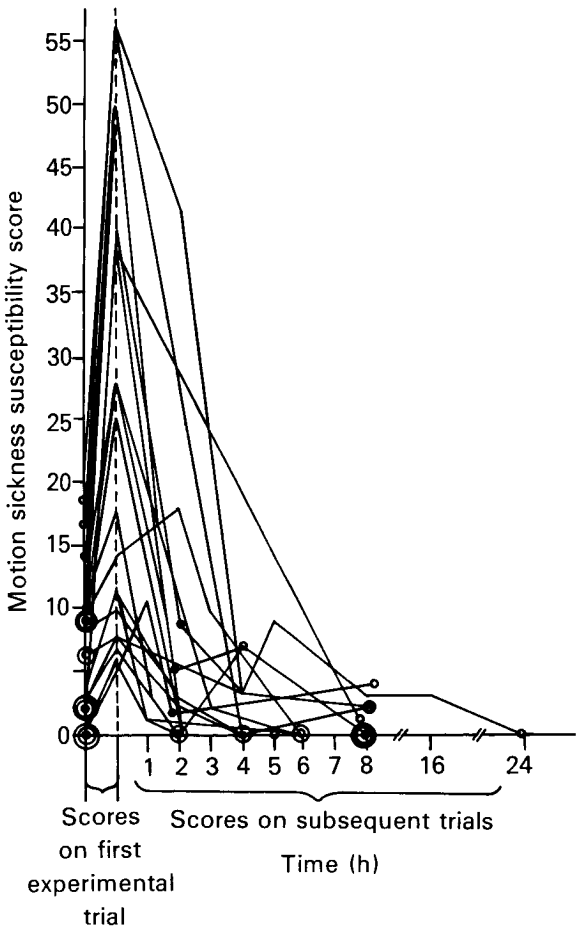


FIGURE 39.—Decay in direction-specific adaptation effects as a function of the time elapsed between completion of a standard incremental adaptation schedule (and return to zero velocity) and execution of head movements at zero velocity. The first two points on the graph represent susceptibility scores obtained in Test 1 of the series, at 6 rpm and after executing head movements at zero velocity, respectively. Thereafter, each point on the graph (or circles in lieu of points) represents susceptibility scores obtained in subsequent tests. An exponential curve characterizes the decay trend. (From Ref. [39])

Figure 40, Part b, shows the measurements obtained on subject 25 during his first four tests. In the second test he was completely symptom-free except for a score of 1 point during the reverse IAS after a 2-hour delay. In Test 1 the score of 6 points on return to zero velocity (a relatively weak challenge) suggests that testing would have been aborted during exposure to a

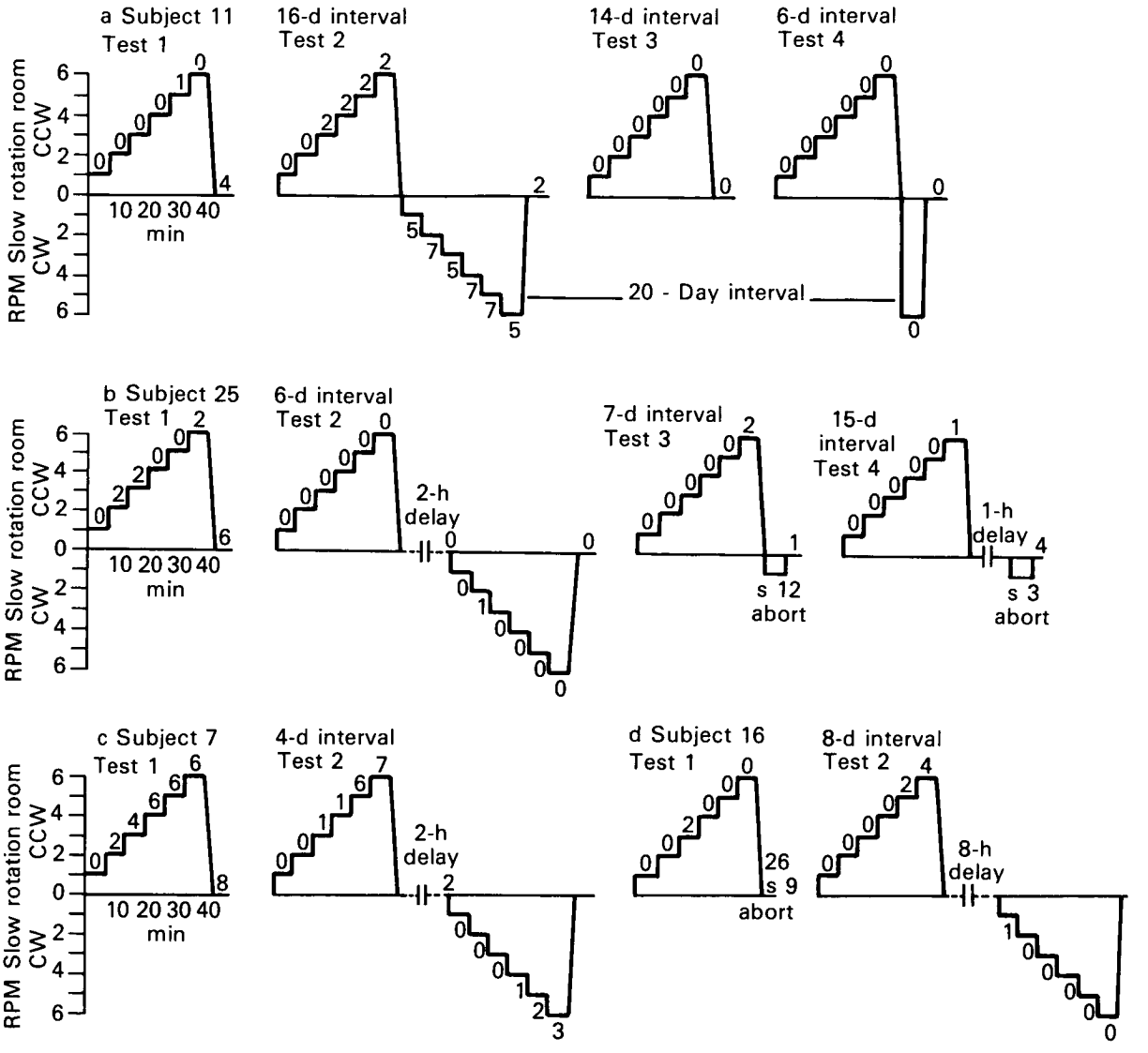


FIGURE 40.—Stress profiles and motion-sickness scores in four subjects, suggesting simultaneous acquisition of direction-specific and nondirection-specific effects. (a) Freedom from symptoms during the execution of 120 head movements after a one-step change from 6 rpm CCW to 6 rpm CW rotation, more likely to be the result of adaptation to CCW rotation (4 exposures) than one exposure to CW rotation, Test 2. (b) Freedom from symptoms during CW rotation and return to zero velocity (Test 2) only explicable by the 2-h delay (see Tests 3 and 4) and the previous adaptation to CCW rotation. (c) The mild symptoms during the reverse IAS and especially the score of 1 point on return to zero velocity, likely explained by adaptation to CCW rotation in Tests 1 and 2. (d) Explanation similar to that in (c). (From Ref. [39])

reverse IAS if it had been done at that time, which was definitely confirmed in Tests 3 and 4. The only reasonable explanation for the virtual absence of symptoms during the reverse IAS in Test 2 and during the challenge after return to zero velocity is that the 2-hour delay was sufficient for the direction-specific effects acquired during the initial IAS to disappear, revealing the non-direction-specific adaptation acquired during that initial IAS and, probably, during the IAS in Test 1.

Subject 7 (Fig. 40, Part c) demonstrated sus-

ceptibility to motion sickness during the initial IAS in Tests 1 and 2 but demonstrated only very mild symptoms during his first exposure, after a delay of 2 hours, to a reverse IAS (Test 2). The score of 1 point on final return to zero velocity suggests that less central vestibular repatterning occurred than in Test 1 (8 points). Only the delay of 2 hours prevented an abort in subject 7, and only prior acquisition of nondirection-specific adaptation could account for the less severe symptoms during the first reverse IAS (and return to zero of Test 2) compared with the initial IAS of Tests 1 and 2.

Figure 40, Part d, shows that for subject 16 in Test 1, testing was aborted during the challenge after return to zero velocity, implying that testing would have been aborted during a reverse IAS if this had been measured at that time. Symptoms during the initial IAS in Test 2 were more prominent than in Test 1, implying that central vestibular repatterning was taking place and that, in the light of Test 1 results, testing would have been aborted during a no-delay reverse IAS had this been done. The 8-hour delay allowed nearly all of the direction-specific effects to disappear, thereby revealing prior acquisition of nondirection-specific adaptation that accounted for the virtual absence of symptoms during the reverse IAS and, more importantly, for the 1-point score on final return to zero velocity.

The findings just described imply that with the disappearance of direction-specific adaptation, with a short time constant, nondirection-specific adaptation with a long time constant is revealed. The practical significance of these findings is twofold. On making transitions from a rotating to a nonrotating portion of a space station, it is necessary to ensure that short-term direction-specific adaptation effects are not present and that long-term adaptation to weightlessness has not been lost. On the transition from the weightlessness to the rotating part, it is only necessary to ensure that adaptation to rotation has not been lost.

It is interesting to speculate on the problem of ataxia and past pointing in making transitions between rotating and nonrotating parts of a space station. Based on the incidental findings [47] that adaptation to rotation with respect to walking in the SRR was preserved during exposure to walking under simulated fractional G-loads and during a subsequent period upwards of 24 hours, it would seem that exposure to weightlessness would not result in loss of adaptation to walking in the rotating environment. With respect to past pointing, visual cues would serve to minimize any tendency to past point in making transitions between the weightless and rotating environments.

Antimotion Sickness Drugs

Numerous reports have been published recommending many drugs, chemicals, and other agents in the prevention of motion sickness, but competent reviewers, pointing to faulty experimental design, have made sweeping criticisms of the validity of many findings. The major criticisms center around: (1) lack of understanding of the complex etiological factors; (2) lack of control over stimulus conditions in the field; and (3) inadequate design, making statistical treatment of the findings of doubtful value. Inasmuch as antimotion sickness drugs are effective in any "motion environment," bioassay under laboratory conditions is recommended. Important aspects in experimental design involve: (1) selection of typically normal subjects; (2) control and measurement of the stressful accelerations; (3) standardization of the laboratory environment; (4) measurement of responses elicited; (5) use of an end point short of vomiting; and (6) use of a double-blind technique in the administration of the pharmacologic agents.

Prior to the introduction of the antihistamines, hyoscine (scopolamine) was generally regarded as the most effective antimotion sickness remedy, although the side effects from moderate doses were annoying and from large doses, unacceptable. The antihistamines ushered in a new and better era in the use of antimotion sickness drugs, although most of the preparations reaching the public have not been thoroughly evaluated for effectiveness.

Recent studies have confirmed the effectiveness of hyoscine [11] and the effectiveness of some drug combinations [4, 15, 81, 135, 136]. Figure 41 summarizes bioassays conducted in a

slow rotation room using mild motion sickness (malaise III) as an end point [136]. A constant (predetermined) level of stress was used, and differences in susceptibility were measured in terms of the number of head movements required to reach the end point. A 10-unit Latin-square design was used (seven drugs and three placebos regarded as drugs). A "placebo" baseline was drawn and findings on the 10 subjects were treated as a group. When these drugs were ranked in order of their effectiveness in reducing susceptibility to acute motion sickness, it was found that they also were arranged in terms of their pharmacologic actions. Drugs with central sympathomimetic or parasympatholytic action were effective not only individually, but also their effects tended to sum. It is not shown in Figure 41 that the relatively high effectiveness of ephedrine 50 mg in combination with promethazine 25 mg have minimal side effects [135].

The procedure just described does not permit valid analysis of the bioassay findings in terms of the individual and has two other undesirable features. The velocity (rpm) of the SRR at which a subject experienced the motion sickness end point after executing about 50 head movements was used as his "baseline." When some subjects were tested after administration of an effective drug, it was impossible to achieve the end point even after 300 head movements. Another handicap was the difficulty in ranking subjects with regard to susceptibility, using both rpm and the number of head movements as a combined score. An experiment just completed on another project (comparing susceptibility with eyes open and eyes closed) used an incremental provocative test schedule (Fig. 25) that yielded a single score (rpm). This permitted measuring and ranking all intraindividual and interindividual differences in susceptibility. An effort is being made at present to reevaluate all drugs and drug combinations that will yield reliable information on individuals as well as groups.

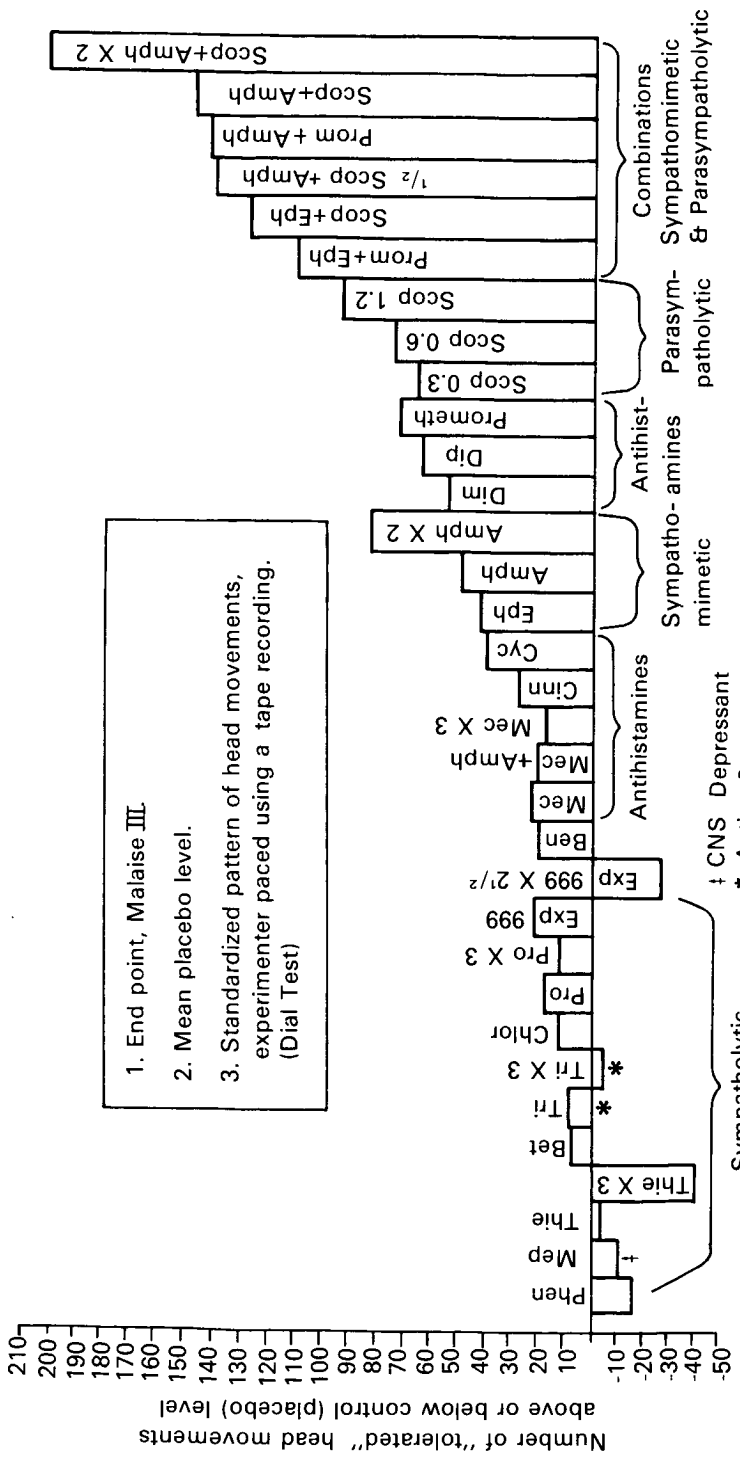
SPACE MISSIONS

The basic difficulty in coping with vestibular problems in space exploration is that our knowledge of vestibular side effects, especially motion sickness, is mainly empirical. Consequently, it is not possible to predict accurately susceptibility to motion under the novel conditions that may be encountered in space. Aside from the use of drugs, we must rely on such countermeasures as the selection process and preflight adaptation in preventing vestibular disturbances.

There are some encouraging aspects. First, the motion environments encountered under nominal conditions are not highly stressful, and vestibular side effects, if experienced, are limited through the acquisition of adaptation. The exception to this generalization regarding adaptation to weightlessness or to a rotating environment arises if the crewman makes rapid transitions between rotating and nonrotating parts of a space station. A second favorable aspect is that the symptomatology of motion sickness is similar even when the eliciting causes are different. In other words, ground-based studies dealing with symptomatology per se have validity in space, which, it appears, also applies to drug therapy. A third favorable aspect is the feasibility (small number involved) to evaluate and test each crewman on an individual basis.

An extensive testing program is needed in view of great individual differences that pervade nearly every mechanism underlying vestibular side effects. Thus, there are differences between susceptibility to reflex phenomena and motion sickness, differences in the rate of acquisition and decay of side effects in different motion environments, and differences in the effectiveness of antimotion-sickness drugs.

A full understanding of the relation between reflex vestibular phenomena and delayed epiphenomena (motion sickness) is needed. Although susceptibility to reflex vestibular disturbances (loss of stability) has some value in predicting susceptibility to motion sickness, there are many exceptions to this generality. Thus, improving the stability of the reflex vestibular system (through training and conditioning) [37, 39, 66, 116] may be quite independent of the ease with which vestibular influences, as soon as they have escaped from their normal confines, may travel along preferential (though common) pathways to sites where first-order symptoms originate. Indeed, it is likely that some nonvestibular etiological factors also exert their influence in this way.



Phenoxybenzamine 20 mg	Benactyzine 3 mg	Dimenhydrinate 50 mg	Scopolamine 0.3 mg +
Meprobamate 400 mg	Meclizine 50 mg	Diphenidol 50 mg	Amphetamine 5 mg
Thiethylperazine 10 mg	Meclizine 50 mg +	Promethazine 25 mg	Promethazine 25 mg +
Thiethylperazine 30 mg	Amphetamine 10 mg	Scopolamine 0.3 mg	Amphetamine 10 mg
Betahistidine 4 mg		Scopolamine 0.6 mg	Scopolamine 0.6 mg +
Trimethobenzamide 250 mg	Meclizine 150 mg	Scopolamine 1.2 mg	Amphetamine 10 mg
Trimethobenzamide 750 mg	Cinnarazine 50 mg	Promethazine 25 mg +	Scopolomine 1.2 mg +
Chlorpromazine 25 mg	Cyclizine 50 mg	Ephedrine 50 mg	Amphetamine 20 mg
Prochlorperizine 5 mg	Ephedrine 50 mg	Scopolamine 0.6 mg +	
Prochlorperizine 15 mg	Amphetamine 10 mg	Ephedrine 50 mg	
EXP 999 10 mg	Amphetamine 20 mg		
EXP 999 25 mg			

FIGURE 41.—Effectiveness of antimotion-sickness drugs in preventing SRR sickness in 70 subjects exposed on 500 occasions in a rotating environment, using the Dial Test. See item 3 (box) in the chart for explanation of Dial Test. (From Ref. [136])

Although the immediate concern at present is the prevention of, or coping with, vestibular side effects in weightlessness, attention is being given to validating aloft the ground-based measurements made in the laboratory and in parabolic flight. Attention is also being given to experimental studies, looking ahead to the possibility that, tomorrow, artificial gravity will be generated by rotation of part of a space station. Thus, tackling the problems aloft will be carried out on an incremental basis.

The crewman necessarily plays a key role in this integrated effort: as subject, he can serve as his own control in validating studies; as onboard experimenter, he is essential in conducting experiments and making observations aloft; as astronaut or cosmonaut, he has responsibilities in connection with the prevention of vestibular side effects during the mission. Prevention involves taking charge, rather than responding to, events which requires close cooperation between the crew aloft and the biomedical representatives in the ground-based control center. Preflight preparations include such major elements as selection (or secondary selection), instruction, and, if needed, preflight adaptation. The inflight period involves making observations and measurements aloft and ground-based monitoring during the mission. Postflight, the debriefing and initial assessment should be followed by measurements at repeated intervals until stable values are obtained.

Weightlessness

The literature dealing with orbital flights is discussed elsewhere in this volume; only a few comments on prevention of vestibular side effects will be mentioned here.

On transition into weightlessness, the crewman's head movements (rotations) generate normal angular accelerative stimuli, but the resulting sensory input encounters unusual central vestibular patterning due to absence of the constant stimulus of gravity. The susceptible astronaut is immediately confronted with the maximum stressful effect possible; the analogous situation in a rotating environment would be immediate transition from zero velocity to terminal velocity. To achieve adaptation, however, head movements must be made. A program based on present knowledge should be helpful. As soon as symptoms are experienced, especially the nausea syndrome, time must elapse before dynamic changes in the vestibular system disappear and restoration through homeostatic mechanisms has taken place in nonvestibular systems. If feasible, it is highly desirable for the crewman to restrict head movements for a period well beyond the time during which symptoms have disappeared. This will allow time for antimotion-sickness drugs taken by mouth to be absorbed (90 min), after which head movements may be cautiously resumed. If it is not feasible to restrict head movements, drugs may be injected—a collar device fixing the head relative to the thorax is beneficial, providing circumstances permit.

Rotating Environment

Although the rotating environment represents a novel experience, the principal unknown element concerns the effect of the fractional G-load. This information will be available, however, long before rotating space stations are a reality. With rare exceptions, the initial transition will be made from the weightless part to the rotating part, spinning at terminal velocity. Thus, the crew making normal head movements out of the plane of passive rotation would be exposed to maximal accelerative stimuli. In the event that symptoms are elicited, head movements (out of the plane of rotation) should be restricted if possible; otherwise, countermeasures described above should be taken. If there is opportunity to restrict head movements until 1 or 2 h have elapsed after symptoms have disappeared, an incremental adaptation schedule is feasible under antimotion-sickness drug therapy. This would be accomplished in a Bárány-type chair rotating opposite the room's rotation, permitting manipulation of the angular velocity between zero velocity and the terminal velocity of the space station. After a demonstration that symptoms were not elicited at (resultant) zero velocity while executing standardized head movements, a cautious stepwise increase (0.5 rpm) in angular velocity should be scheduled.

Sudden transitions between rotating and nonrotating parts of a space station involve novel stimulus conditions. Experience in the rotating room has demonstrated the need to distinguish between direction-specific and nondirection-specific adaptation effects. If this is kept in mind, the prevention of vestibular side effects on making rapid transitions between rotating and nonrotating portions of a spacecraft should not pose a problem [39, 120].

Postural disequilibrium, on making the transitions, is a separate problem because receptor systems serving touch, pressure, and kinesthesis are involved mainly, and because direction-specific effects, it would seem [47], do not disappear spontaneously but require active whole-body motions.

The suggested preventive measures indicated today will almost surely be different tomorrow. The need for full understanding of vestibular side effects, including self-diagnosis, prevention, and treatment may not change.

VESTIBULAR INVESTIGATIONS IN SPACE MISSIONS

Operational Aspects

The character of prolonged space missions will inevitably change with advances in spacecraft technology, and the emphasis will gradually change from exploration to exploitation of extraterrestrial opportunities. Travelers at present must be able to withstand the severe stresses incidental to launch and reentry which demands a state of fitness that seems to dwarf the subtle effects of weightlessness. Even among travelers in superb health, maintenance of fitness during prolonged exposure in a weightless spacecraft will make great, continuous demands on the spaceman's time; illness aloft, precluding exercise, could pose a hazard. With tomorrow's advent of a space shuttle or its equivalent, stresses incidental to launch and reentry will be greatly reduced; the limiting factor with regard to fitness for travel will be conditions aloft, and the most important of these factors is weightlessness. The generation of artificial gravity by causing the spacecraft to rotate represents a "technological fix," and this alleviates an otherwise potentially continuous hazard, weightlessness.

The major need (it was indicated earlier) is to be able to predict, on the basis of ground-based tests, the responses (mainly or partly of vestibular origin) of space flyers in the novel environments of the weightless space vehicle and the rotating space station. The limitations in simulating such novel stimulus conditions force an extension of ground-based studies to include validating observations and experiments conducted aloft. Identifying motion sickness as the chief vestibular problem still leaves the problem to be solved, and this must be accomplished in ground-based laboratories.

Scientific Aspects

It is doubtful if the precise role of gravity under terrestrial conditions (distinguishing between gravitoinertial forces and agravitoinertial mechanical forces) can be made without the opportunity to conduct studies in space. Transition into weightlessness abolishes the stimulus to the otolith organs due to gravity in an elegant and harmless manner, and also abolishes the stimulus to receptors serving touch, pressure, and kinesthesis due to weight. Psychophysical experiments using mechanical pressure can be conducted in weightlessness that should add to our knowledge of these perceptual systems. For example, experiments conducted in Gemini 5 and 7 [48] dealing with egocentric visual localization suggested that elicitation of the A and E phenomena depends not only on otolithic inputs (already known) but also on nonotolithic mechanoreceptor systems. The vestibular experiments to be conducted in Skylab 2 and 3 flights will not only extend the measurements made in Gemini 5 and 7 but will also include measuring changes in canalicular susceptibility, susceptibility to motion sickness, and two-dimensional perception of nonvisual extrapersonal space [99]. Devices designed for these purposes (see Figs. 21, 26, and 42) have many uses in ground-based laboratories.

It is not an overstatement to say that the opportunities to study the vestibular system aloft constitute a major historical landmark in the advancement of knowledge not only in the vestibular but also in related areas. Resting dis-

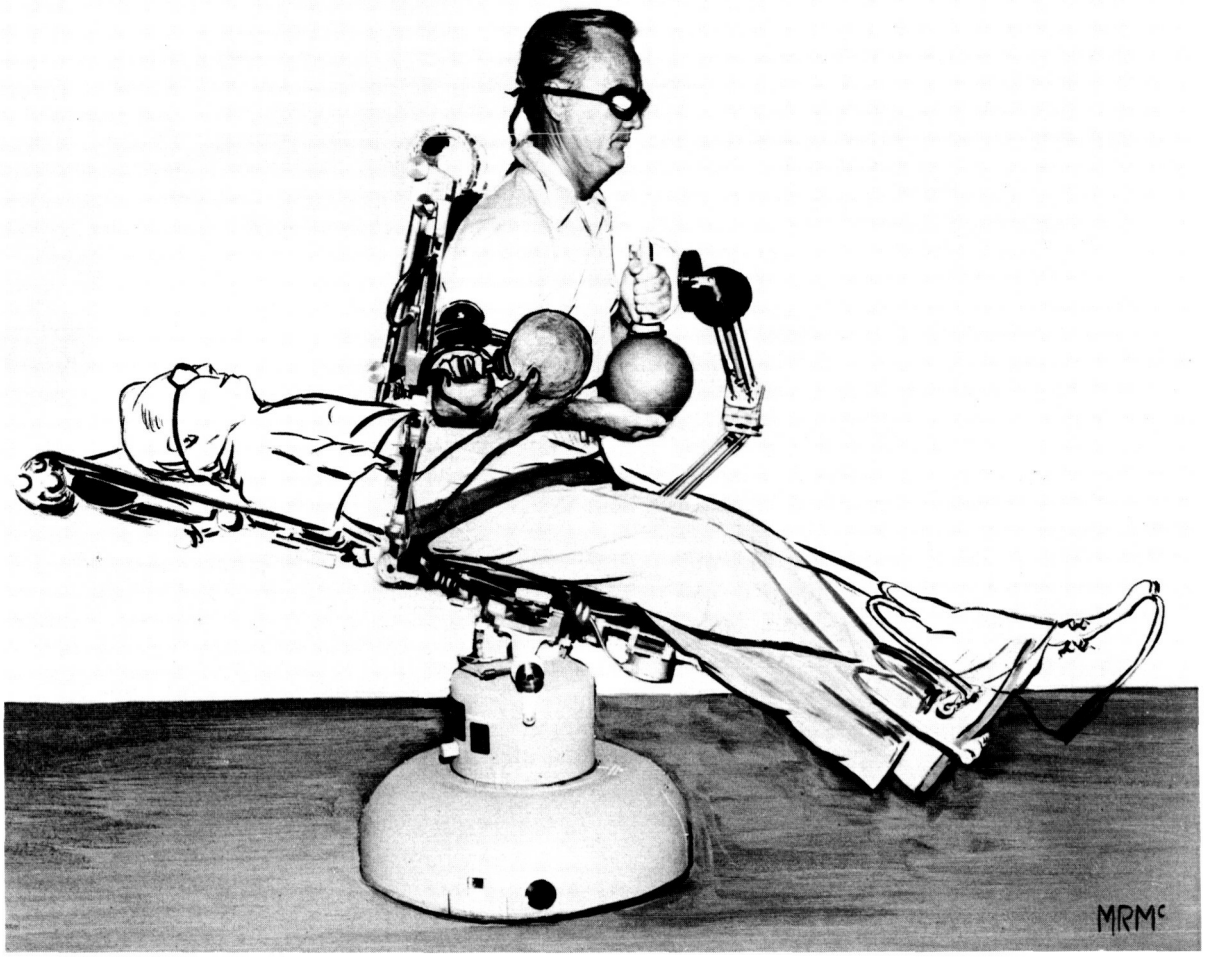


FIGURE 42.—Rod and sphere device for measuring nonvisually perceived personal and extrapersonal space. The device has a pointer held by magnetic attraction to a hollow steel ball. With eyes covered, the subject slides the rod over the ball until spatial localization is achieved; note absence of constraints that are usually provided to maintain the indicator in one plane. The readout is semiautomatic.

charges [54] and the contribution of tonic otolithic sensory inputs modulating stretch reflexes and muscle tone in man [16, 73, 75, 84, 104, 115] can be investigated. Distinctions between otolithic and canalicular influences that are so closely intertwined might be unraveled.

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Chapter 8

WEIGHTLESSNESS[1]

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

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

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

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

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

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

WEIGHTLESSNESS AS A UNIQUE AND EXTREME SPACEFLIGHT FACTOR

Significance of Gravitational Forces in Regulating Homeostasis

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

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

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

Certain basic life processes apparently depend on the presence of gravity; included are growth

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

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

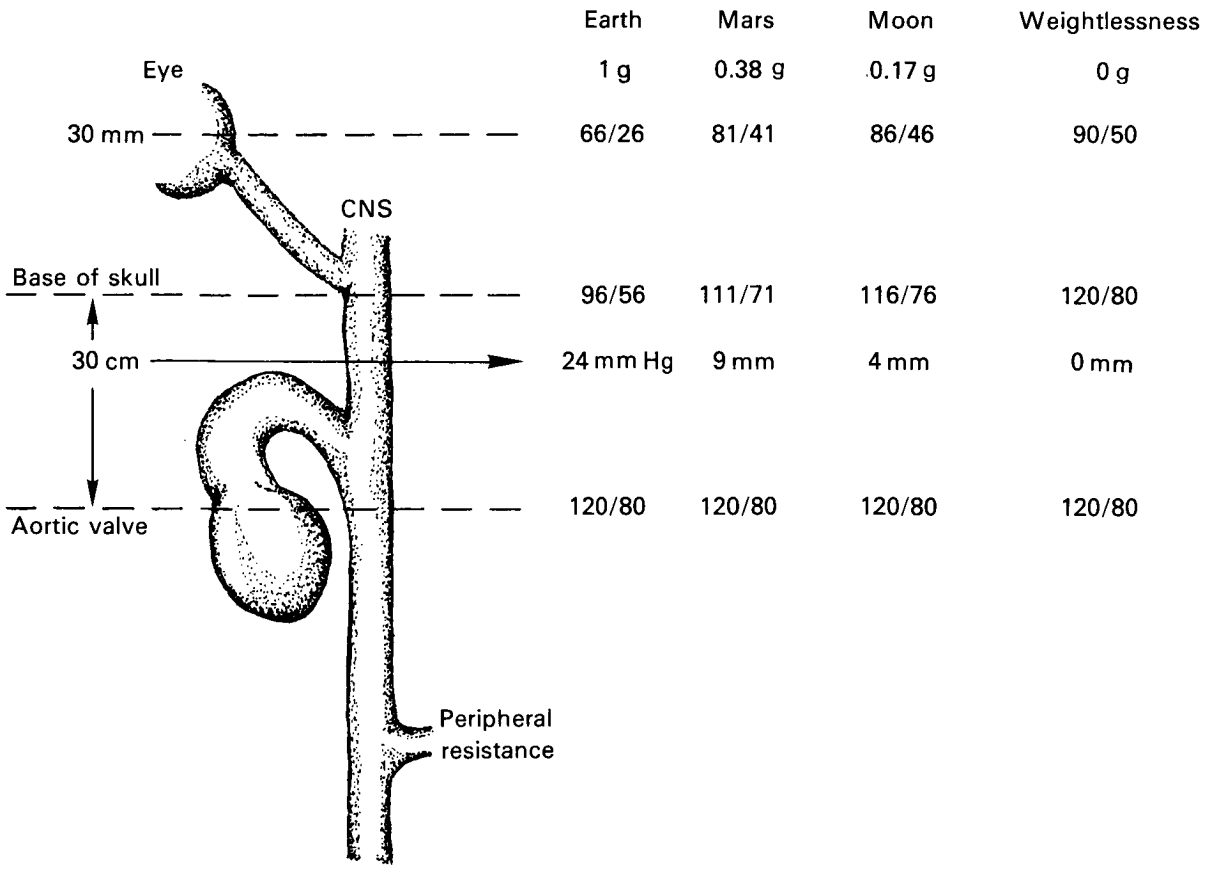


FIGURE 2.—Levels of systolic and diastolic blood pressure in man and their alteration under various subgravity conditions [6].

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

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

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

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

Investigation of Effects of Weightlessness on the Human Organism

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

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

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

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

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

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

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

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

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

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

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

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

Experiments were conducted with complete water immersion up to 7 d, and 120 d bed rest, to determine the effects of simulated weightlessness on the body's weight-bearing structure, internal intravascular hydrostatic pressure, metabolism, fluid and water balance, mineral exchange, cardiovascular and respiratory func-

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

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

Theories on biodynamic and biogravic effects of changing accelerations and systematic treatises of biological problems in space, including comparative and methodologic aspects of space physiology and medicine as related to weightlessness [76, 90, 191, 193, 244];

Processes and mechanisms of deconditioning, adaptation, homeostasis and biological rhythms in zero-G [3, 12, 37, 55, 72, 111];

Specific effects and interaction of various sensory and neural analyzers or systems [22, 140, 143, 257, 278]; and

Hormonal, immunologic, regenerative and hematogenic functions [2, 3, 7, 20, 222];

Mathematical modeling and statistical treatment of medical and human factor problems associated with subgravity and weightlessness [132, 153, 190, 249, 262].

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

State of Reduced Weight (Subgravity)

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

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

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

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

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

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

a.

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

b.

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

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

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

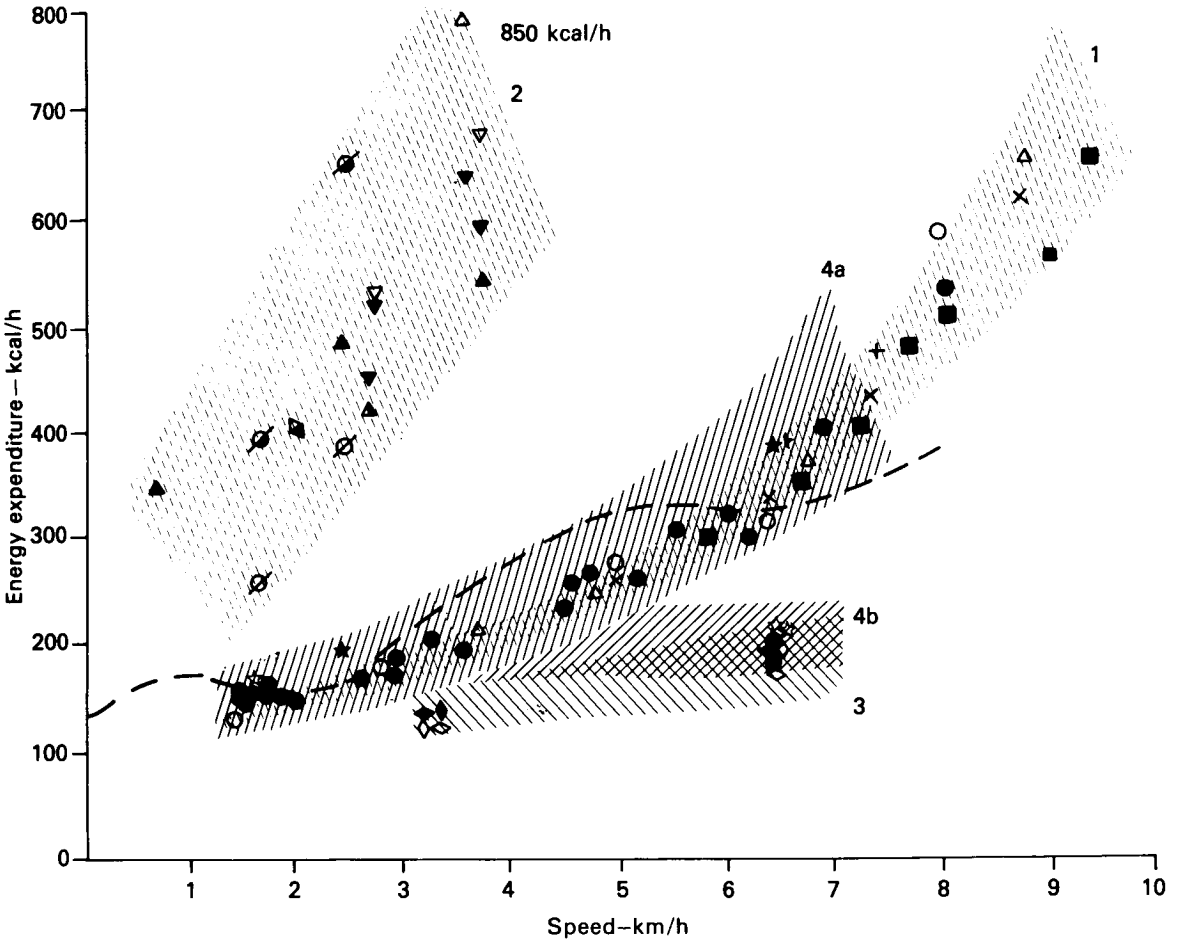
Lunar Surface Activities

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

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

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

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



Terrestrial gravitation

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

Lunar gravitation

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

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

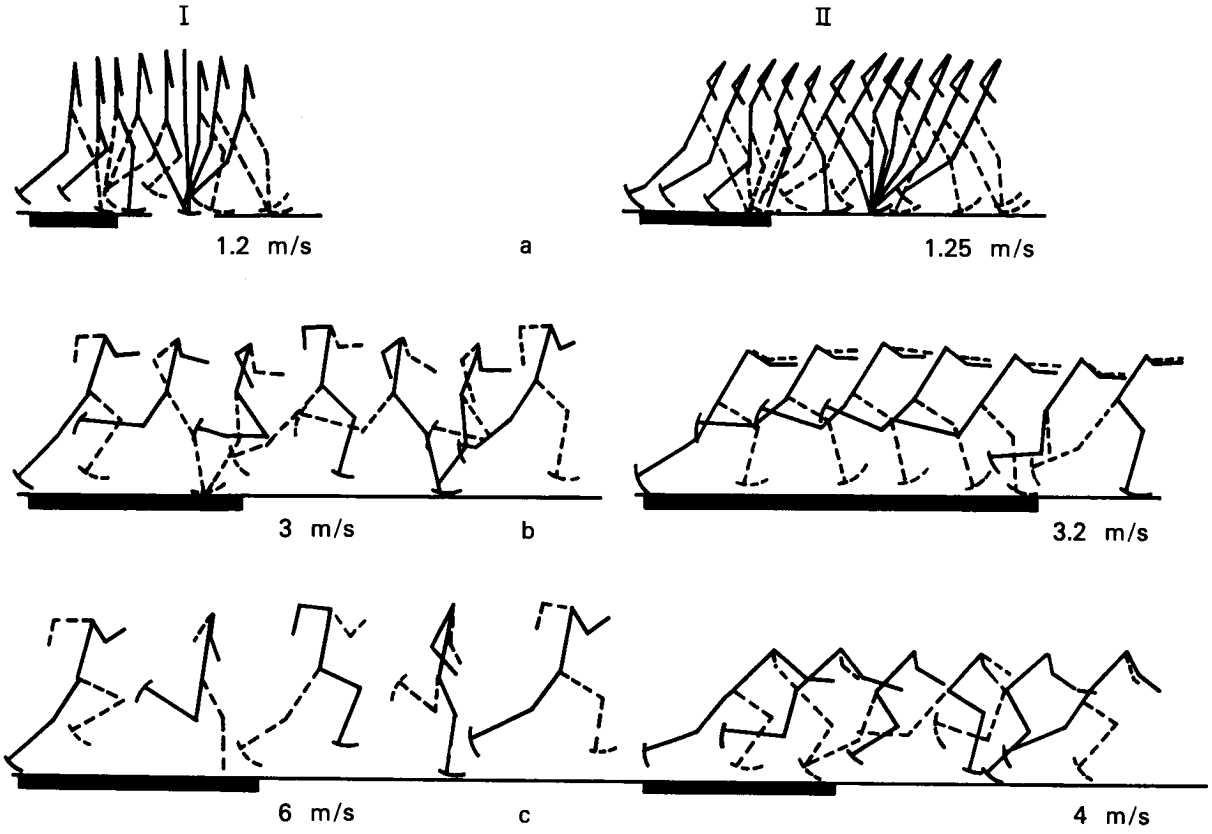


FIGURE 4.—Change in body kinematics during locomotion under lunar and terrestrial gravitation conditions. (After Spady [31]) Heavy line is length of stride; distance between figures 0.16 s. a, walking; b, running and jumping; c, running. I, terrestrial gravitation; II, lunar gravitation.

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

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

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

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

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

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

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

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

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

Nervous System

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

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

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

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

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

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

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

Cardiovascular System

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

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

Metabolism

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

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

Reactions	Conditions and objects of observations [1]	Sources in literature (Ref)	Notes
1	2	3	4
Sensations of an unsupported position, floating, falling, spinning, turning, flow of blood to head, deterioration of orientation in space, predominance of visual information role in evaluating position of body in space	Man (TW, KP, SF)	[14, 15, 92, 93, 94, 140, 180, 211, 217, 244, 259, 260, 273, 275, 281]	Emotional coloring of sensations (fear, joy, etc.) depends on experience and training of subjects; in orbital flight-adaptation
Displacement of successive visual image during G-forces – downward (oculogravic illusion), and upward during weightlessness (oculoagravic illusion): illusions are characteristic of initial periods in weightlessness	Man (KP, SF)	[92, 93, 141, 211, 260]	Actual position of visual targets during G-forces – above the successive image, and below it during weightlessness; with gaze fixed on a target, the successive image coincides with it
Slowing down of speed and accuracy of movements; errors in trying to hit center of a target (deviation of hits upward)	Man (KP, SF)	[92, 94, 184, 211, 217, 244, 259, 260]	Only in initial phase of SF, then adaptation
Deterioration of ability to carry out measured muscular efforts and evaluate differences in mass of objects not fastened down	Man (KP)	[93, 211, 281]	
Pulse frequency: slowing of normalization following action of G-forces; subsequent tendency toward slowing, increase in variability (possible arrhythmias of the bigeminal type); in final stage of long SF, slight increase	Man, animals (SF)	[9, 17, 21, 60, 78, 94, 129, 134, 211, 217, 218, 249, 260]	With PBR following initial decrease in frequency of pulse, increase in frequency (lack of training)
Arterial pressure: moderate decrease, followed by stabilization, tendency toward decrease in pulse pressure	Man (SF)	[7, 17, 76, 133, 134, 136, 211, 256, 258]	In PBR, initial decrease followed by increase (sympathetic effect)
Heart: decrease in size (according to data from x-ray studies); symptoms of decrease in the contractile ability (according to electrocardiographic and seismocardiographic data and results of phase analysis of cardiac cycle)	Man (SF, R)	[21, 125, 190, 217, 258, 266]	Descriptions of cases of increased mechanical activity of heart during flight
Bone tissue: demineralization (according to the data from x-ray photometry) due to loss of Ca^{++}	Man, animals (R)	[14, 17, 18, 21, 26, 114, 196, 211, 260]	No changes observed when using method of photon absorption
Muscles: decrease in volume and strength	Man, animals (SF, R)	[21, 45, 94, 204, 258, 260]	Primarily atrophy of antigravitational musculature
Dehydration (decrease in plasma volume, followed by loss of intracellular fluid)	Man, animals (R)	[14, 15, 16, 18, 125, 196, 260]	Decrease in plasma volume develops on 1st or 2nd (Henry-Gauer reflex); recovery possible later

[1] See footnote at end of table.

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

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

[1] See footnote at end of table.

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

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

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

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

Musculoskeletal System

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

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

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

It is also clear from this discussion that one of

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

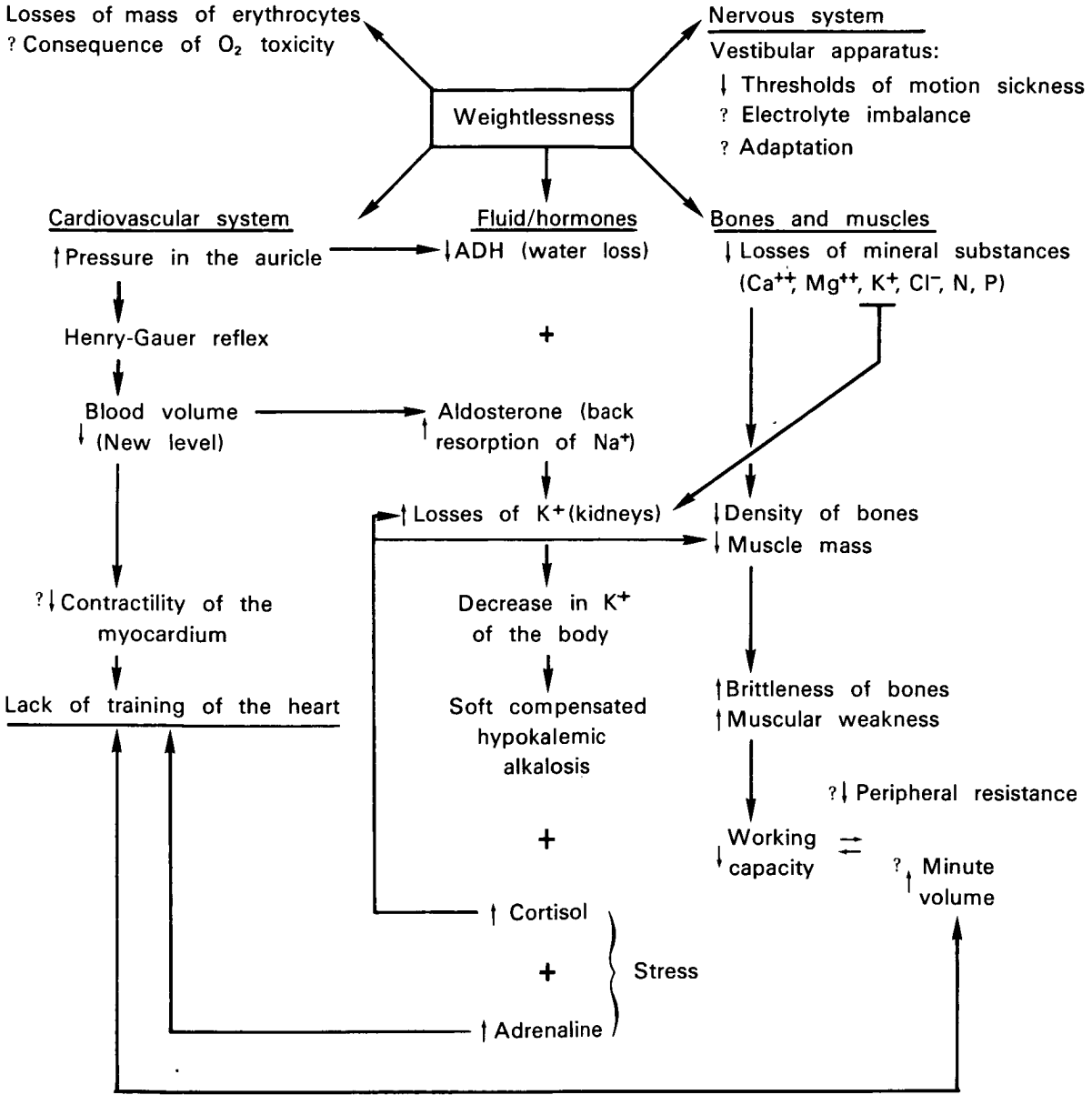


FIGURE 5.—Effects of the influence of weightlessness on man. (Working hypothesis adopted from [266])

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

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

Reactions Caused Primarily by Changes in the Afferent Nervous System

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

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

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

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

Proper vestibular functioning is undoubtedly associated in several ways with proper function-

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

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

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

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

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

Reactions Caused Primarily by Lack of Hydrostatic Blood Pressure

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

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

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

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

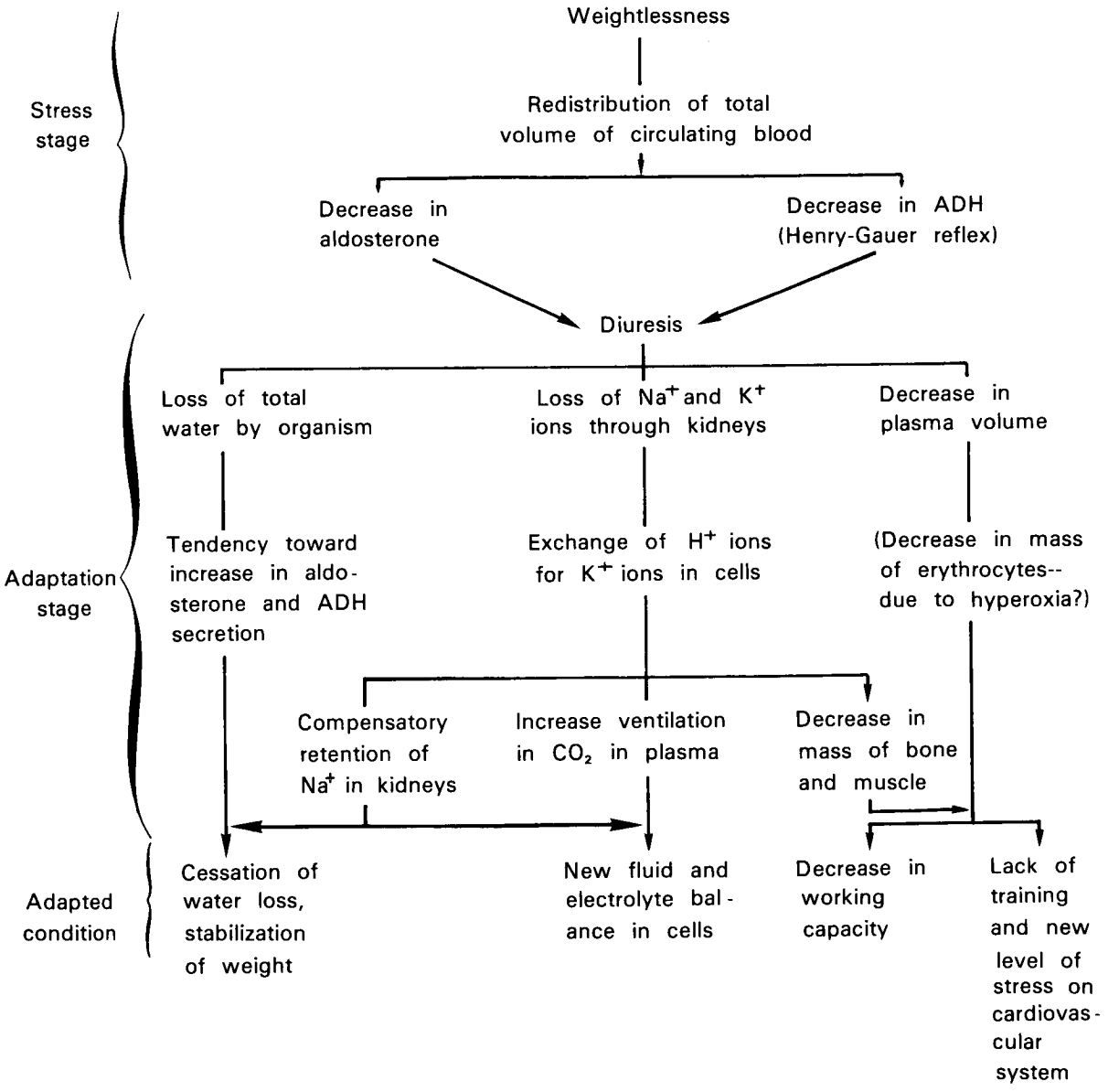


FIGURE 6.—Proposed process of adaptation to weightlessness [159a].

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

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

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

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

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

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

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

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

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

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

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

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

Orthostatic Stability

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

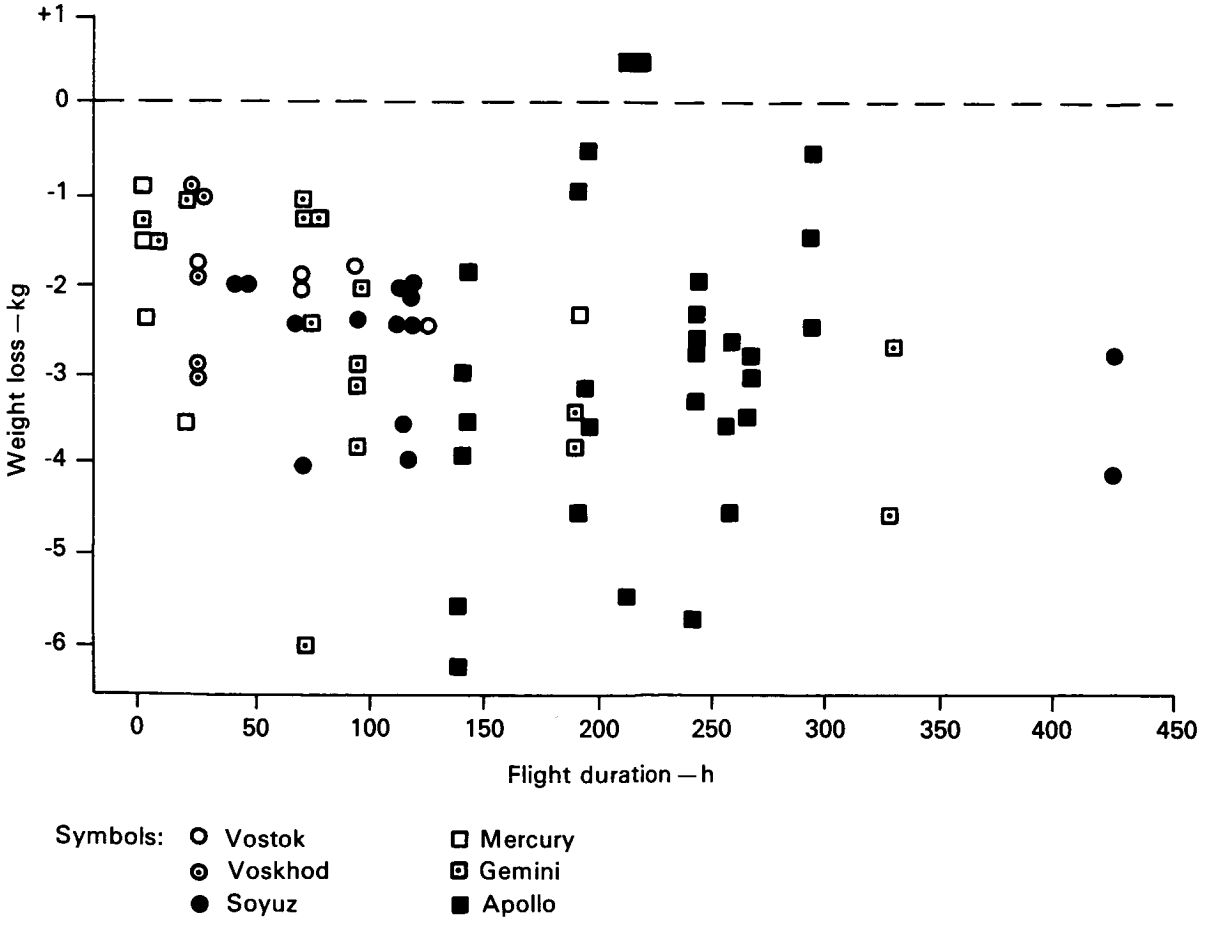


FIGURE 7. — Changes in body weight following space flights of varying duration.

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

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

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

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

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

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

Reactions Caused Primarily by Lack of Weight on the Musculoskeletal System

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

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

Prolonged experiments on the ground with controlled limitation of motor activity, especially its motion (hypokinesia) and force (hypodynamia) components, indicated a systematic decrease in basal metabolism ranging from 3–7% to 20–22% [56, 138, 159, 173]. Indirect determination of the gas exchange level under spaceflight conditions, carried out by Soviet and US investigators on the basis of results of chemical analysis of regeneration material, showed a slight decrease in energy

consumption to 83.5–97.2 kcal/h [23, 261]. Individual direct measurements of the gas exchange level during space flights do not permit final conclusions, since both increases and decreases in oxygen consumption have been found [133, 135].

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

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

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

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

Muscular Effects

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

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

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

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

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

Cardiac Effects

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

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

When a horizontal position is prolonged, the electrocardiogram shows position changes, relative slowing of the intraauricular, atriventricular, and intraventricular conductivity as well as the $T_{r1} > T_{r6}$ syndrome [122, 123, 262]. Changes in phase structure of the cardiac cycle during laboratory simulated weightlessness usually combine in the sympton complex called the *phase syndrome of cardiac hypodynamia* [123, 131, 188]. The symptom complex includes: lengthening of isometric contraction phase, shortening of expulsion period, decrease in rate of intraventricular pressure rise, intrasystolic index, and increase in myocardial stress index. In pathology, this syndrome is encountered in various forms of myocardial ischemia and reflects a disturbance of its contractility. Although several weeks are required for development of these symptoms with deconditioning hypodynamia effect on the cardiovascular system, some have already become evident in varying degrees during periods spent in weightlessness.

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

Hence, elimination of weightload on bone and muscle apparatus is a distinctive and important causative mechanism in the development of various disturbances attributed to weightlessness. It is sometimes given primary responsibility, although this leads to insufficient evaluation of other pathogenetic mechanisms [126, 157]. Hypodynamia is widespread in clinical practice and there is an analogy to this mechanism in daily life. Therefore, problems in investigating the influence of hypodynamia on the organism and com-

bating its consequences are not limited to space medicine, but have general clinical significance.

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

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

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

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

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

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

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

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

Changes in immunological reactions and resistance to infection were noted in simulated weightlessness experiments and after an 18-d space flight [49, 175, 260]. These alterations, linked to general deconditioning and metabolic changes, were accompanied by increased sensitivity to disease, which could be critical during flight [84]. Illness can also be transmitted from one crewmember to another through pathogenic microbes and fungi [18]. Therapy under these

conditions may be limited by change in the organism's reactivity in regard to pharmacologic preparations resulting from the action of weightlessness [243, 246]. On short flights, no significant changes involving immunological reactivity were observed [2].

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

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

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

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

PROTECTION OF THE HUMAN ORGANISM AGAINST ADVERSE EFFECTS OF WEIGHTLESSNESS

Preventive and Therapeutic Measures

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

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

The second concept is more realistic for current needs of astronautics, since it allows partial adaptation of the organism to weightlessness, but also provides for measures that can be taken to prevent or reduce the principal unfavorable consequences of adaptation.

Solution of the problem will be satisfactory if the preventive measures by the crew during

the flight and directly after landing preserve their health and working capacities. The effectiveness of the protective measures will, therefore, be based primarily on maintenance of a sufficient level of physical working capacity, motor coordination, and orthostatic stability, since changes in these functions postflight appear to be the most critical. Such measures may be comparable with flight conditions in terms of technical and operational characteristics and medically, will not produce discomfort or harmful side effects.

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

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

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

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

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

Preventing Primary Effects of Lack of Hydrostatic Blood Pressure in Weightlessness

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

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

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

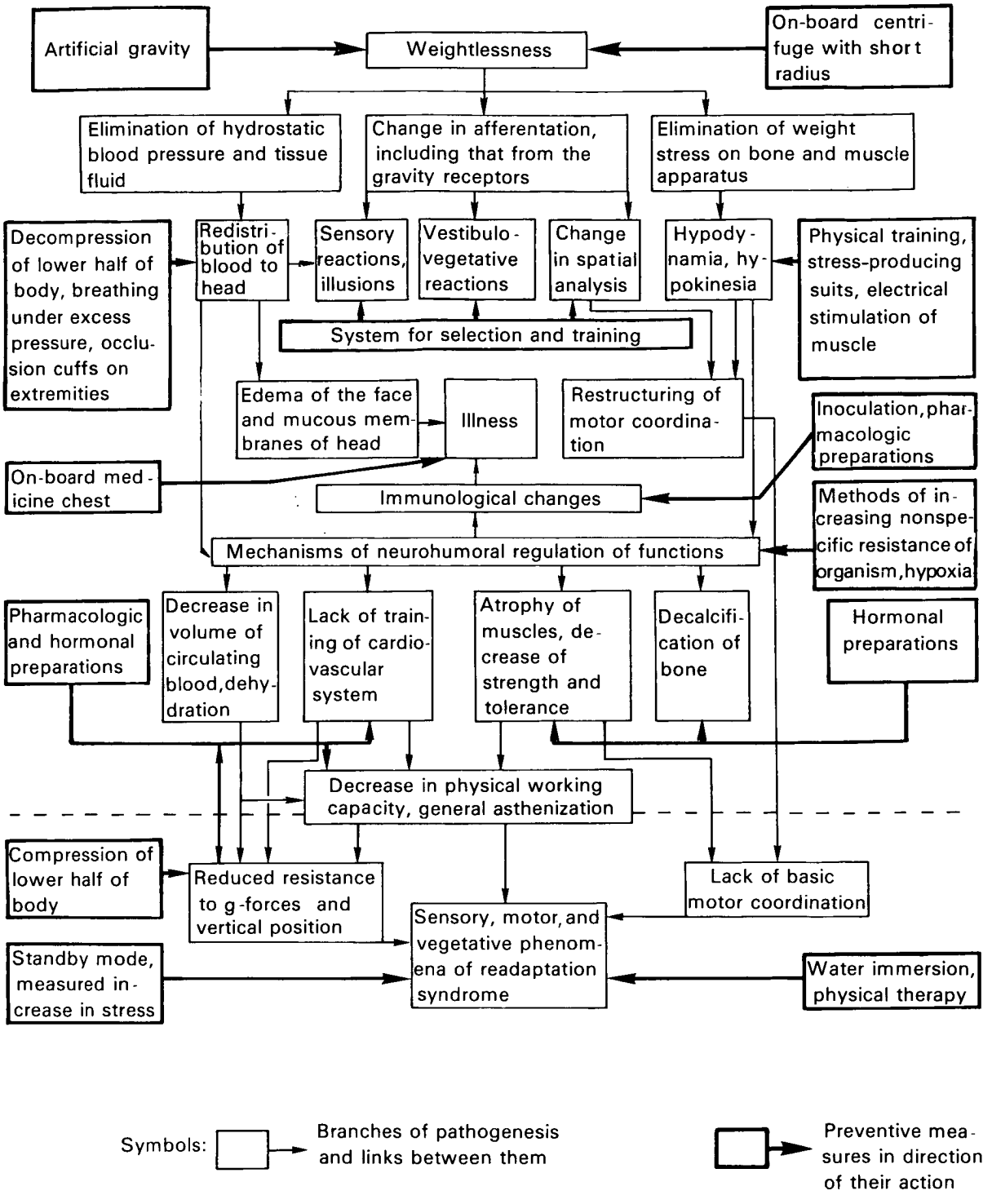

FIGURE 8.—Pathogenesis of problems caused by influence of weightlessness and directions of preventive actions. (Modified version of the system in [81])

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

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

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

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

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

Lower Body Negative Pressure (LBNP)

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

organism, normalization of circulating plasma volume, and orthostatic stability under conditions of simulated weightlessness.

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

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

Simulated Weightlessness Experiments

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

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

Pharmaceuticals

Preventive action aimed at certain intermediate links of the pathogenetic chain can be effected with pharmacologic and hormonal preparations [73, 167, 197, 200, 229, 243, 245, 246]. Such substances proved effective in laboratory experiments and prevented phe-

nomena of deconditioning and orthostatic instability following a certain period in a horizontal position [32, 118].

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

G-Suits

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

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

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

Preventing Adverse Effects of Hypodynamia

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

When insufficiency of muscle stress is caused by unfavorable changes in the condition of the organism, physical training is not only justified, but also necessary. Physical exercise studies with controlled limitation of motor activity, its spatial and force components, has promoted

normalization of phenomena associated with the hypodynamic syndrome. Changes involving gas exchange [138, 173], nitrogen metabolism [234], the cardiovascular system [150, 198, 216], neuropsychic functions [30, 163, 189, 212] and immunobiologic reactivity [49] have been less prominent. The positive action of physical training has also been observed in states of the musculoskeletal system, physical working capacity, motor coordination [44, 100, 126, 137], and stress tolerance [44, 148].

Physical Exercise

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

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

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

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

by singular methods, but must be approached on a complex basis.

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

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

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

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

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

Other Methods

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

The action of most of the preventive measures mentioned is not strictly selective, but frequently extends to combined branches of pathogenesis

and thereby goes beyond the limits of the proposed classification, which emphasizes only primary effects for which a specific measure was designed. For example, the effect of LBNP, in addition to blood redistribution, is likewise accompanied by an axial load on the organism, the magnitude and point of application of which are determined by design of the vacuum device or garment. LBNP can also create sensations that are characteristic of the force of gravity action. A vacuum device used during bed rest creates, in particular, the feeling of being in a vertical position. A broad spectrum of action, which affects all triggering mechanisms associated with weightlessness, is obtained by the use of on-board centrifuges. Desirable preventive effects may be achieved only with a combination of preventive measures aimed at various links of the pathogenetic chain.

Methods of Nonspecific Prevention

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

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

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

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

Another approach to increasing the organism's nonspecific resistance to counteract weightlessness may be the use of conditioning measures used widely under terrestrial conditions—ultraviolet irradiation and acclimatization to high altitude [149, 155, 247, 248]. In simulated weightlessness experiments, hypoxia prevented a decrease in erythrocyte mass but did not prevent plasma loss [231]; there were also decreases in electrolyte excretion, total urinary nitrogen, and bone substance demineralization [163]. Physio-

logic reactions to hypoxia are considered counter-reactions in the hypodynamic syndrome, similar to reactions to physical training [155, 237]. Within the total of preventive measures, periodic changes in spacecraft gas composition and other environmental parameters may find justifiable usage in time [82].

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

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

SUMMARY OF SKYLAB MISSIONS

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

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

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

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

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

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

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

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

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

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

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

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

A retrospective analysis of the state of the art indicates that the level of scientific theoretical thought at all stages in the development of astronautics has been sufficient to satisfy practical requirements in a timely fashion. Long before the practical need for eliminating unfavorable effects of prolonged weightlessness on the human organism, US and USSR laboratories had begun testing effective preventive measures. It was precisely the development of

these measures that made it possible to plan space flights of increasing duration. However, as the length of the flights increase, new problems may arise, making even more important further studies linked to the effects of weightlessness on the human organism [266].

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

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

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

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

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

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

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

control techniques for future manned space missions.

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

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Chapter 9

NOISE AND VIBRATION [1]

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Noise and vibration have been undesirable byproducts of aviation from its beginning. An appreciable percentage of propulsion power has always been radiated as noise potentially disturbing to persons on the ground and transmitted inside vehicles to be received by passengers as airborne noise or structure-borne vibration. The large propulsion units of unprecedented thrust developed for manned space flight obviously raised questions about tolerability of the associated noise and vibration environments for crewmembers aloft as well as on the ground. Added to the noise and vibration impacts introduced by propulsion units, other phases of flight, such as reentry into the Earth's atmosphere, introduced phenomena of potential noise and aerodynamic buffeting, with which there had been little prior experience. Consequently, space efforts during a 15-year period (1958–1973) stimulated new research into human response to noise and vibration, to enable adequate planning and design to guarantee crew safety and performance capability, and avoid annoyance of exposed individuals and communities on the ground.

Airborne acoustic energy at sufficiently intense levels may interfere with routine activities, damage the auditory system, diminish the quality of performance, modify physiologic functions, and induce annoyance in exposed individuals and communities. The acoustic energy fields generated by aerospace systems are of intensity levels adequate to produce some or all of these adverse effects.

Mechanical vibration transmitted to human operators can degrade comfort and human performance. In some circumstances, vibration which is intense, prolonged, or repeatedly applied to man can affect operational safety and occupational health. The adverse effects of vibration may be immediate, developing as soon as the person is exposed to the stress (e.g., mechanical degradation of visual acuity by whole-body vibration); or the effects may be cumulative, being manifested only with passage of time under vibration stress or with repeated vibration exposure (e.g., fatigue effects on performance, vibration disease). The unifying field of bio-

[1] This chapter is based on extensive material compiled by USSR contributors I. Borschevskiy and U. V. Krylov, and US compilation material prepared by E. M. Roth and A. N. Chambers (*Compendium of Human Responses to the Aerospace Environment*. NASA CR-1205 (II), Vol. II, Sections 7–9. Washington, D.C., NASA, 1968). In addition, the vibration portion is based substantially on material published in Reference [50].

dynamics, stimulated largely by the urgent problems of manned space flight, has evolved to deal with the effects of all kinds of mechanical force on biologic systems.

Noise and vibration are two closely related phenomena, not only because of their common origin, but also because of their effects. As soon as airborne noise is transmitted from the air to the human body, it travels through the tissues as vibration, which in principle is not distinguishable from structure-borne vibration transmitted to the body. Vibration transmitted to any part of the body can be propagated through the tissues and received by the ear as sound and airborne noise, and if intense enough, can be felt as vibration by other body systems besides the ear. Thus, the mechanical characteristics of body tissue and the reception, transmission, and attenuation of vibration in tissue are of interest to human noise as well as vibration research. (These research areas overlap to some extent and are frequently treated under the same heading, as in this chapter.)

The first section is concerned with a comprehensive discussion of the noise factor in space systems. General characteristics of the physical stimulus of noise and corresponding psychologic and physiologic reactions of man are discussed. Space system noises are also considered, including special factors of infrasound, ultrasound, and impulsive sound and their effects on crewmembers, support personnel, and communities. Current practices of noise control from the standpoint of the source and receiver are discussed relative to specific aerospace system noises.

The results of vibration research obtained in support of the space efforts (also discussed) include physiologic and performance research, basic laboratory studies, operational tests, and evaluations of actual and simulated space missions. A new generation of vibration simulators evolved which could produce complex and random vibration in several degrees of freedom. Vibration capabilities have been incorporated into man-carrying centrifuges and into spaceflight simulators. The main emphasis in recent research, with such machinery, has been on man's short-term tolerance limits and his specific performance capabilities. The interaction of vibration with other spaceflight stressors such as acceleration, heat, noise, and radiation has also been studied. Finally, practical exposure criteria and protective measures in both the noise and vibration areas for various phases of space missions are discussed.

THE NOISE FACTOR

Nature and Characteristics of Acoustic Energy

Acoustic energy, a physical quantity, in space biology and medicine is generally considered from the standpoint of its undesirable effects on man. Physiologic and performance effects are related to descriptive parameters of physical exposure for interpretive as well as predictive purposes. Characteristics of the magnitude of the energy, the frequency components present, and the duration or time history of the exposure are primary determinants of human responses. To evaluate the impact of acoustic exposures on man, the nature and relevant parameters of the acoustic energy must be defined.

Sound

Sound waves are variations in the air pressure above and below the ambient pressure. Sound waves are described by the physical characteristics of intensity, spectrum, and the time history of the event.

Intensity. The intensity of the sound wave is determined by the amount its pressure varies above and below the ambient level. The wide range of pressures of interest to space biology and medicine is described by a logarithmic scale which expresses a ratio of sound pressure to a reference pressure in decibels (dB). The decibel is a unit of level commonly used to describe levels of acoustic pressure, power, and intensity; its scale is logarithmic expressing the magnitude of the ratio between two quantities.

Atmospheric or ambient level is measured in dynes/cm^2 (dyn/cm^2) or microbar (μbar) with 1 atm equaling about 1 000 000 μbar. The smallest periodic variation in ambient pressure (sound wave) occurring at a rate of about 1000 times/s can be detected by man at a pressure amplitude of approximately 0.0002 dyn/cm^2 or μbar or about

2×10^{-10} atm. This just detectable level was arbitrarily selected as the standard reference sound pressure for the practical decibel scale for sound measurement in gases in terms of sound pressure level (SPL). The relationship between sound pressure and SPL is shown in Table 1 with the more recently adopted reference of 0.00002 N/m^2. The intensity of a pressure (P), in terms of SPL is defined by

$$\text{SPL} = 20 \log_{10} \frac{P_1}{P_0}$$

where $P_0 = 0.0002$ μbar and the SPL value is quoted as dB re 0.0002 μbar.

TABLE 1.—*Scales Commonly Used to Describe Magnitude of Acoustic Energy*

Sound pressure level (dB)	Sound pressure (μbar)	Sound pressure (N/m^2)	Pressure (lb/in^2)
174	100 000	10 000	1.47
134	1 000	100	14.7×10^{-3}
94	10	1	147.0×10^{-6}
74	1	0.1	14.7×10^{-6}
54	0.1	0.01	1.47×10^{-6}
14	0.001	0.0001	14.7×10^{-9}
0	0.0002	0.00002	2.94×10^{-9}

Spectrum. Sound waves of periodic (sinusoidal) oscillations in single or simple components are discrete tones, described in terms of oscillations per unit time or frequency, i.e., either cycles per second (cps) or hertz (Hz). Noises and complex sound are made up of many simple sounds distributed in frequency. Noises of concern to aerospace biology and medicine are frequency-dependent in terms of their effects on man; noise is commonly described in terms of levels of successive passbands of octave, half-octave, and third-octave bandwidths [5]. Spectrum is the plot of the various band levels as a function of frequency. The total sound pressure of a complex noise is expressed as overall sound pressure level (OASPL). Contributions of the various frequency bands of the spectrum are referred to as octave band sound pressure level (OBSPL), third octave band sound pressure level, and so forth.

The spectrum of acoustic energy which is important to man's perception ranges from small fractions of a single cycle to over 20 000 cps (Hz). The young, normal human ear is sensitive to energy in the range of about 15 to 20 000 Hz, which is termed the audiofrequency range. Energy at frequencies below about 20 Hz is subaudible sound or infrasound. Although the term ultrasound has classically been defined as acoustic energy above 20 000 Hz, the term is applied to energy ranging as low as 8000 to 10 000 Hz and above.

Time history. Pressure (sound) waves consist of rather specific individual patterns of fluctuations or changes in pressure with time that relate directly to the kind of source generating the pressure variation. Various types of sound waves are differentiated and identified by their time courses. Steady-state sounds are those with a time course or duration greater than 1 s. Impulse sounds, individual pressure pulses of sudden onset, are those with a duration of less than 1 s and a peak to root-mean-square (RMS) ratio greater than 10 dB. Impulse sounds are described by their rise time, peak level, and duration. The frequency content of impulsive sounds is determined by energy-spectral-density analysis. Pressure time histories describe variations in sound pressure of a signal as a function of time. The frequency content is not quantified in pressure-time histories of signals. Analytic techniques must be applied to the signal to obtain frequency or spectrum characteristics.

Propagation. Theoretically, sound waves in open air spread spherically in all directions from an idealized point source. As a result of this spherical dispersion, the sound pressure is reduced to half its original value as the distance is doubled, which is a 6-dB reduction in SPL. Sound propagation is further influenced by such factors as atmospheric attenuation, air temperature and turbulence, topography, and obstacles in the sound field. The general effects are those of propagation losses and distortion brought about by absorptive and reflective properties of obstacles encountered, scattering by irregular ground surfaces and meteorological turbulence, and shifting due to strong winds. The speed of sound in air is temperature-dependent and is

about 344 m/s (1128 ft/s) at a temperature of 21° C (70°F).

Noises from aerospace sources do not radiate uniformly as from a point source but follow characteristic forms or patterns. This directivity of sound propagation from particular sources is considered in noise evaluations, to insure that exposure levels within noise fields have been adequately defined relative to placement of personnel and exposure of communities in the vicinity of the noise sources.

Aerospace Noises

Major sources of acoustic energy of concern in aerospace operations are vehicle propulsion systems and auxiliary equipment which provide maintenance support on the ground and mission (life) support on-board vehicles. The operational phases which must be considered are launch, orbit or cruise, and reentry. The manner in which acoustic exposure from various operations influences ground personnel, flight personnel, and other persons on the aerospace complex and in exposed communities must be defined. Relative energy levels and frequency content of noise exposures of various aerospace operations are shown in Figure 1.

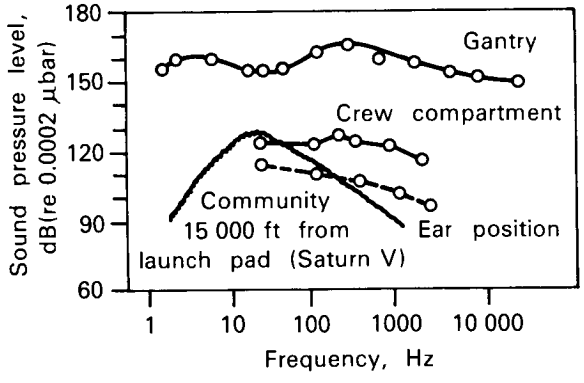

FIGURE 1.—Relative energy levels and frequency content of aerospace noises at launch [56].

Airborne noise is generated by propulsion systems, its magnitude increasing with the thrust of the engines. Jet and rocket noise have a continuous noise spectrum of random character, whereas propeller and turbine noise have spectra which are dominated by discrete frequency components determined by the number of blades and the speed of revolution (rpm). Aerodynamic or boundary layer noise occurs at high flight velocities through the atmosphere as a result of pressure fluctuations in the boundary layer rushing over the vehicle skin. Figure 2 shows the relative contributions of propulsion and aerodynamic noise as a function of time after ignition of a space rocket launch.

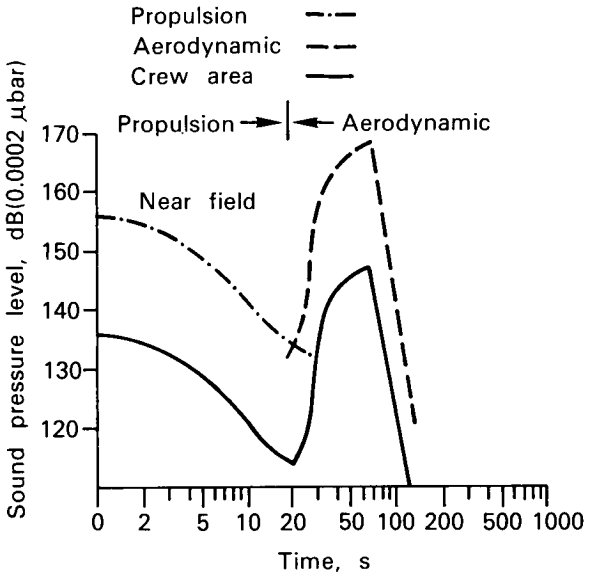

FIGURE 2.—Relative levels of propulsion and aerodynamic noise as a function of time after launch [32].

Jet noise from the propulsion system of a space vehicle predominates at launch and the zone of maximum intensity on the ground is in the form of a ring spreading outward from the launching pad. As the rocket gains altitude, the noise heard from below grows fainter and changes to a low-frequency rumble which extends far into neighboring areas and often disappears abruptly. Aerodynamic noise at the vehicle exceeds the propulsion noise with increasing flight speed but subsequently decreases as the vehicle progressively leaves the Earth's atmosphere. In the crew compartment, maximum noise exposures also occur after ignition from propulsion noise and as the vehicle passes through the range

of maximum dynamic pressure (max q) from the aerodynamic or boundary layer noise. The overall sound pressure level time histories for an Apollo mission shown in Figure 3 were measured as a function of time from lift-off. The external noise levels are effectively reduced by the space-cabin structures and by the helmet-space-suit system as indicated by the relative levels at the crew station and at the ear. Aerodynamic noise is also encountered upon reentry of the capsule into the Earth's atmosphere. The levels of acoustic energy in the spacecraft cabin during reentry are comparable to those shown in Figure 3; however, the duration may be longer because of broader angles of trajectory and increased amount of time in the atmosphere.

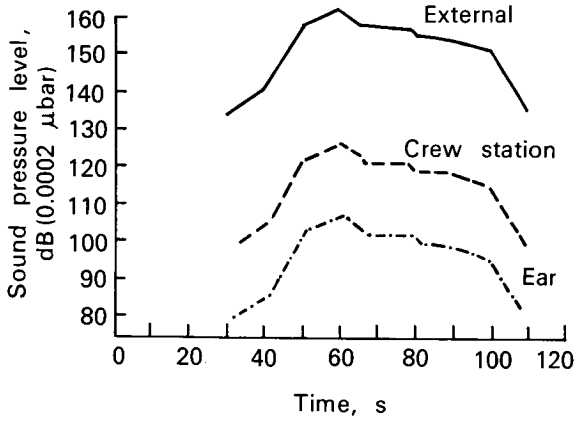

FIGURE 3.—Overall sound pressure level time histories as a function of time from lift-off of Apollo [32].

When supersonic speeds are reached by vehicles traveling in the atmosphere, shock waves or sonic booms are generated and propagated in a conical pattern behind the moving body [1]. If the flight angle relative to the ground is appropriate and if the pressure pulses are strong enough, the shock waves are perceived by observers on the ground as identifiable explosive-type sounds.

The magnitude or overpressure is arbitrarily defined as the positive peak pressure component of the pressure-time history of the sonic boom. During launch, the downrange flight angle and the altitude at which the downrange maneuver is executed largely determine whether or not the sonic boom reaches the Earth. Space activities, such as the US Space Shuttle Program in which pilot-controlled space vehicles will reenter the atmosphere at supersonic speeds and decelerate to accomplish a conventional landing, will also generate sonic booms. The nature of the reentry trajectories are such that large areas of the Earth's surface may be exposed to low-level sonic booms.

Primary noise sources are mission- and life-support systems during the orbital or cruise phases of space flight. The noise generated by several on-board systems during nonpowered flight is shown in Figure 4. The potential problems of continuous long-term exposure to moderately intense noise, as well as its influence on sleep and rest, were initially evaluated relative to spaceflight applications. Since that time, emphasis has been expanded to include man's important daylong exposures to all categories of noise in our present societies.

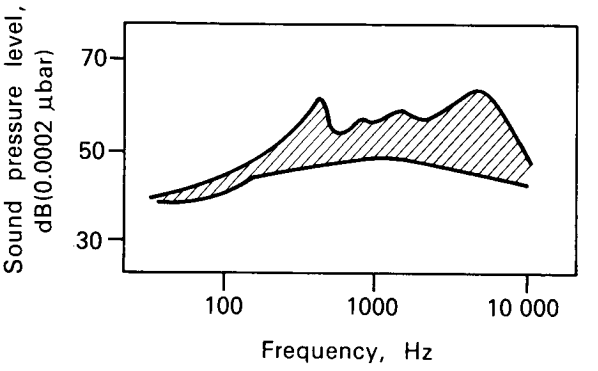

FIGURE 4.—Estimated range of noise exposure from on-board systems during cruise [56].

A significant characteristic of noises generated by space propulsion systems is the presence of very high levels of infrasound and low audio-frequency energy. As the exhaust diameter of such systems increases, the frequency at which the maximum acoustic energy occurs is lowered. The low and infrasonic energy is not effectively attenuated by the atmosphere; consequently, it is propagated long distances into adjacent areas

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and nearby residential and business communities. It is also more effective than higher frequency energy in causing structures to shake and rattle.

Airborne ultrasound, present around some aerospace propulsion systems, is effectively attenuated by the atmosphere and not propagated great distances. Adverse effects of airborne ultrasound have not been demonstrated for general outdoor conditions. Potential adverse effects of exposure to ultrasound on hearing and acceptability by individuals located close to ultrasound sources are discussed in a later section.

Pressure pulses of higher magnitude than those described as sonic booms accompany explosions, weapons fire, and the like, and are usually characterized as blast waves. Their magnitude and frequency spectrum depend on, among other variables, the explosive charge and distance from the source.

Effects of Noise on Man

The basic responses of persons influenced by space operations noises are broadly described as physiologic, those involving directly and indirectly physiologic mechanisms, and as psychologic, those which relate the basic attributes of sound to man's perception, judgments, attitudes, and opinions. In spite of this widely accepted dichotomy, in many noise exposure situations both elements are present, and the overall effects are mixed. The interactions of physiologic and psychologic responses to noise are too often ignored.

Physiologic Effects

Primary among the physiologic effects of noise is the response of the auditory system and the hearing function. Effects of acoustic energy have also been investigated relative to the vestibular system, mechanical stimulation of the body, autonomic nervous system, sleep, and startle. These latter effects, although described as nonauditory are, with few exceptions, also mediated through the auditory system.

Auditory response. The human auditory system is an extremely sensitive and highly specialized mechanism. The hearing threshold level or threshold of audibility is an individual's hearing sensitivity expressed in decibels relative to the normal threshold of hearing or standard hearing reference zero. The range of audible frequencies in the normal young human ear extends from about 15 to 20 000 Hz. The most sensitive region of the ear is from approximately 500 to 4000 Hz—the band most important for understanding speech. Infrasound, energy below the audible frequency range, is not detected by the human ear except at very high sound pressure levels. Harmonic components of intense infrasound may appear in the audiofrequency range at sufficiently high levels to be heard. Airborne ultrasound, i.e., acoustic energy above about 20 000 Hz, is not ordinarily perceived by the ear. An upper boundary of hearing is represented by the sound pressure levels at which tickle, ear discomfort, and pain may occur.

The auditory mechanism reacts in the presence of intense sound with a number of protective actions to reduce acoustic transmission to the inner ear [3]. At high intensities, the vibration of the stapes changes from a pistonlike movement to a rocking motion in the oval window due to subluxation of the ossicular joints. The stapedius and tensor tympani muscles contract also in response to appropriate loud sound, producing an increase in stiffness and possibly damping of the ossicular chain. The muscle reflex fails to provide protection from sudden and impulsive sounds shorter than about 15–20 ms because of its response latency which is nominally 25 to over 100 ms.

Acoustic stress. Excessive exposure to noise is a common cause of both temporary and/or permanent changes in hearing sensitivity or hearing loss. Temporary threshold shift (TTS) will return to normal or preexposure hearing levels within a reasonable time, whereas permanent threshold shift (PTS) does not recover, irrespective of time. Relationships have been established between noise exposure and TTS, and between PTS and noise exposure experienced daily over many years [73]. Noise-induced TTS is assumed to be an integral part of, and an essential precursor to, noise-induced PTS. Furthermore, it is assumed that without TTS, no PTS will occur. PTS also develops similarly to TTS but on a different time scale, and finally,

all noise exposures which produce equal amounts of TTS are considered equally noxious with regard to PTS. These assumptions based on TTS data from the laboratory and TTS/PTS data from actual everyday noise exposures, have made it possible to formulate hearing risk criteria which relate noise exposure and hearing loss.

Excessive noise exposure may produce hearing loss associated with two general syndromes. Hearing loss may result from mechanical stress or damage in the tympanic membrane-middle ear system, or in the inner ear. A mixed syndrome reflected in both mechanical and sensorineural components in the hearing loss may result from intense noise exposures, particularly from those with impulsive characteristics.

Continuous and impulsive aerospace noise exposures may cause mechanical damage to the tympanic membrane and ossicular chain, and, in some instances, the inner ear as well. Hearing loss resulting from this mechanical type acoustic trauma is characteristically flat or about the same magnitude for all frequencies when there is no sensorineural involvement. Sensorineural hearing loss, if a result of an intense impulsive signal, may not be determined for several months after exposure because of the slow course of recovery.

Auditory pain due to noise is associated with excessive mechanical displacement of the middle ear system, and is believed to occur near the damage threshold. This pain, occurring almost independently of frequency at levels of 130–140 dB SPL and above, acts as a rather ineffective warning mechanism for overexposure. No pain is associated with overexposure of the inner ear which is often recognized only after inner ear damage has occurred and the hearing function has been adversely affected.

Continuous noise exposure may produce a slow, progressive loss of auditory sensitivity; this loss is first observed between 2000 and 6000 Hz with the greatest and most rapid decrease at 4000 Hz. The loss of sensitivity increases in magnitude and spreads in frequency with continued exposure. The manner in which noise-induced permanent threshold shift progresses with a number of years of exposure has been widely documented.

The susceptibility of individual ears to noise-induced hearing loss varies greatly, i.e., the amount of TTS produced by a specific noise exposure will differ markedly in each case. The capability of determining an individual's noise susceptibility prior to his assignment to a noise environment would be most valuable; however, despite considerable research, there has been no satisfactory method for arriving at such a decision. Exposure criteria have not incorporated a susceptibility factor because of wide variance from person to person and the inability to predict TTS for a specific ear.

Vestibular system. Subjective reports of disorientation, vertigo, nausea, and interference with postural equilibrium during high-intensity noise exposure suggest that intense acoustic energy may stimulate the vestibular system [13]. Empirical efforts to substantiate vestibular responses to noise have not been conclusive; however, this evidence does identify the vestibular system as the most probable site of acoustical stimulation [54, 107].

Sensory systems other than the vestibular receptors are clearly affected at levels above 140 dB and mechanoreceptors and proprioceptors may be the primary mediators of the physiologic response [71, 141].

General physiologic responses. The influence of noise on human physiologic responses other than audition is unclear, and consistent deleterious effects have not emerged. Changes in various physiologic indicators are measured under laboratory conditions and in real-life situations; however, the magnitude of changes are frequently no greater than those experienced in daily living activities. In addition, physiologic responses which accompany individual noise exposures are frequently transitory. Generally, humans adapt very well to stimuli such as noise; however, questions yet to be answered concern possible adverse effects on health and well-being due to regular long-term exposure to noise over many years. Neither long-term adaptation to noise nor the manner in which widely varying individual differences affect physiologic reactions are well understood.

General and specific physiologic responses to sound have been measured by a number of in-

vestigators [19, 65, 68, 69, 141]. The results are complementary and include effects on peripheral blood flow, respiration, galvanic skin response (GSR), skeletal muscle tension, gastro-intestinal (GI) motility, cardiac response, EEG, pupillary dilation, renal and glandular function. Many of these response changes have been reported at relatively low sound pressure levels (70–90 dB).

Studies of nonauditory effects in industrial settings suggest that noise does influence general health. According to Kryter [72], Andriuken has reported greater arterial blood pressure in workers exposed to high-frequency lathe noise and to very intense broadband noise found in ball bearing production shops than in men working in less intense noise. Shatalov et al [120] showed differences in various cardiovascular responses of persons who worked in a spinning mill noise of 85–95 dB compared with those who worked in 114–120 dB of industrial noise. The incidence of symptoms of vascular disorders, cardiac arrythmias, and pale, taut skin conditions were higher in employees who worked in noise levels greater than 90–95 dB than in those working in less intense exposures [67]. Subjective reports of fatigue, loss of appetite, irritability, nausea, disorientation, headache, and even inability to remember, continue to be reported as a result of noise exposure.

Numerous other factors in industrial noise situations where physiologic problems have been observed indicate that caution must be exercised in attributing adverse effects solely to noise. An apparent corollary indicates that as noise exposure in work situations increases in intensity, other elements of the same environments, considered stressful to physiologic functions, increase correspondingly. The contributions to physiologic problems of temperature extremes and poor ventilation, threat of accidental injury or death, demands of specific tasks, and other nonnoise factors which tend to grow with intensity of noise exposure cannot be ascertained without being controlled in test populations.

Sleep interference. Interference with sleep due to noise may be a serious effect, for there is widespread agreement that adequare sleep is a physiologic necessity. There are two general aspects of sleep interference due to noise: actual arousal or wakening, and changes within the sleeping individual who does not awaken to the noise. Sleep is in stages or levels, which are revealed by patterns of electrical (EEG) activity of the brain. In terms of arousal, individuals are more resistant to noise stimuli during some stages of sleep than others. During sleep stage 2, subjects are more susceptible to behavioral awakening than during the other stages; they are most resistant during stage 4 and REM (rapid eye movements, with dreaming) sleep. Recent work by Lukas and Kryter [83] indicates an age factor in sleep interference due to noise. Aircraft noise and sonic boom-type stimuli perceived in the home environs awakened older persons (67–72-year-old males) about 70% of the time, younger persons (21–22-years-of-age) less, and children (5–8-years-of-age) hardly at all. Williams [138] reports the threshold for behavioral wakening has been measured at only 20 dB or thereabouts above the hearing threshold of audibility, while Kryter reports awakening thresholds of 30 dB in stage 2, and 50 dB in stage 4.

Sleeping individuals not awakened in response to noise stimuli have nevertheless shown changes in peripheral vasoconstriction as well as in EEG. Finger pulse amplitude changed at noise levels 15 dB below arousal threshold, and heart rate changes were measured at 10–15 dB below arousal threshold. These responses confirm that measurable effects of noise on biologic responses in man during sleep are observable even though the sleeper is totally unaware of the acoustic exposure.

Myasnikov [100] describes an interesting investigation of sleep in which subjects experienced broadband continuous noise exposure of 75–78 dB during simulated space flight. A dichotomy emerged: those who fell asleep rapidly, slept well and awakened feeling well; those who fell asleep with difficulty, did not sleep well and did not feel well on awakening. Other effects were generally bimodal corresponding to the two types of sleepers. The author concludes that selection of candidates for astronauts or cosmonauts should include screening of sleep characteristics to eliminate poor sleepers.

Startle. Startle may be evoked by a wide variety of stimuli but is particularly susceptible to sudden,

unexpected noises. The physiologic aspects of the startle response are not specific to the stimulus. They include increased pulse rate, increased blood pressure, and diversion of blood flow to the skeletal musculature. Startle responses are not known to have a direct adverse physiologic effect on personnel. They do not occur frequently in everyday life and generally are not considered to constitute a widespread problem.

Psychologic Effects

Psychologic responses to noise of interest to aerospace biology and medicine are potential problems in voice communication and crewmember performance.

Voice communication. The technical discussion of voice communication which follows, based largely on research and experience with standard American English, may not be directly appropriate for non-English languages. Processing different languages by a common space-communication system may be of concern as international cooperation in aerospace medicine and biology increases. Factors which influence operational voice communication have been systematically examined as a function of language. The statistics of language may vary significantly from one to another, and communication capability may likewise be differentially influenced. Voice communication as a function of language, although essentially ignored to the present, requires further definition in future aerospace research activities.

Speech communication may be adversely affected by noise exposures in two basic ways: the speech signal may be masked or drowned out by the noise, and/or temporary hearing loss due to the noise exposure may reduce the individual's ability to understand messages. Temporary hearing loss, if it occurs in this situation, is highly variable and cannot conveniently be included in schemes for estimating or predicting voice communication efficiency in noise. Masking effects of noise on speech communication, which are well understood, form the basis for quantitative predictive schemes and criteria. These criteria do not include low-frequency and infrasonic exposures. The extent to which such exposures affect the prediction of speech intelligibility has yet to be determined. Subaudible airborne sound is effective in eliciting body vibrations and responses, which, as they are reflected in speech production, may prove a problem.

Influences on voice communication have been categorized by Webster [136] as environmental, personal, message, and equipment. Noise, both acoustical and electrical, is the predominant environmental factor responsible for masking and degrading speech. Conditions of whole-body vibration and of artificial atmospheres such as $He–O_2$ mixtures have demonstrated clear-cut influences on the speech communication process [106]. Combined stresses, i.e., noise and vibration, may produce greater decrements than those found in either element experienced singly. Task requirements, possible danger, other health effects and stresses may also cause communication to deteriorate.

Personal factors are concerned with the manner in which the speech message is produced and perceived by the individual. Poor speech production habits, regional and national dialects, and word usage are important. Hearing loss, either temporary or permanent, will also degrade perception. Experience in the communication environment facilitates efficiency as does an adequate program of training concerned with the environment in which the trainee will perform and the speech materials and equipment he will use.

Type of material or messages which result in reduced intelligibility involve large vocabularies, unexpected terms, and phrases used infrequently. Equipment degradation of speech can be effectively engineered out using principles such as noise-cancelling microphones, microphone noise shields, adequate passband of the system, appropriate peak clipping, low impedance characteristics, and the like. Most communication systems using these principles account for very little speech degradation. Engineers, to insure a successful design, must know characteristics of the system and the manner in which the system is to be used.

Various procedures are in widespread use for analyzing and predicting the effectiveness of electronically aided (headset) and face-to-face speech communication in noise. These procedures involve a physical description of the noise ex-

posure in both level and spectrum, a nominal or measured speech level and spectrum, and an analytic procedure based upon experimental data relating masking effects of noise to speech reception and a descriptor of expected efficiency of speech communication as a function of the noise. The least sophisticated and easiest to use method is the A-weighted sound pressure level (dBA). Speech Interference Level (SIL or PSIL) is the simplest method using octave band levels. A more refined procedure than SIL and PSIL developed for use in a very wide range of applications is Noise Criteria (NC or PNC). The most comprehensive and accurate procedure for predicting speech communication efficiency in noise environs is the Articulation Index. A final procedure, probably the most time-consuming and expensive, is to attempt to simulate the communication environment and directly measure the response of the system through intelligibility testing.

Sound level. The A-weighted sound level in decibels (dBA) is a single number representation of a noise measured with a sound level meter [8]. The A-weighting approximates sensitivity of the normal human ear to moderate level sound. Measured dBA values referenced in Figure 5 [135] provide relationships between communication capability and noise. This procedure is ideal for survey and monitoring purposes; however, it is unsuited for noise control and engineering purposes because detailed spectral information is lacking in the descriptor.

Speech interference level—speech interference level, preferred frequencies. SIL and NC procedures permit estimates of the acceptability of noises for communication based on octave band descriptions of the noise. Recent changes in noise

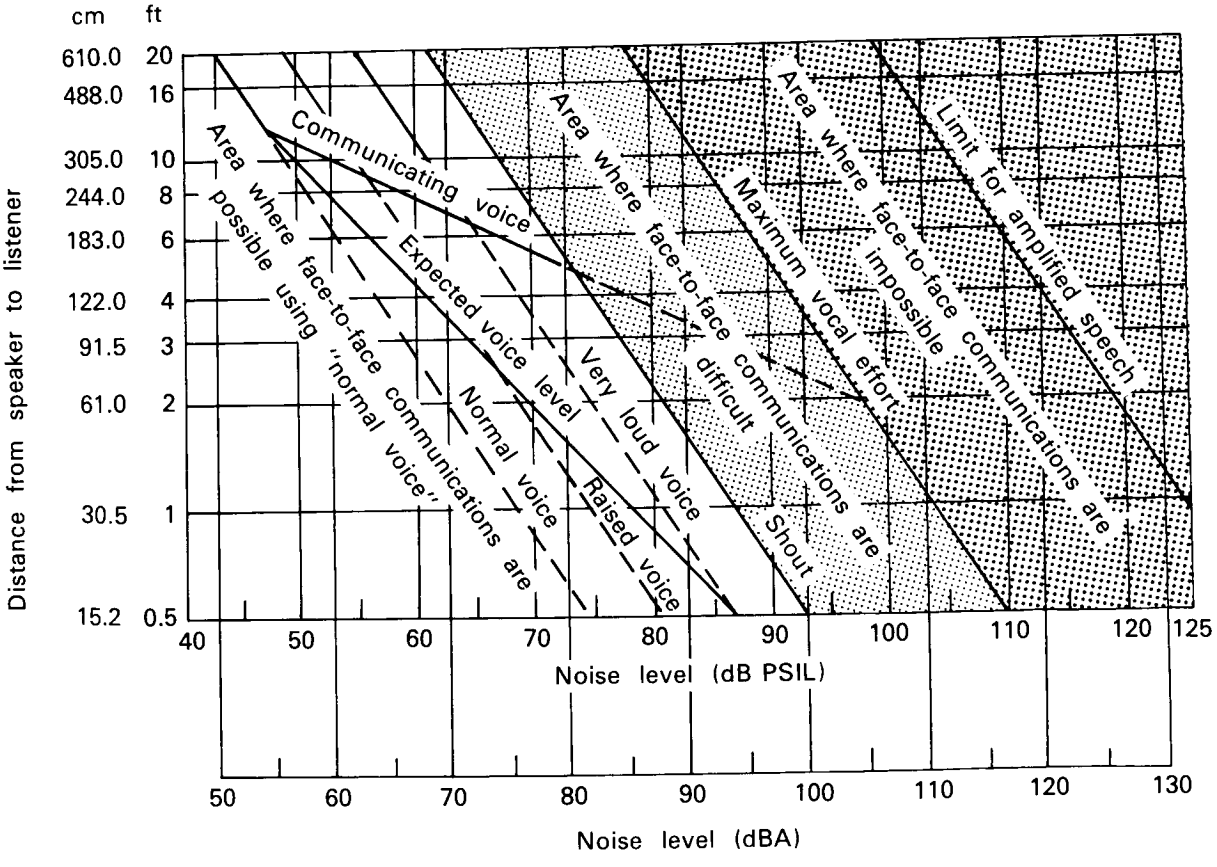


FIGURE 5.—Objective measures of noise level (PSIL and dBA) and corresponding communications capabilities [135].

measurement standards have resulted in two slightly different descriptions of the noise. New octave bands have been standardized for general use, and current noise measuring equipment is constructed to comply accordingly. The new octave bands, which have different center frequencies from the old octaves, are called *preferred* frequencies or octaves. The preferred center frequencies and the nonpreferred center frequencies of octave bands are presented in Table 2. To identify speech intelligibility prediction procedures that use the preferred center frequencies, the letter P is added to the nomenclature to produce PSIL and PNC.

SIL and PSIL [135] are single number criteria valid for noise exposures having a relatively uniform spectrum. The SIL is defined as the arithmetic average of the sound pressure levels (dB) of the noise in the three octave bands which contain most of the speech energy: 600–1200, 1200–2400, and 2400–4800 Hz. The PSIL, defined as the average octave band level of new or preferred octave bands centered at 500, 1000, and 2000 Hz, is called the three-band preferred octave speech interference level. PSIL and SIL levels for reliable communication at various distances and voice levels are shown in Figure 5. PSIL values are generally 3 dB higher than SIL values for the same noise exposure. It is acceptable practice to convert from one to the other by adding or subtracting 3 dB.

Noise criteria. Noise criteria (NC) are basically an expansion of SIL from a single number to sets of numbers representing octave band criteria. Noise criteria assume a reasonably steady and continuous spectrum. A new set of criteria curves has been formulated, which uses the new octave bands. These curves, called preferred noise criterion curves (PNC) [16], have levels in the bands below 125 Hz and above 1000 Hz that are lower than those of the original NC curves by 2–5 dB. Criteria curves and corresponding recommended indoor functional activity areas are described in Tables 3 and 4 for both NC and PNC.

To estimate communication performance for a given noise environment using either of these criteria:

1. determine the noise in octave bands
2. compare the octave band spectrum to the appropriate PNC criterion curve in Table 3
3. the criterion value just above the highest octave band level describes the noise environment
4. consult Table 4, which contains functional activities, to determine the level and quality of communication to be expected for that environment.

Articulation index. The most comprehensive procedure for predicting intelligibility in noise is the articulation index (AI) [7]. The AI is a calculation from physical and acoustical measurements made on a communication system which describes the intelligibility that might be expected for that system under actual test conditions. The speech spectrum and effective masking spectrum at the ear of the listener are required for the computation. The method is applicable for communication situations which involve male talkers.

TABLE 2.—*Preferred and Nonpreferred Center Frequencies of Octave Bands*

Preferred center frequencies	Band limits	Nonpreferred center frequencies	Band limits
31.5	22.4– 45	26.5	18.8– 37.5
63	45 – 90	53	37.5– 75
125	90 – 180	106	75 – 150
250	180 – 355	212	150 – 300
500	355 – 710	425	300 – 600
1000	710 – 1400	850	600 –1200
2000	1400 – 2800	1700	1200 –2400
4000	2800 – 5600	3400	2400 –4800
8000	5600 –11 200	6800	4800 –9600

TABLE 3.—*Octave-Band SPL Values Associated with Recommended 1971 Preferred Noise Criterion (PNC) Curves* [16]

Preferred noise criterion curves	31.5 Hz	63 Hz	125 Hz	250 Hz	500 Hz	1000 Hz	2000 Hz	4000 Hz	8000 Hz
PNC-15	58	43	35	28	21	15	10	8	8
PNC-20	59	46	39	32	26	20	15	13	13
PNC-25	60	49	43	37	31	25	20	18	18
PNC-30	61	52	46	41	35	30	25	23	23
PNC-35	62	55	50	45	40	35	30	28	28
PNC-40	64	59	54	50	45	40	35	33	33
PNC-45	67	63	58	54	50	45	41	38	38
PNC-50	70	66	62	58	54	50	46	43	43
PNC-55	73	70	66	62	59	55	51	48	48
PNC-60	76	73	69	66	63	59	56	53	53
PNC-65	79	76	73	70	67	64	61	58	58

Procedures for calculating AI may be based on the spectrum level of the noise and of speech present in 20 contiguous bands of frequencies, octave bands, or 1/3 octave bands of frequencies. The greatest precision is obtained with the 20-band procedure, the least with the octave band method. An appropriate worksheet must be used to calculate the AI. Sample worksheets are shown for the 20 contiguous bands (Fig. 6) and the octave bands of frequencies methods (Fig. 7). An example of the calculation of an AI by the octave band method is contained in Figure 8 for a relatively flat noise spectrum of moderate intensity. This calculation procedure may be followed in the example which provides an AI of 0.54:

1. Plot the octave band levels of the steady state noise reaching the listener's ears.
2. Adjust the idealized speech peaks curve to reflect the speech value in the system under test.
3. Determine the difference in decibels at the band center frequencies between the speech and the noise spectra. (Assign 0 to differences less than 1, and 30 to differences greater than 30.)
4. Multiply the difference values in each band by the weighting factor for that band, and add the resulting numbers to obtain the AI.

A number of factors which influence speech intelligibility scores, either individually or in combinations, may be quantitatively evaluated using the AI principle. Some of the factors are: (a) masking by steady state noise, (b) masking by nonsteady state noise, including the interruption rate, (c) frequency distortion of the speech signal, (d) amplitude distortion of the speech signal, (e) reverberation time, (f) vocal effort, and (g) visual cues. Of the many factors not evaluated by AI, there are: (a) sex of the talker, (b) multiple transmission paths, (c) combinations of distortions, (d) monaural vs binaural presentation, and (e) asymmetrical clipping, frequency shifting, and fading.

The relationship of AI to various measures of speech intelligibility is shown in Figure 9. The intelligibility score is dependent on the constraints placed on the message, i.e., the greater the constraint, the higher the intelligibility. No single value AI can be established as an acceptable communications criterion because of variations in proficiency of talkers and listeners, and in the nature of messages to be transmitted. AI is a consistent, reliable procedure for predicting relative performance of communications systems operating under given conditions. Present-day communication systems usually have design goals of AIs in excess of 0.5. An AI of 0.7 appears appropriate as a goal for systems which will operate under a variety of stress conditions and with many different talkers and listeners of varying degrees of skill.

Measurement of intelligibility. In some situa-

tions the speech and/or noise characteristics may not satisfy the basic assumptions underlying the standard calculation procedures. Unusual noise environs, whole-body vibration in noise, and artificial atmospheres and noise are examples. The communication efficiency with talkers and/or listeners in the environment of interest must then be measured. Some intelligibility assessment procedures are widely accepted through standardization and through usage. One sensitive test of speech intelligibility is the Phonetically Balanced (PB) Monosyllabic Word Intelligibility Test [6]. This procedure consists of trained talkers reading lists of phonetically balanced material to trained listeners under communication system features being evaluated. A score of about 70% on the PB word lists corresponds to more than 90% intelligibility for sentences.

Speech communication, using good sound protector-communications units (i.e. earphones under ear protectors and a shielded microphone reducing speech masking by the ambient noise) is adequate in most operational aerospace ground-maintenance situations. The performance of these units has not been determined in the noise fields of present and future rocket systems, of large jet engines of the C–5A or SST, and with VTOL and VSTOL type aircraft.

Artificial atmosphere. Speech communication has been evaluated in special or unusual environments of interest to aerospace operations. Helium, once considered a possible component of the life-sustaining atmosphere of some space vehicles and orbital stations, was investigated [70, 106]. This research described speech responses in helium concentrations ranging from 0–80% at pressures of 760–258 mm Hg. Effects of helium were found positively related to the amount of helium present, i.e., the greater the amount of helium, the greater the effect on speech. In general, helium speech showed: (1) good intelligibility, (2) less vocal output than air, (3) shifts of speech energy (vowels) to higher frequencies, (4) greater susceptibility to masking by ambient noise than speech in air, and (5) a strange, unnatural quality. These characteristics are imposed by elements of the physical environment, thus cannot be significantly improved by crewmember training and experience.

Vibration. Various powered phases of space missions as well as high-speed, low-altitude flight are characterized by severe vibration, buffeting, and intense noise. The speech of individuals subjected to these stimuli is altered to a tremolo-like voice quality corresponding in some degree to the frequency of the vibration [103]. Word intelligibility is reduced, particularly by vibrations at 6 to 7 Hz. The vibrated speech is masked by noise to a greater extent than might be expected. Speech continues to deteriorate with increasing levels of acceleration.

Performance

Adverse effects of noise on sensorimotor performance and cognitive function have not been

TABLE 4.—*Recommended Noise Criteria Ranges for Steady Background Noise as Heard in Various Indoor Functional Areas* [16]

Type of space (and acoustical requirements)	PNC curve	Approximate sound level (dBA)
For sleeping, resting, relaxing; bedrooms, sleeping quarters, hospitals, residences, apartments	25 to 40	34 to 47
For fair listening conditions; laboratory work spaces, drafting and engineering rooms, general secretarial areas	40 to 50	47 to 56
For moderately fair listening conditions; light maintenance shops, office and computer equipment rooms	45 to 55	52 to 61
For just acceptable speech and telephone communication; shops, garages, power-plant control rooms, etc. Levels above PNC–60 are not recommended for any office or communication situation	50 to 60	56 to 66
For work spaces where speech or telephone communication is not required, but where there must be no risk of hearing damage	60 to 75	66 to 80

consistently demonstrated. Performance efficiency has been variously reported to increase, deteriorate, or remain unaffected by noise. In general, efficiency may improve when noise exposure functions to isolate performance from acoustic distractions. The efficiency may deteriorate when the noise itself is a distracting influence on tasks which require attention and concentration over long work periods. Although numerous, experimental investigations on effects of noise on performance have failed to provide an integrated framework for the establishment of exposure criteria. Questions remain unanswered concerning the amount of performance impairment to be expected for specified sets of noise exposure conditions.

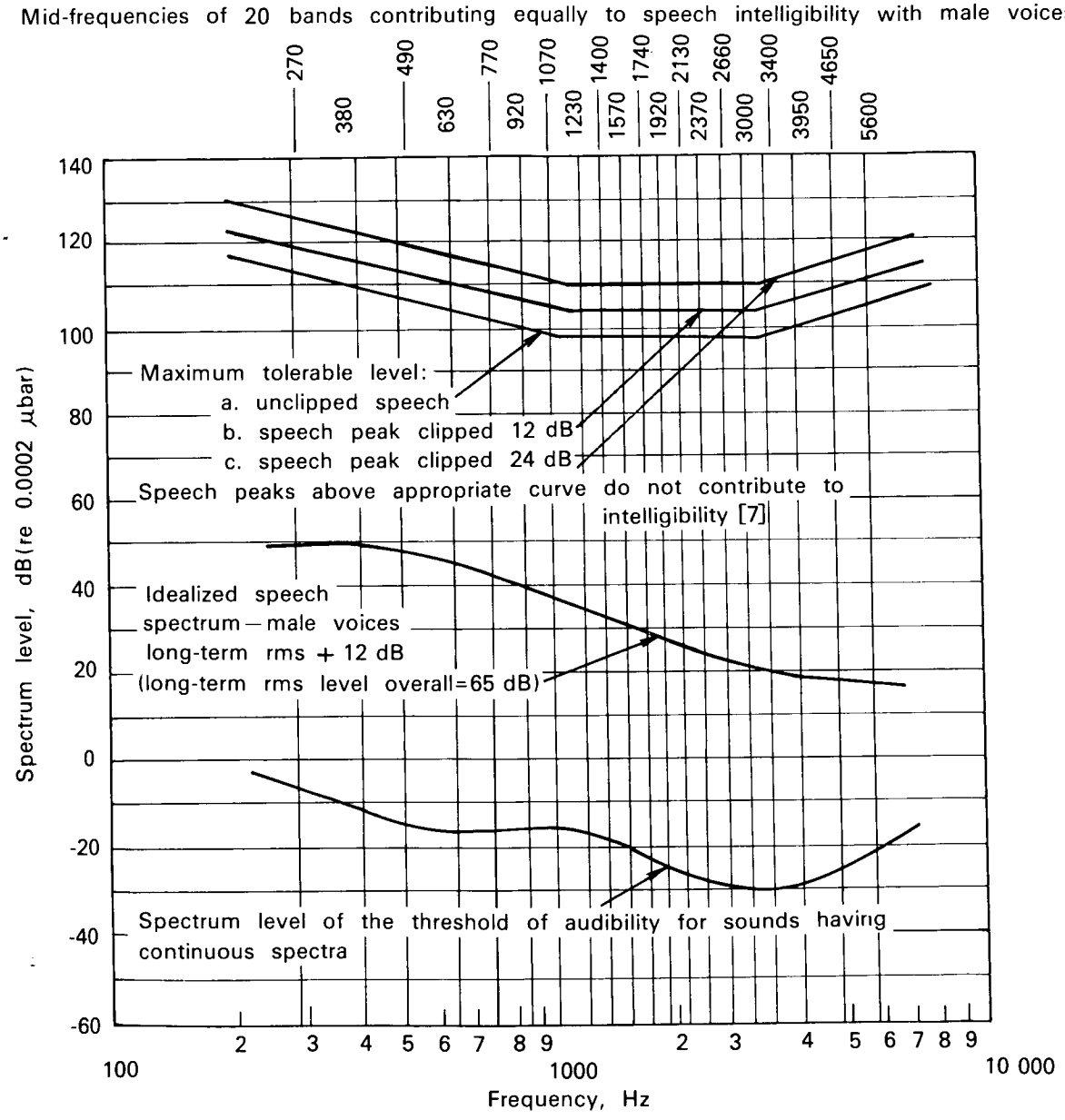


FIGURE 6.—Work sheet for articulation index, 20 contiguous bands method [7].

Kryter [72] presents a comprehensive discussion of a great deal of key work accomplished over the past 10 years. He reviews the results as well as various theories to explain motor performance in noise. In summarizing, he suggests that noise will not "directly interfere with mental or motor performance." He asserts noise effects on mental and motor nonauditory tasks to be negligible below about 27 dBA, possibly beneficial between about 27 and 67 dBA due to arousal and isolation from distraction, and possibly detrimental above about 67 dBA due to overarousal, aversion, and distraction from the task.

Noise Combined with Vibration

Simultaneous exposure to noise and vibration is exceedingly common in current transportation systems and in powered flight phases of space activities. The effects of these combined stimuli on performance cannot be predicted from knowl-

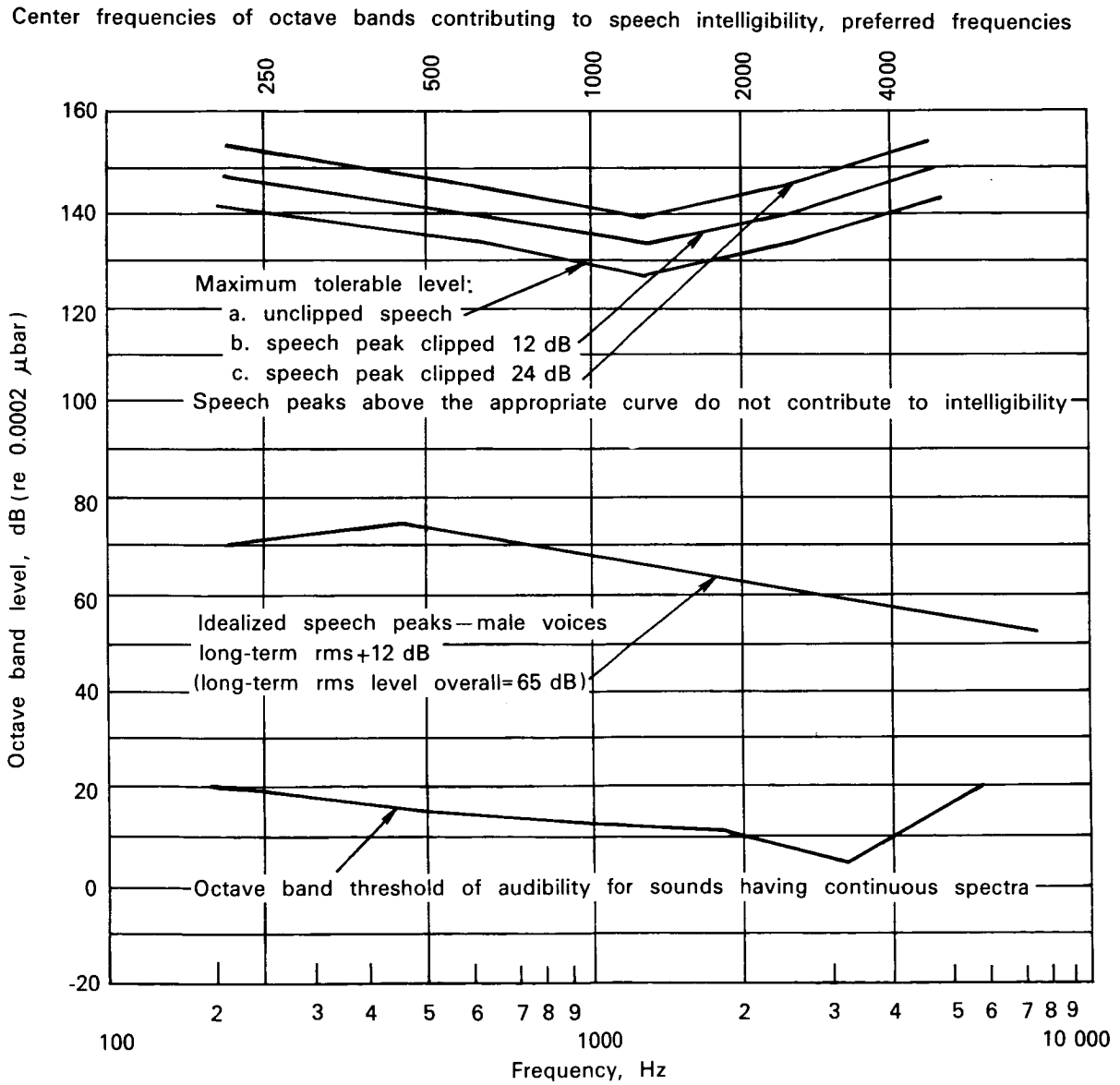


FIGURE 7.—Work sheet for articulation index, octave band method, preferred frequencies [7].

edge of single-stress effects. Since consistent information is lacking about effects on performance from noise and vibration individually, it is not surprising that even less information exists relative to their combined effects. Scientific interest in the experimental investigation of this combined stimulus is relatively recent. In a few studies, motor performance has been examined on a two-dimensional complex tracking and reaction time task, and cognitive performance on a short-term memory/subtraction task. Results from motor performance studies were not conclusive. However, there was some consistency between studies for the cognitive task [125]. An additional study of the effects of the combined noise and vibration on the mental arithmetic task as a function of time of day revealed no significant differences in performance measured at 6 a.m. and at 3 p.m. Ioseliani [63] reports decreased intellectual performance in noise combined with

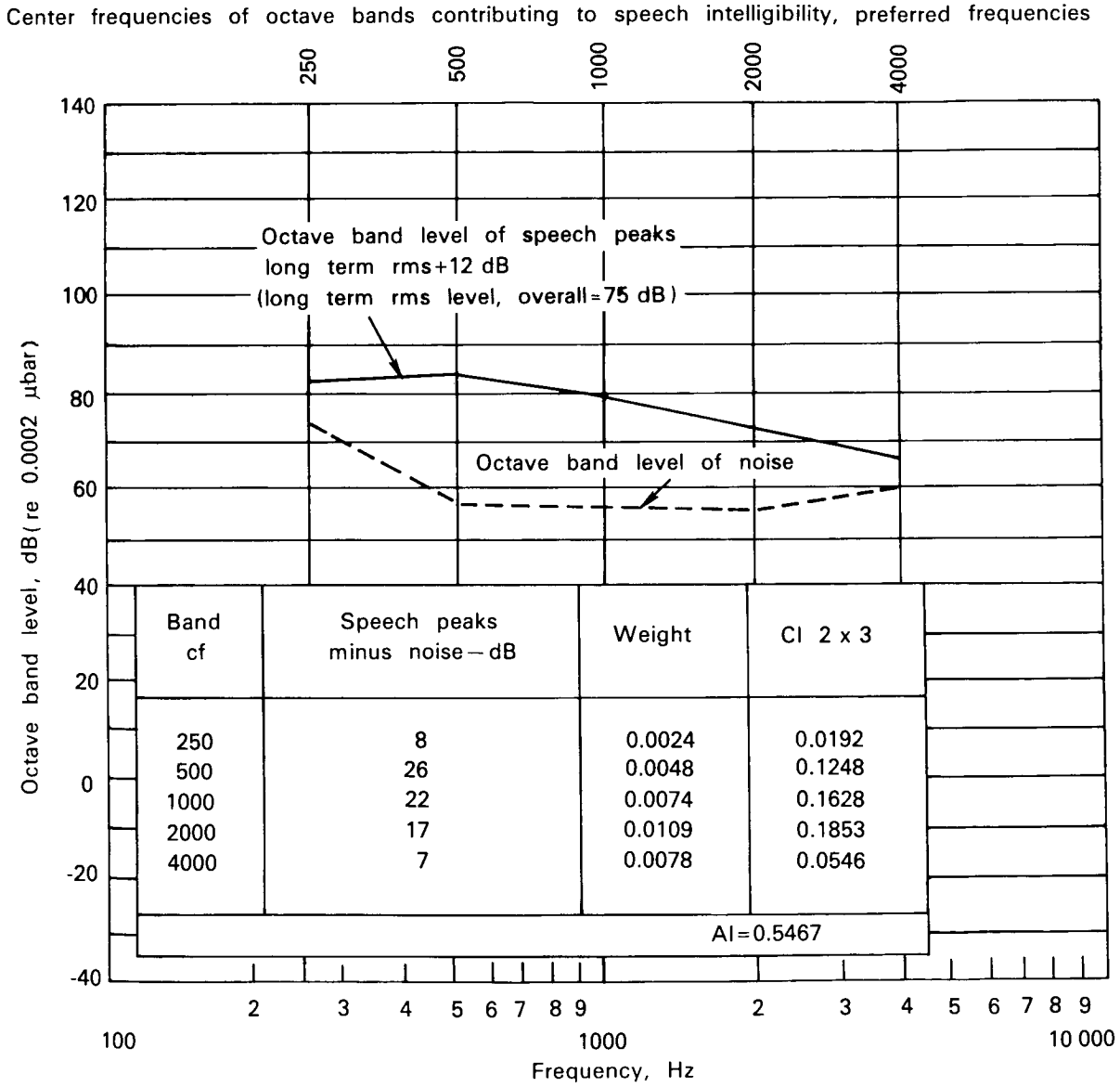
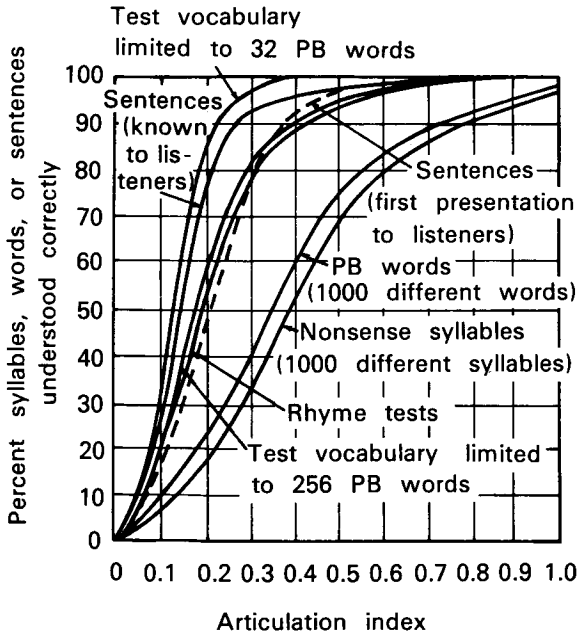


FIGURE 8.—Example of articulation index calculation using the octave band method [7].

vibration: 70% of the degradation was due to vibration, and 30% due to the noise component.

The environmental stress of heat was added to that of noise and vibration by Grether et al [44, 45] in two studies which examined effects on performance and were specifically oriented to the combined stress of space activities. The subjects were exposed to heat 49° C (120° F), noise (105 dB), and z-axis vibration (5 Hz, 0.30 g peak) singly and in various combinations. Results suggest that the combined stress condition produced less of an effect on performance than the individual stressors. The greatest impairment of performance resulted from the vibration stimulus alone. These results should not be interpreted as conclusive because of the limited number of investigations and meager amount of information.

Stresses are typically encountered simultaneously in real life situations, instead of individually, as they are ordinarily investigated.



Note: These relations are approximate. They depend upon type of material and skill of talkers and listeners.

FIGURE 9.—Relation between AI and various measures of speech intelligibility [7].

Investigators working in the area of combined stresses point out the complexity of these multi-stress situations which are further confused by interactions relating to task, instructional, and situational variables. The problems encountered in single-stress research and the little experience accumulated when stresses are combined suggests that the prediction of human performance capability in combined-stress situations is likely to be very difficult for some time in the future. There are, however, no documented situations in which acoustical energy has directly acted upon individuals so as to seriously interfere with task performance in environments typical of those experienced by aerospace crews.

Complex Reactions

Numerous psychologic factors in the lives of individuals contribute to the manner in which they respond and will respond to noise and sonic booms from aerospace activities of the present and future. The interaction of these psychologic factors with noise exposure results in the wide range of behavior in response to noise, and is described as complex reactions. Some general models have been proposed for various actions of the intruding noises and corresponding responses of those exposed to it.

Noise. Acoustic energy is undesirable when attention is called to it unnecessarily or it interferes with routine activities in the home, office, shop, recreational area, or elsewhere. Numerous techniques based on physical stimuli are available and in use to assess noise exposure effects on people in work and living spaces and to estimate individual and community reaction to them. In the past, most approaches to this question have been based upon loudness functions and methods for calculating loudness of sounds. A current concept, which has gained widespread acceptance and usage, maintains that individual and community reaction to a sound is determined by the annoyance or unwantedness of the sound instead of its loudness. The subjectively judged unwantedness of a sound is described as its perceived noisiness (PN). The perceived noisiness concept supposes that unacceptability of a sound may be adequately determined from physical

measures of sound. The unit of noisiness obtained from calculations—using the physical or objective measurements of the sound—is defined as the perceived noisiness in decibels or PNdB.

Relationships between various PNdB levels and the nature of community reactions that correspond to them have been defined on the basis of data from airport noise experiences as well as both laboratory and field research. These relationships are compiled for use in estimating reactions and a step-by-step procedure is available for arriving at PNdB values from the physical measurements of the noise. A comprehensive discussion of the basic concept of perceived noisiness, including various modifications and refinements intended to extend the usefulness of the procedure, is presented in detailed form in Kryter's discussion [72].

Most schemes currently in use throughout the world for estimating total exposures are based upon some form of loudness function or of the perceived noisiness concept. Each nation also modifies whatever basic concept is used relative to its own needs, criteria for percent of population affected, basic research data of most interest to them, and the like. The wide variety of techniques for describing the acoustic stimulus can be reduced to a common denominator for convenient comparison [33]. Approximate equivalences between noise exposure indices from a number of different nations are shown in Figure 10. Each of these procedures is used to estimate responses of communities and to determine compatible land usage for corresponding noise exposures.

Present indices for predicting complex reactions to total noise exposure may not be directly appropriate to aerospace activities. Total noise exposure implies numerous individual exposures daily over a minimum of many days. Aerospace activities, other than those such as static rocket firings, will likely occur one or two times per week as a maximum, at least for the foreseeable future. Appropriate corrections might be applied to the basic procedures to permit their use with noise exposures of the aerospace systems.

Sonic boom. National and international attention is directed at human response to sonic boom from the standpoint of commercial supersonic transport aircraft, as well as current and future aerospace activities which will involve frequent exit from, and reentry into, the Earth's atmosphere at supersonic speeds. Investigative efforts continue in a number of areas to determine valid tolerance criteria. Recent research activities in both laboratories and communities have provided a framework of information within which this stimulus may be better understood [40]. Estimates and observations of sonic boom exposures are summarized in Table 5.

Direct physiological injury of humans due to exposure to the level of sonic booms typically experienced in communities and to special experimental studies has not been documented. The auditory mechanism is exceedingly sensitive to variations in pressure; however, no adverse effects of sonic booms on hearing acuity have been measured. Startle and interference with routine living and work activities may lead to complex reactions of annoyance, which are problems of considerable proportion. The extent to which individuals adapt to startle after repeated exposures over days and weeks is unknown.

High-Intensity Noise Effects

Some noise environs during launch and static firings of aerospace vehicles are short-duration exposures at overall sound pressure levels ranging from 120 to 170 dB and greater. When individuals are without adequate hearing protection against these noises, likely they will have pain and severe acoustic trauma during relatively brief exposures. Whole-body or nonauditory effects may be experienced at these intensity levels in spite of using good hearing protection.

Steady state. Steady-state acoustic energy at these levels, and particularly for lower frequencies, is clearly felt as well as heard. The threshold of feeling for the airborne sound is about 10 dB below the threshold of aural pain for energy in the midfrequency range. The acoustic energy activates mechanoreceptors throughout the body [71, 141]. The stimulus is perceived by cutaneous receptors, viscera, and the vestibular system. Sinuses, mucous membranes, and proprioceptors also respond. Overall sensations are strange and somewhat disturbing even to individuals accustomed to noise exposure. Vertigo, nausea, vomiting, and occasional disorientation are reported

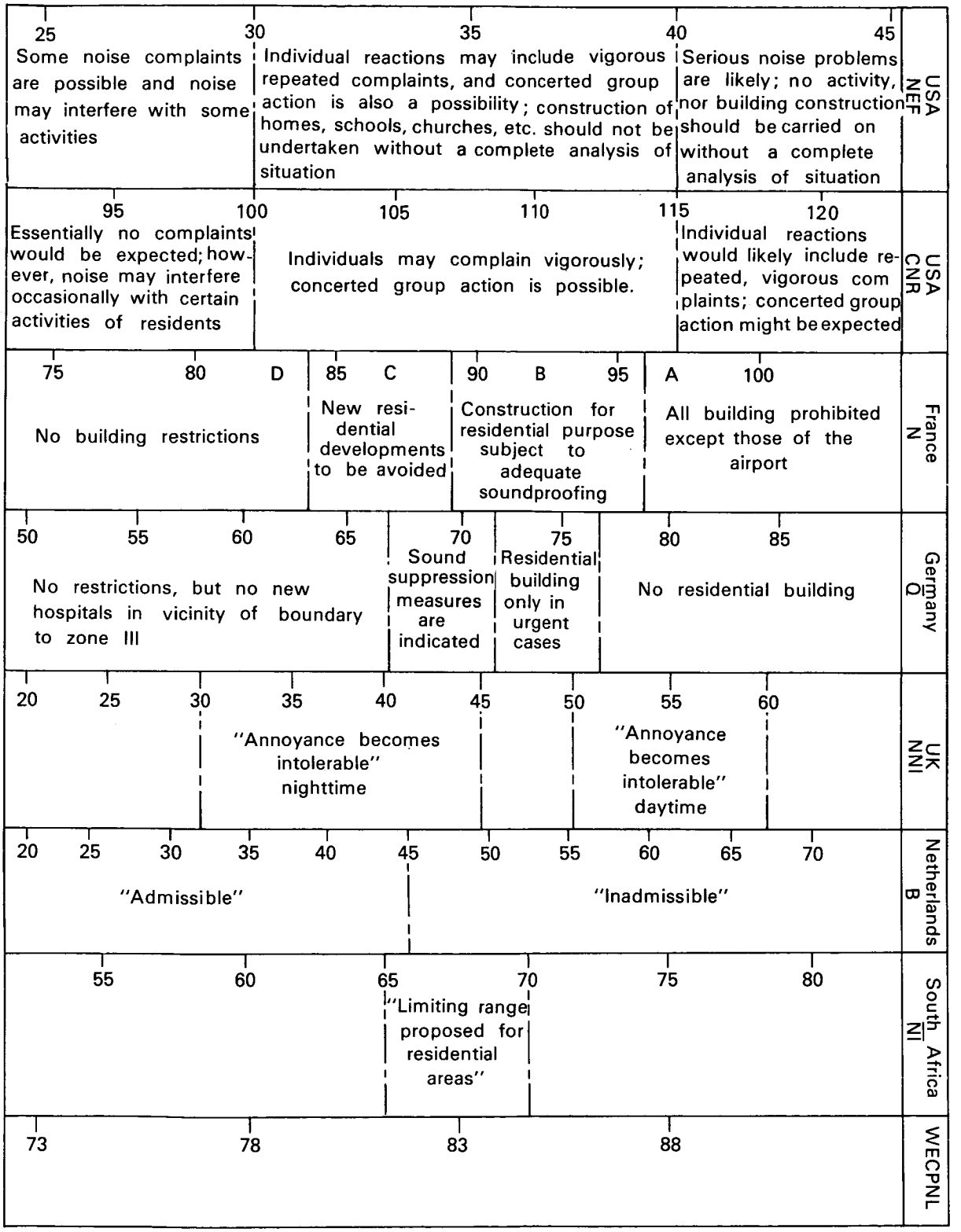


FIGURE 10.—Approximate relationships between noise exposure indices [33].

TABLE 5.—*Estimates and Observations of Sonic Boom Exposure*

Peak overpressure		Predicted and/or measured effects	
lb/ft^2	dyn/cm^2		
0–1	0–478	Sonic booms from normal operational altitudes: typical community exposures (seldom above 2 lb/ft^2, or 957 dyn/cm^2)	No damage to ground structures; no significant public reaction day or night
1.0–1.5	478–717		Very rare minor damage to ground structures; probable public reaction
1.5–2.0	717–957		Rare minor damage to ground structures; significant public reaction, particularly at night
2.0–5.0	957–2393		Incipient damage to structures
20–144	957×10^3–6.8×10^4	Measured sonic booms from aircraft flying at supersonic speeds at minimum altitude; experienced by humans without injury	
720	3.44×10^5	Estimated threshold for eardrum rupture (maximum overpressure)	
2160	1.033×10^6	Estimated threshold for lung damage (maximum overpressure)	

or observed during, and sometimes after, the acoustic exposure is terminated. Continuous exposures produce irritability and fatigue, which may persist for many hours after exposure.

Personnel should not be permitted in noise fields of 150 dB, as a rule, regardless of the hearing protection worn, because of possible adverse nonauditory effects. In environs near these levels, individuals who are susceptible to nonauditory or auditory effects should be monitored closely.

Impulse. Impulse noises, with signal durations of less than 1000 ms, commonly occur at peak positive pressure values ranging from 120 to 170 dB and greater for weapons fire, explosions, impact devices, and near field sonic booms. The relatively little energy in the very brief and rapidly rising and falling single impulse is significantly less effective in adversely affecting man than is steady-state noise. When high-level impulses occur repeatedly, however, their potential effect on the auditory system increases. Aerospace impulsive noises are likely to be single impulses and may be limited to low-level sonic booms for present generation systems.

Infrasound. Aerospace propulsion systems are a major source of intense infrasound during launch. Noise spectra containing intense low-frequency and infrasonic energy may excite body parts such as the chest, abdomen, eyes, and sinus cavities, and cause concern, annoyance, and fatigue. Psychologic responses accompanying these physiologic effects may result in even more complex reactions to such exposures.

In one comprehensive study, an attempt was made to systematically assess effects on various human responses of a number of existing high-intensity infrasound and low-frequency energy sources [97]. Representative spectra and levels of acoustic energy to which noise-experienced subjects were exposed in a series of separate tests are shown in Figure 11. Subjects wore hearing protective devices in those exposures containing high-level audiofrequency energy, but participated open ear or experimented with various types of protectors when the high-frequency energy was relatively low.

Subjective human tolerance data relating to the various noise exposures are also summarized in Figure 11. Voluntary tolerance limits were approached for frequencies below 100 Hz at levels of 150–154 dB as evidenced by symptoms of nausea, giddiness, coughing, choking, and the like. This confirms the maximum permissible exposure limit of around 150 dB for infrasound. The levels and behavior described are approach-

ing maximum subjective tolerance for the durations experienced, although subjects reported that tolerance limits had not been reached. Lower levels of exposure are presumed to be safe and/or acceptable for longer periods.

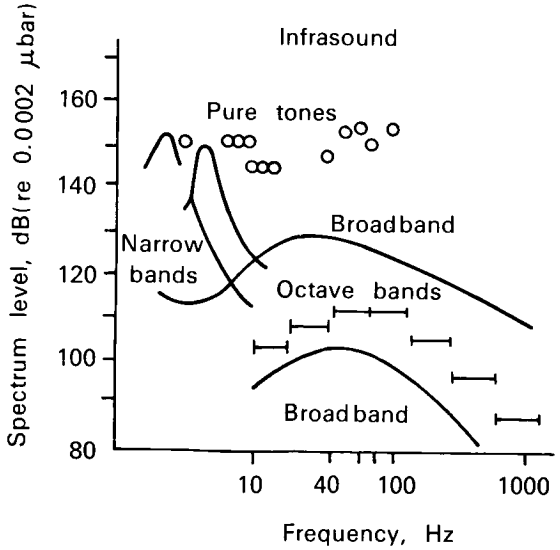
Ultrasound. Numerous ultrasound noise sources are present in aerospace activities and equipment such as rocket and jet noise, cleaning and measuring devices, drilling and welding processes, and power and communication control. Documented evidence of detrimental effects on personnel exposed to airborne ultrasound is scarce, in part because ultrasound is particularly amenable to atmospheric absorption and to noise control measures. The use of standard hearing protective devices essentially eliminates complaints of undesirable exposures.

Subjective symptoms of ultrasonic exposure were attributed earlier to apprehension of the exposed individual; however, recent evidence correlates symptoms with specific exposure conditions [2]. Energy at frequencies above about 17 000 Hz and in excess of 70 dB produces subjective effects. Individuals who cannot hear in this region do not experience the subjective symptoms. Women appeared to experience symptoms more often than men, and younger men more often than older men. This would appear to be consistent with the relative hearing abilities of the three groups and the described relationship with the energy above 17 000 Hz and 70 dB.

Many ultrasound exposures also contain substantial energy in the audiofrequency range and this lower frequency energy is commonly responsible for the complaints. In these instances, reducing the level of the audio portion of the exposure results in disappearance of subjective symptoms. Nevertheless, when airborne ultrasound at the position of the operator's head exceeds acceptable levels, subjective responses of ill effects may be expected from exposed personnel.

Noise Effects in Space Operations

The aerospace noises (described in the first section of this chapter) vary as a function



Tolerance data

Exposure	Observed behavior
0 to 50 Hz up to 145 dB	Chest wall vibration, gag sensations, respiratory rhythm changes, postexposure fatigue; voluntary tolerance not exceeded
50 to 100 Hz up to 154 dB	Headache, choking, coughing, visual blurring and fatigue; voluntary tolerance limit reached
Discrete frequencies	Tolerance limit symptoms
100 Hz at 153 dB	Mild nausea, giddiness, subcostal discomfort, cutaneous flushing
60 Hz at 154 dB 73 Hz at 150 dB	Coughing, severe substernal pressure, choking respiration, salivation, pain on swallowing, giddiness

Representative low-frequency and infrasonic test environments

FIGURE 11.—Infrasound exposures and corresponding subjective responses.

of the phases of the spaceflight profile and in their potential effects on the space vehicle crewmembers, ground-support crews, and residents in communities where the acoustic energy may intrude. A summary of space operations noise exposure and potential environmental impact is contained in Table 6.

Launch. At ignition, rocket exhaust noise suddenly attains very intense sound pressure levels which radiate very great distances from the launch site.

Flight crew. Noise reaches the crew compartment through structure-borne and airborne transmission. However, transmission loss in space systems such as Apollo is sufficient to reduce outside levels in excess of 150 dB to crew station levels of 120–125 dB. Additional protection from the acoustic energy is provided by crewmembers' space suit-helmet configurations. Sound levels at the ears of crewmembers range from a maximum of near 120 dB for the very low frequencies to 90 dB and less at the higher frequencies above 2000 Hz. As the vehicle lifts off, the level of propulsion noise decreases and that of aerodynamic noise increases. Approximately 60 s after launch, maximum levels of around 120 dB are again encountered at the crew stations. From 60 to 110 s, the noise gradually decreases to relatively low levels below 100 dB which are dominated by on-board systems.

Noise exposures experienced by crewmembers during launch are not of sufficient magnitude in the short exposure periods to create adverse biomedical or performance effects. The total very brief duration and maximum levels are attained only momentarily before they gradually decrease. Voice communication is the most vulnerable potentially threatened function under these conditions. Its efficiency is limited by the basic instrumentation system as well as the acoustic isolation and protection of the headset and special features of the microphone designed to effectively operate in noise environs. Voice communication system technology and the experience of several space launches in the USSR and US indicate that voice communication is adequate for current rocket-system launch noises.

Shirt-sleeve crew environments provide less whole-body protection against noise exposure than pressurized space suits. Whole-body exposure levels of about 125 dB may be sufficient to stimulate mechanoreceptors in some individuals. However, the training and experience of crewmembers, in addition to the very brief durations of the exposures, again suggest that no significant adverse effects will occur.

In general, space suit and shirt-sleeve crew environments contain intense acoustic energy during launch; however, the brief duration of the intense exposures and special provisions for the situation preclude adverse physiologic or psychologic effects.

Ground crew. The rocket noise at ignition is the most intense exposure experienced by ground crew personnel. Overall levels at the exhaust of vehicles such as Saturn V reach 175 dB decreasing to levels of 150–155 dB in the near field around vehicles as close as 182.9 m (600 ft) from the pad. The overall level decreases as the vehicle accelerates away from the launch site. Levels are of sufficient intensity to produce both physiologic and psychologic effects; however, such undesirable effects may be avoided easily with adequate protection of the ground crews. Concrete bunkers and other structures, as well as personal hearing protection, will provide sufficient protection to insure no adverse effects on crewmembers and their tasks. Ground crew voice communication may be assured with the use of appropriate hearing protector-voice communication systems.

Communities. The low frequency and infrasonic components of the launch noise propagate freely over great distances with relatively little attenuation. Sound pressure levels of 105 dB for energy below 20 Hz have been measured 16.09 km (10 mi) from a rocket site during launch. Communities as far away as 32.2 km (20 mi) clearly experience this low-frequency energy. It is possible that band pressure levels above 100 dB may excite vibration in structures and furnishings where people reside and work, causing disturbances and annoyance. Unless structures are so close to the launch site that minor property damage is precipitated, community acceptance may be relatively high for the infrequent exposures of present space operations.

Cruise. The controlling noise exposures in crew compartments are produced by on-board support equipment. Data from measurements taken in various crew areas in the Apollo command module indicate relatively moderate overall levels of 65–70 dB. These levels have proven acceptable, although not necessarily ideal, for space ventures of several weeks. No undesirable aftereffects have been reported due to noise.

Effects of exposure to relatively low level (60–70 dB) on-board noise for long-duration missions have not been fully described. In nonspace

TABLE 6.—*Summary of Space Operations, Noise Exposure, and Potential Environmental Impact*

Operation	Exposure	Spacecrew	Groundcrews	Community
Industrial support of space systems	Noise		Industrial noise exposure; 8-h d; compliance with DoL 90 dBA criteria	Potential problems where noises intrude into neighboring communities
Launch	Noise	Brief exposures of 125–130 dB SPL in crew area; less than 120 dB at ear; hearing protection and voice communication adequate with current systems; no adverse effects due to protection and brief exposures	Very intense levels as high as 150 dB SPL at 600 ft from pad; adverse effects without protection provided by structures and/or hearing protectors	Intense levels perceived at great distances; low frequencies of 115 dB 3 miles from pad; 105 dB at 10 miles; infrequent occurrence, brief duration contribute to acceptability
	Sonic boom	Not perceptible		
Cruise	Noise	On-board systems; ambient levels of 60 70 dB; noise levels higher during certain operation, levels tolerable for brief missions of several days; acceptable levels for missions of 6–18 mo not determined	Not applicable	Not applicable
Reentry	Noise	Noise similar to maximum aerodynamic noise at launch; greater duration, may need to assume voice comm capability for space shuttle type reentry	Brief, low-level exposures at landing	Negligible; infrequent
	Sonic boom	Not perceptible	Not perceptible, boom occurs some distance from landing site	Space shuttle-type reentry may expose large areas of Earth's surface; impact depends on number of people exposed, etc.
Static firing	Noise	Not applicable	Very intense levels of 150 dB at 600 ft; must use protection; durations and frequency of occurrence much greater than launch	Noise propagates far distance into communities; duration of runs; frequency of occurrence, time of day, etc., will contribute to acceptability; this may be worse community exposure situation

activities, noise exposure is generally considered "off" during sleep periods at which times the affected biologic systems may recuperate. During cruise phases of space flight, noise exposure is continual, recuperation periods are not available, and potential effects during many months are uncertain. The maximum permissible level originally proposed by Yuganov et al [141], of about 65 dB, is considered acceptable for 30–60 d missions; however, it may be too high for continuous exposures 24 h/d over many months and even years. He does indicate that 50–60 dB is desirable in general and required for sleep and rest, and that 85 dB or less is maximum for a 4-h watch.

Some on-board systems which may produce high noise levels are used only periodically and may not be reflected in the measured figures of 60–70 dB overall noise level. Systems which produce higher level noises for periods less than 24 h should be designed so that noise exposures comply with appropriate hearing damage risk and voice communication criteria (24-h criteria are preferable, otherwise use 8-h criteria).

Reentry. The impact of noise exposure during reentry is dependent upon the specific reentry vehicle and mode of operation. Current systems which utilize the atmosphere to retard the vehicle's speed upon reentry and a parachute delivery of the capsule to the Earth's surface involve noise exposures to only the crewmembers. Aerodynamic noise of approximately the same maximum levels experienced during launch will also occur during reentry. The duration of reentry exposure is longer than at launch. However, overall impact of the exposure appears to be no greater than during launch and is acceptable.

Future space systems are expected to reenter the atmosphere in an operational mode similar to that used in pilot-controlled high-performance aircraft. The maximum aerodynamic noise levels should not differ markedly from those of other systems on reentry; however, the exposure duration will likely be prolonged due to the relatively flat trajectory of the vehicle. Adverse effects of noise exposure on crewmembers are not expected.

Sonic booms are generated by the supersonic speeds of vehicles on reentry to the atmosphere from space. Parachute-delivered systems' landing areas are generally located in remote regions over land or water. Thus, the impact of the sonic boom on structures and people may not be a matter of major concern. Pilot-controlled systems will gradually decelerate and land at a few designated spaceport facilities, generally close to populated areas. Sonic booms are expected over large areas of the Earth's surface during these operations, the magnitudes of which are estimated to be small. Their impact on communities is not yet determined. Similar to sonic boom exposures in general, the acceptability is related to such factors as frequency, whether or not minor property damage accompanies the booms, and, of course, magnitude of the booms.

Sonic booms at launch will reach the ground only for certain flight trajectories. Launch corridors, selected for safety and other reasons, usually restrict the use of these areas by non-space-related personnel and activities. It is expected that the effects of sonic boom on structures and persons exposed during launch will follow the same rules for acceptability.

Static firing. Propulsion systems generate broadband noise which radiates from the test site during captive firing. Although the directivity may be significantly affected by exhaust deflectors, the nature of the physical stimulus is similar to that at ignition. Maximum energy is in the low and infrasonic frequencies, but intense groundborne noise is also present with the airborne noise during static testing. The frequency of the firings and duration of individual exposures during rocket engine test are considerably lengthened. If the test site is not sufficiently distant from residential communities, the possibility of vibrating buildings and creating noise annoyance may be significantly increased. Similar to launch noise, intensity levels close to the pad are hazardous for unprotected personnel.

Control Measures

Quantitative engineering analysis and prediction techniques are available for treating elements of the acoustic-exposure problem ranging from the noise source to the human receiver.

Control of noise at its source is most desirable from both engineering and human exposure standpoints. Since this form of control is not practical in many situations, other measures must be implemented in dealing with particular noise environments.

Source. The engineering capability to reduce noise exposure should be exploited as the initial step in control programs or efforts. Many sources, however, are not amenable to such treatment. Even after engineering treatments, levels are not reduced below limiting exposure values. Additional measures to control the noise at its source must be considered.

Noise exposure may be reduced, in many situations, by modification of the operational activity producing, or associated with, the noise. Shorter running periods, operations at slower speeds, appropriate rest intervals, and the like, may reduce power, noise level and duration, and total exposure. The overall health, safety, and well-being of personnel affected is the primary concern in a modification of activities to reduce noise exposure. Generally, this approach can be implemented without any compromise of the operational activity.

A practical and highly effective noise control measure is simply to increase the distance between a noise source and receivers. Major noise sources such as rocket and engine test, and maintenance facilities may be located far distant from occupied areas. The majority of such operations usually achieve noise reduction through remote siting of projects. The amount of attenuation to be expected with increased distance may be grossly estimated using the inverse square law which dictates a 6 dB change in sound pressure level for each halving or doubling of the distance from source to receiver. Small items of noisy equipment should also be physically located at the greatest practical distance from the receivers to take advantage of the distance attenuation provided by nature.

Receiver. Noise control is accomplished at locations occupied by personnel with sound treatment of the facility or vehicle and by providing personal protection against the noise. Sound treatment may involve increasing the transmission loss characteristics of structures against external noise, increasing the absorptive properties of work and living spaces against the noise, directly treating the internal source, or all of these.

Sound treatment in aerospace vehicles usually includes action against both internal (air conditioner, pneumatic pumps) and external (aerodynamic, engine) noise. Noise exposures may be below levels which threaten hearing yet be of sufficient magnitude to interfere with speech communication or cause general discomfort and annoyance. More effective sound treatment is then required. Sound treatment involving additional acoustic material to the vehicle is accomplished at a weight cost. Consequently, the amount of noise reduction realized in aerospace vehicles may be determined by compromise between weight cost and allowable exposures for crewmembers or speech communication capabilities. This compromise may be significantly influenced by the availability and use of personal ear-protective devices. Sound treatment of ground facilities is not ordinarily hampered by weight penalties, making noise reduction relatively easier to accomplish in this respect than in airborne systems.

Protection of the Organism

When excessive noise exposures cannot be reduced by generation and propagation noise control measures, general protection of the organism must be considered. Personal hearing protective devices are those inserted into the external ear canal or those that cover the external ear to reduce the amount of acoustic energy at the eardrum. The expected range of hearing protection (in dB) provided by good protective devices is summarized in Figure 12. Hearing protectors permit individuals to undergo more intense and longer duration exposures than with the unprotected ear and still remain within established health standards. Exposure criteria are essentially extended by proper use of hearing protection. The amount of protection obtained with these devices is limited by tissue and bone conduction of the head. Sound bypasses the protector and reaches the inner ear through tissue and bone pathways of the head [39].

Intense noise exposure may induce a variety of nonauditory effects including those on the abdomen, chest, internal organs, respiration, and vibrotactile sensitivity [71, 97]. Total head enclosures, which include antinoise helmets, will increase tolerance to noise influences primarily mediated via the auditory system and tissue and bone conduction pathways of the head.

Maximum general protection of the organism against the most intense noises may require antinoise suits or total body enclosures. An antinoise suit (such as that shown in Figure 13) worn with conventional hearing protectors provides additional protection and comfort against the whole-body effects of intense noise. Antigravity flying suits and space suits provide some additional protection and comfort for the organism against noise.

Hearing protection	Frequency, Hz				
	1-20	20-100	100-800	800-8000	> 8000
Earplugs	5-10	5-20	20-35	30-40	30-40
Earmuffs	0-2	2-15	15-35	30-45	35-45
Earplugs and earmuffs	10-15	15-25	25-45	30-60	40-60
Communication headsets	0-2	2-10	10-30	25-40	30-40
Helmets	0-2	2-7	7-20	20-50	30-50
Space helmet (total head enclosure)	3-8	5-10	10-25	30-60	30-60

Entries show approximate minimum and approximate maximum protection available from various devices

FIGURE 12.—Expected range of hearing protection for good protective devices.

Limiting Noise Levels

Aerospace noise sources generate acoustic energy over a wide spectrum ranging from below 1 Hz to well above 100 000 Hz. The differential effects on man produced by various segments of acoustic-exposure frequencies necessitate the definition of limiting noise levels for a number of portions of the spectrum. Generally, exposure limits may be defined specifically for infrasound

FIGURE 13.—Antinoise suit designed to provide general protection of the organism in intense noise.

(1–20 Hz), audiofrequencies (20–20 000 Hz), ultrasound (20 000–100 000 Hz) and impulsive sound. Some of the exposure limits considered are well-substantiated by experimental evidence and experience; others must be considered tentative until more evidence is forthcoming. Exposure criteria or guidelines are summarized for various categories of acoustic energy in Figure 14.

Infrasound

Range 1–20 Hz. Limiting noise levels considered acceptable are 150 dB at 1–7 Hz, 145 dB at 8–11 Hz, and 140 dB at 12–20 Hz. These values apply to discrete frequencies or octave bands centered at the stated frequencies. Maximum exposure duration is 8 min with 16 h rest between exposures. Satisfactory insert earplugs will increase permissible levels by 5 dB for the same exposure times; earplugs are strongly recommended for all intense infrasound exposures to minimize subjective sensations. Levels above 150 dB should be avoided even with maximum hearing protection because general nonauditory responses occur.

Range 20–100 Hz. The tentative limiting levels

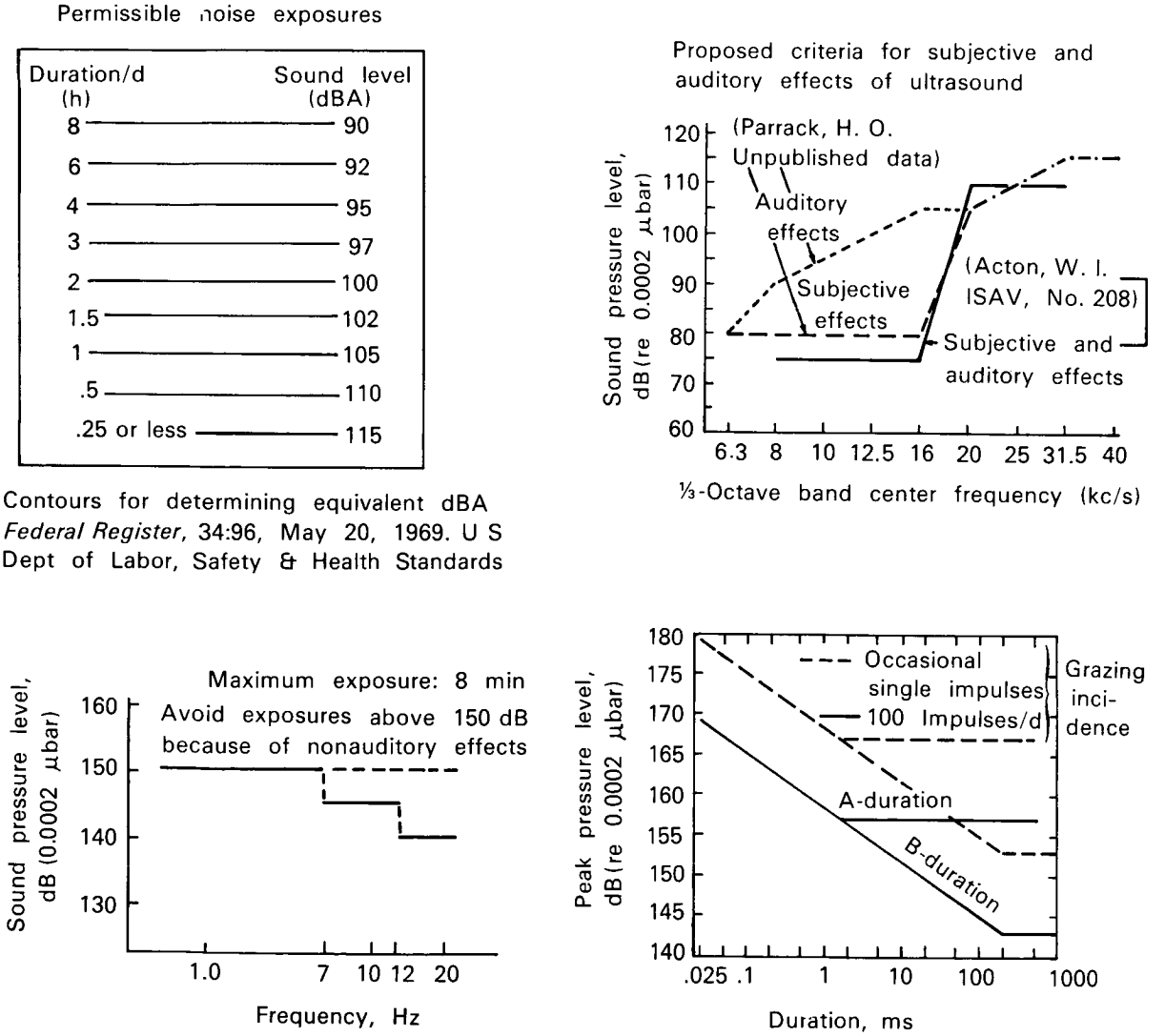


FIGURE 14.—Exposure guidelines for various categories of acoustic energy.

for this range for both discrete tones and octave bands is set at 135 dB for a single daily exposure of 20 min. This permissible level may be increased to 150 dB with the use of good earplugs for the same exposure duration. Again, the 150 dB maximum is intended to minimize nonauditory symptoms experienced by many individuals at these levels.

Audiofrequency

Range 100–6300 Hz. Damage risk for continuous exposure has been defined for up to 6 h by Borschevskiy [19] and for an 8-h workday by Kryter et al (CHABA) [74]. The limiting levels for typical workdays are considered compatible with unimpaired hearing for conversational speech signals after a work history of more than 10 years in the noise. Exposure criteria have been converted to equivalent A-weighted values in decibels (dBA) to simplify the measurement and assessment of noise-exposure risk. A-weighted values are currently in widespread use for noise monitoring purposes; however, for other purposes, such as engineering noise control, more detailed information about frequency content is essential.

Range 6300–20 000 Hz. Aerospace propulsion systems do not generate intense acoustic energy in this frequency range at locations occupied by personnel. Consequently, no limiting levels of noise are appropriate for rocket noise exposures. However, other aerospace sources may generate more intense energy in this region. Limiting values for subjective and auditory effects of ultrasound (determined independently by Parrack and Acton) are contained in Figure 14. There is good agreement among values for subjective effects; however, Parrack allows higher exposure levels from 6300 to 20 000 Hz than Acton does for auditory effects.

Ultrasound

Range above 20 000 Hz. Proposed criteria for energy in the frequency range above 20 000 Hz is also contained in Figure 14. Limiting effects in this inaudible range are confined to subjective symptoms such as malaise, headache, and fatigue. Compliance with the proposed values will greatly minimize adverse effects. Rocket propulsion noise in this frequency region dissipates rapidly and is not a problem. Personal hearing protective devices are very efficient against energy above about 8000 Hz. Use of these devices in ultrasound noise fields is usually sufficient to eliminate overexposure problems relating to hearing and to subjective symptoms of ill-feeling.

Impulse noise. Limiting noise exposure values for impulsive stimuli have been established and are presented in a form consistent with damage risk for continuous exposures in Figure 14 [15, 28]. Exposures which comply with these criteria should produce, on average, no more TTS than 10 dB at 1000 Hz, 15 dB at 2000 Hz, and 20 dB at 3000 Hz and above in 95% of the ears exposed. The curves represent criteria for a daily exposure of 100 impulses during any period ranging from 4 min to several hours. The criterion values are increased for fewer than, and decreased for more than, 100 impulses per day by a factor of about 1.5 dB for each doubling or halving of the number of impulses. In practice a 5-dB decrease in the allowable level must always be subtracted for those impulses which strike the ear at normal incidence.

Summary

Acoustic energy or noise is present in varying degrees from the time before launch of manned space missions until landing. In spite of the impressive quantity of work accomplished on the effects of noise on man, the noise problems of cosmic flight have not been fully resolved. Scientific knowledge coupled with the highly successful manned space programs of the USSR and the US provides the grounds for one to conclude, from a large base of objective evidence, that noise has not been a major limiting factor for space teams or the population through present generation systems and missions. Recommendations of permissible levels of noise for various phases of past missions have proved tolerable. Such levels, however, are not considered ideal and important questions concerning prolonged missions of many months remain to be answered.

THE VIBRATION FACTOR

Nature and Characteristics of Acoustic Energy

Vibration, in everyday language, means shaking, usually imposed by a mechanical agent such as the engine of a vehicle in which a person is riding, or by interaction between the vehicle and surface irregularities or air turbulence in the medium through which it moves. In physical terms, vibration may be defined [29] as a series of reversals of velocity, a process in which both displacement and acceleration necessarily take place. Disturbing vibration may reach man in several ways [50, 61]. It may affect man principally through a supporting surface such as an astronaut's or cosmonaut's couch; through some secondary contacting surface such as a headrest, sighting device, or control stick; through a fluid medium in which the body is immersed (akin to the acoustical transmission of noise through the body surface); or vibration may be disturbing indirectly, for instance, when the vibration of a space vehicle's instrument dials and pointers makes them difficult to read during launch. The chief descriptive parameters of vibration affecting man are frequency, intensity (amplitude), direction (with regard to the anatomical axes of the human body), and duration of exposure. A description of each follows.

Frequency. Frequency is an important descriptive parameter of vibration affecting man. The frequency of periodic (i.e., regularly recurring) oscillation is the number of complete cycles of motion taking place in a unit of time, customarily 1 s. The international standard unit of frequency is the hertz (Hz) which is 1 cycle/s.[2] Vibration in aerospace operations is often complex, irregular, or essentially random (e.g., the response of an airframe to turbulence) and consequently not obviously periodic in nature. Nevertheless, it is still possible and appropriate, with the application of spectral analysis techniques, to describe the motion in terms of frequency.

Amplitude. A second important characteristic of vibratory motion is its intensity or amplitude, i.e., the extent of the oscillation. When the vibration is a simple sinusoidal oscillation about a position of rest or equilibrium (the simplest kind of vibration), the amplitude is defined as the maximum displacement from that position. It is properly measured in meters but smaller metric units are often used for convenience.[3]

By extension, the term "amplitude" is commonly used with a qualifying word (e.g., "velocity-amplitude," "acceleration-amplitude") to describe the maximum or a related value of a vibrational velocity or acceleration. These quantities are determined by the frequency and the displacement-amplitude of a vibratory motion. In the case of sinusoidal vibration for which the frequency and amplitude are known, the corresponding values of velocity and acceleration may be determined with these simple formulas. Given the frequency, f, and the (displacement) amplitude, A:

$$\text{Velocity-amplitude} = 2\pi fA \qquad (1)$$

$$\text{Acceleration-amplitude} = 4\pi^2 f^2 A \qquad (2)$$

The same formulas apply approximately to narrow-band random vibration. Each successive time-derivative of displacement is obtained by an additional multiplication using the factor $2\pi f$; and the vibrational acceleration (a physiologically important parameter) corresponding to a given displacement rises with the square of the frequency of vibration.

A time-averaged or root-mean-square (rms) value of the intensity of a vibration must be computed, for example, when evaluating nonperiodic or complex vibrations. Many electronic vibration-measuring instruments yield an output proportional to the rms value of velocity or acceleration. In sinusoidal vibration, the rms value is $\sqrt{2}/2$ (0.707) times the maximum (peak) value. The relationships between sinusoidal vibration frequency, displacement, velocity, and acceleration are conveniently determined from the kind of nomograph shown in Figure 15 [50].

Directions and axes of vibration in man. The human response to a given vibration depends upon the point of application of the force to the

[2] This unit, cycle per second—c/s or cps—(replaced by Hz) is still in widespread use and commonly found in the literature on human response to vibration.

[3] In the English-speaking world, the inch (0.0254 m) remains in frequent use as the unit of displacement in vibration work.

body and the direction in which the force acts upon man. Directions of vibration entering the human body have received standardized definition [62] in relation to anatomical axes; the principal ones are illustrated in Figure 16. When evaluating vibration affecting man, the description of the vibration should apply to the force or motion at the point of entry into the body. It is important to beware of ambiguity which can arise, for instance, when vehicle vibration is measured at some point remote from man and is related to some frame of reference apart from the coordinate system of anatomical axes of the human body.

Time-course and duration of exposure to vibration. Human response is also influenced by the

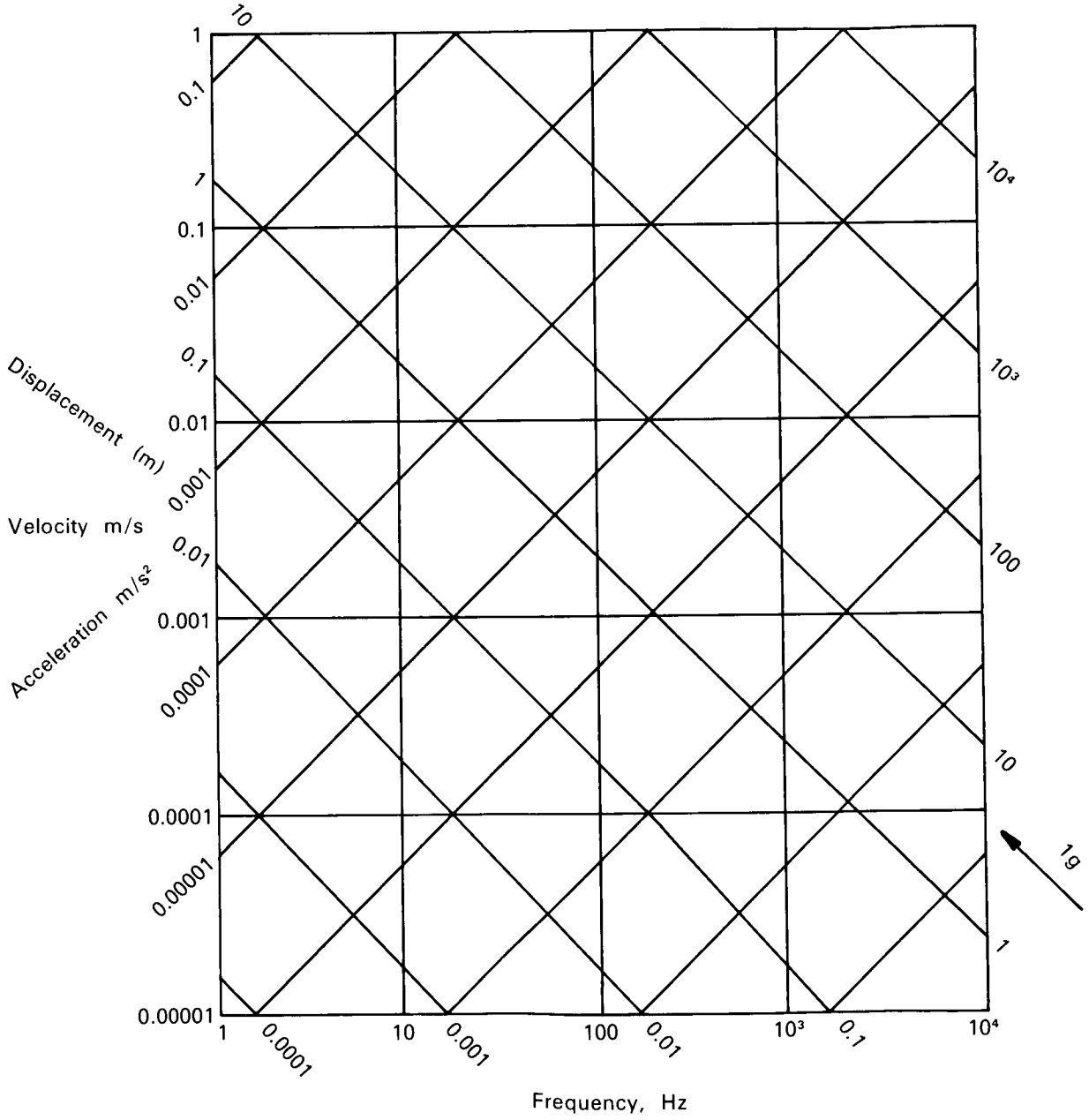


FIGURE 15.—Nomograph relating the principal parameters of sinusoidal vibration.

duration of exposure to a steady-state vibration or by the time course of a fluctuating or transient vibration. This aspect is considered in more detail in subsequent sections. In broad terms, human tolerance of continuous vibration declines with increasing duration of exposure [50, 61]. The extent to which this general tendency is mitigated by adaptation or habituation to vibration stress remains an open question, since little definitive research has been devoted to it so far. The expression, *long-term vibration*, is sometimes used (particularly in the US literature) to denote exposures exceeding 1 h. The corresponding expression, short-term (or short-duration) is not clearly defined but usually denotes exposures lasting 1 min to 1 h. Short-lived vibration, lasting for only a few seconds or a few cycles of motion, can usually be treated as transient vibration or shock motion.

Varieties of Vibration

The principal varieties of vibration observed in engineering practice are illustrated in Figure 17, showing representative waveforms and idealized spectra. Vibrations resembling these varieties can be experienced frequently in aerospace operations. The main distinction to be drawn is between deterministic and non-deterministic vibrations.

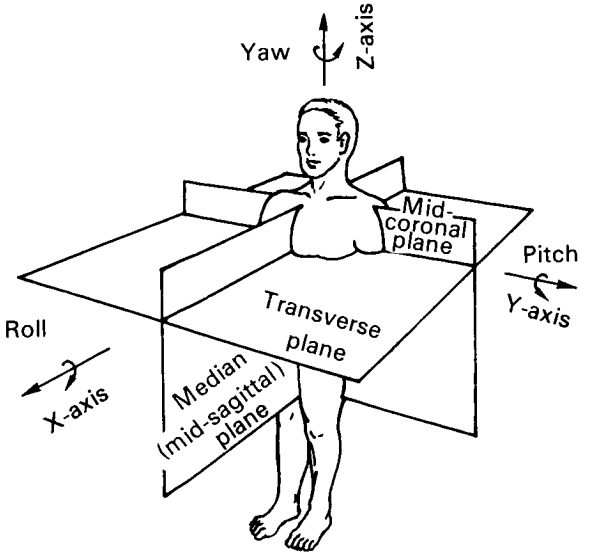


FIGURE 16.—Coordinate system used in biodynamics.

Deterministic vibrations. A deterministic vibration is one for which the magnitude of the displacement or its derivatives can be predicted for any instant from knowledge of its preceding characteristics (frequency, amplitude, phase angle). The simplest example of such a vibration is sinusoidal vibration, which has only a single frequency and, theoretically, a single line spectrum (see uppermost diagrams in Fig. 17). Although rarely encountered outside laboratory conditions, sinusoidal vibration is frequently approximated in practice (e.g., when a vehicle is vibrated by internal machinery running at a steady speed).

In many practical situations where machinery is running (e.g., space cabin conditioning equipment), complex harmonic vibration occurs. This is a deterministic vibration which can be regarded analytically as a mixture of two or more simultaneous sinusoidal vibrations. An example is in Figure 17(b). The lowermost component in the spectrum, called the fundamental, is not necessarily the most disturbing

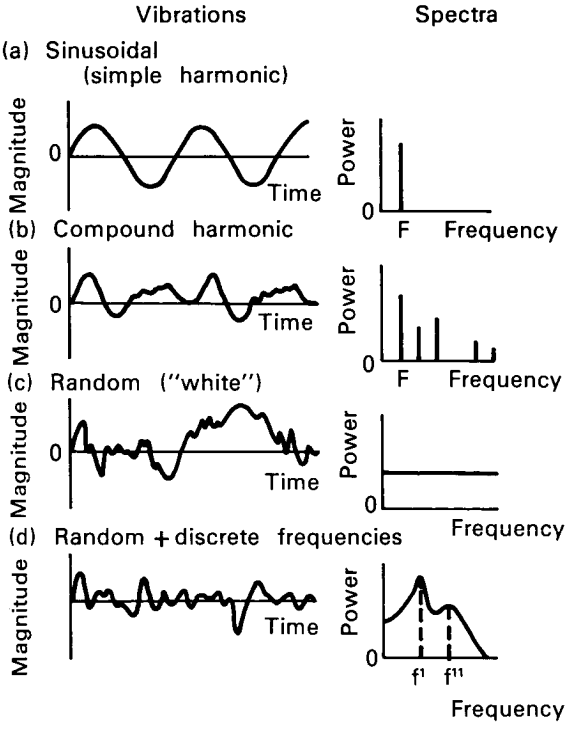


FIGURE 17.—Diagram of waveforms and idealized power spectra of typical varieties of vibration [50].

frequency component. The quality and biologic effect of such a vibration depend upon the relative, as well as the absolute, magnitude of each component and upon their phase relationships.

Nondeterministic or random vibration. When the vibration is irregular, lacking any recognizable periodicity, its time course is essentially unpredictable and is considered nondeterministic or, loosely speaking, random. Analytically, it has a continuous spectrum in which the energy of motion is distributed continuously and more or less uniformly over a range of frequency which can be of infinite extent. Certain sources of vibration, such as atmospheric turbulence, appear to be inherently random at source. When a vehicle with a flexible structure is subjected to random aerodynamic forces (e.g., during launch and ascent of a space vehicle), the crew is subjected to a composite vibration resembling that illustrated in Figure 17(d) [50]. In this case, one or more discrete frequency components, due to the aeroelastic response of the structure, are superimposed upon the essentially random input from the passing airstream.

Transient vibration and mechanical shock. When a vibrating system is subjected to an impulsive force or an abrupt displacement, the vibratory motion resulting within the system is typically short-lived (depending upon the amount of damping in the system) and may change rapidly with time before decaying to a negligible motion. Such a response is called transient vibration or shock motion (the latter term frequently connotes a relatively violent or potentially damaging response). Examples of transient vibration are the motions felt during separation of booster stages, during docking procedures in space, and upon impact with the ground or sea when a spacecraft returns to Earth.

Vibrating Systems and Resonance

Vibrating systems. Any mechanical system possessing the elementary properties of mass and elasticity can be set into internal motion by impressed forces. Engineering structures, such as buildings and airframes, and the living body are examples of such systems. Another essential property always present in any real system is damping, which is the physical process that opposes vibratory motion. Damping forces limit the vibration amplitude of a system subjected to maintained vibratory motion and bring a freely vibrating system eventually to rest. The system, if lightly damped (damping less than critical), will oscillate freely before achieving rest [50]. A lightly damped system, when forced to vibrate continuously at a characteristic frequency, is also capable of exhibiting resonance. In engineering and biodynamic practice, the value of damping in a system (including the human body) is customarily expressed as a fraction of the critical value.

Resonance. The simplest realizable vibrating system (a single mass, spring, and damper) is illustrated diagrammatically in Figure 18(a). The next simplest theoretical system is shown in Figure 18(b)—a two degree-of-freedom system. The characteristic response to forcing vibration as a function of frequency is illustrated to the right of each system. At a frequency or

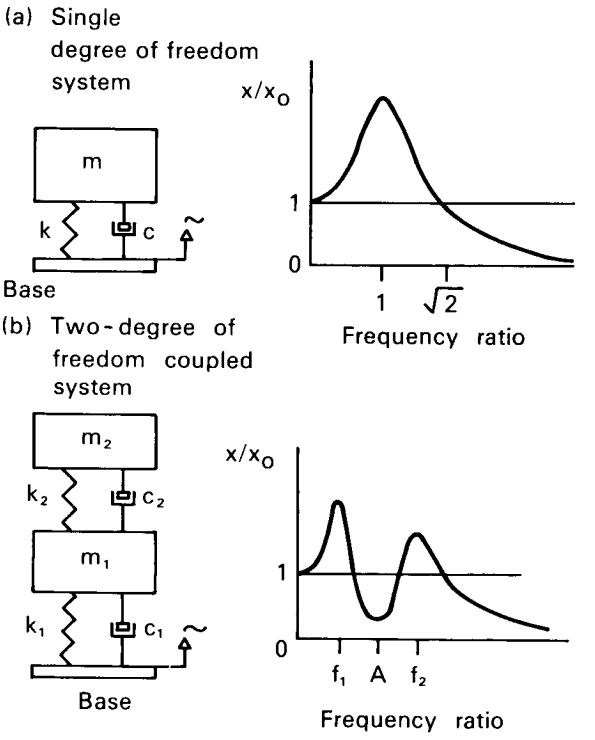


FIGURE 18.—Diagrams of simple vibrating systems and their responses to sinusoidal forcing motions applied to the base.

frequencies characteristic of any particular system, forcing vibration will elicit maximum response, i.e., maximum amplification of the impressed force or motion. It is said that the system resonates at that frequency. The degree of amplification at resonance is inversely related to the amount of damping in the system. The phenomenon of resonance, where relatively small forces at a critical frequency can sometimes excite large vibrations in a system, is often a nuisance in engineering and can be highly destructive. Much of the practice of vibration engineering is concerned with avoiding or suppressing resonance conditions. Biodynamic studies have shown that the human body is a complex vibrating system containing a number of resonant subsystems [36], some of which are illustrated diagrammatically in Figure 19. The characteristic response of man to low-frequency vibration in the z-axis [27, 35, 50] is illustrated in Figure 20.

The mechanical impedance of man determines the mechanical energy transmitted to the body in a vibration environment; consequently, it has recently been studied specifically with regard to the supine position (as in the astronaut's couch) and the simultaneous influence of sustained preloading accelerations of interest in current space operations [25, 133, 134]. Examples of responses observed under such conditions are in Figure 21. Such measurements and mathematical models have made it possible to predict changes in man's dynamic response to vibration in the weightless state—predictions, however, which still require verification from studies in space [133].

Vibration in Space Operations

Appreciable vibration is often present during flight in aircraft and space vehicles [50]. In certain operations, it can be a serious nuisance and threat to the safety and health of the aviator or astronaut. Troublesome vibration during space operations can arise from prime movers (rocket engines), from aerodynamic causes, and from auxiliary-powered equipment running in space vehicles. At source, the vibration problems in space vehicles are of the same general nature as those in aircraft [50]; but space vehicle vibration may disturb the astronaut in substantially dif-

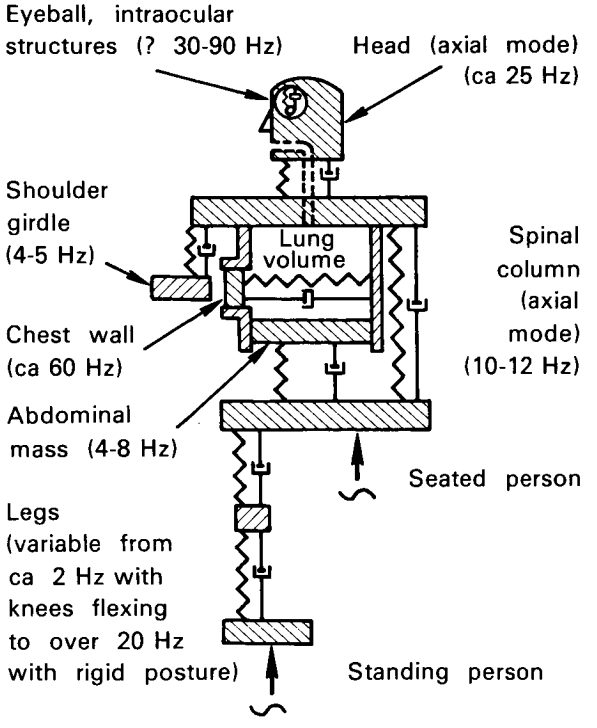


FIGURE 19.—Mechanical model (diagrammatic) of seated and standing man [35].

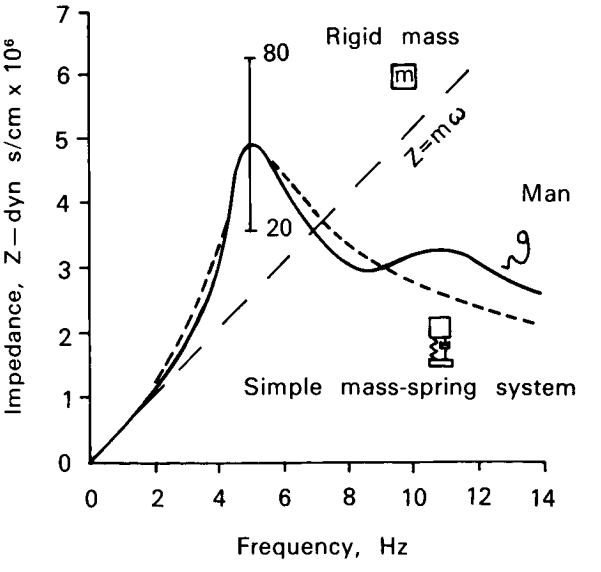


FIGURE 20.—Median z-axis impedance of seated male subjects [26].

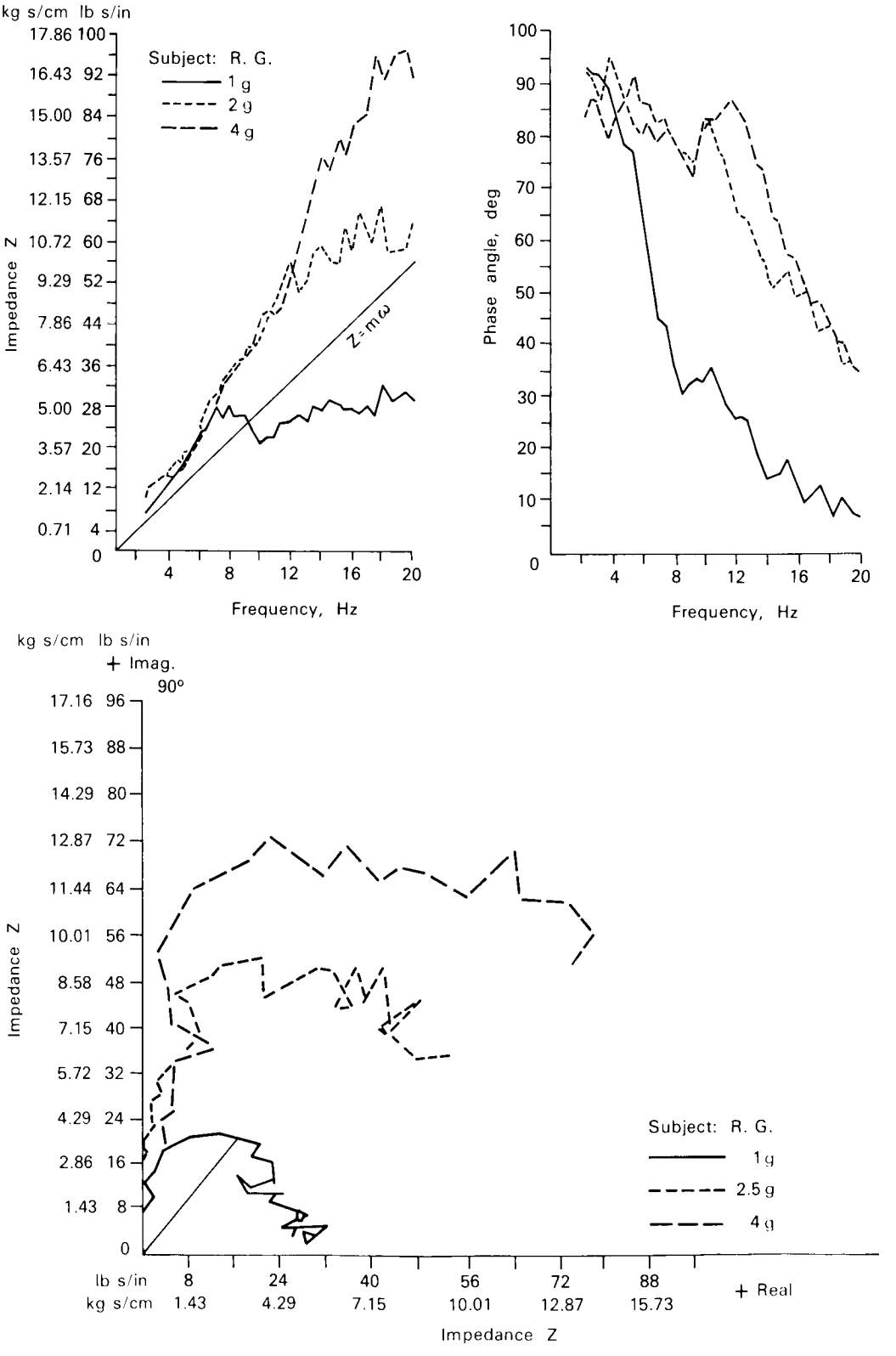


FIGURE 21.—Whole-body mechanical impedance under bias accelerations [134].

ferent ways and to varying degrees during different phases of a space mission.

Launch and ascent. When a large, multistage rocket vehicle carries man into orbit, intense distributed vibration enters the airframe of the vehicle and is transmitted to crew sites as vibration and noise. This vibration arises from the processes of combustion and the violent turbulence of the rocket exhaust. Low-frequency periodic vibrations, which can also disturb the astronaut in some vehicles, is caused by excitation of lateral bending modes and longitudinal ("pogo-stick") vibration of the vehicle structure. Such vibrations are induced by aerodynamic stresses of high-speed penetration of the atmosphere, rapid movement of fuel masses feeding the rocket engines, and operation of the flight guidance system. Transient oscillations are caused by impulses generated by starting up and burnout of the sequentially firing rocket engines in a multistage ascent, and by separation of stages. Major structural vibration frequencies in large spacecraft launching assemblies lie typically in the range 2–15 Hz [38].

Aeroelastically induced airframe vibration is worst during periods of transonic flight and maximum aerodynamic drag, which occur a minute or two after lift-off. After this maximal aerodynamic effect, the effect of the vehicle gathering speed is offset by the increasing rarefaction of the atmosphere. Changes in the pattern of vibration during ascent are also caused by loss of mass (due to consumption of fuel) and separation of stages. In some space vehicles, vibration during launch can be sufficiently intense to interfere with visual tasks such as reading instruments. The manner in which the astronaut is supported and constrained in a couch results in the vehicle vibration being transmitted to the whole body and to the head without attenuation normally provided by the upright body in the sitting position (as in an aircraft seat) [122, 128]. However, the increasing size and power of spacecraft launching vehicles is not necessarily accompanied by worsening vibration problems affecting the astronaut. Vibration during the launch phase in the recent US Apollo program was not apparently a serious nuisance, although noticeable by the astronauts [17].

Oribital and extended space flight. After the rocket engines have been shut down and the spacecraft is moving freely in a ballistic trajectory beyond the atmosphere, the primary sources of vibration (motors and aerodynamic forces) are absent. In the weightless state, the journey is subjectively motionless and essentially vibration-free. Vibration from secondary sources such as life-support equipment or other apparatus running in the spacecraft may, however, be noticed visually or upon contact with interior vehicle structures. Such vibration, even of low intensity, may be objectionable in some circumstances—when constantly or frequently present during extended space flights or long-duration orbital missions, or when the astronaut must perform a delicate task such as using an optical instrument.

Vibration in lunar and planetary expedition vehicles. The vibration problems in vehicles landing on, or exploring other worlds, remain largely hypothetical at present, although some problems can be anticipated [50]. Limited experience from lunar landings in the Apollo series revealed a vibration problem, minor so far, affecting vehicles of light construction standing on airless bodies. Astronauts on the Moon in the Apollo LEM vehicle occasionally reported that minor vibration and noise from equipment running in the module can be irritating and possibly interfere with rest and sleep during extended missions.

A peculiar problem can arise in connection with vehicle ride or with equipment vibration in vehicles standing on bodies with low gravity, such as the Moon or the planet Mars. Under reduced gravity, vertical vibrations of correspondingly lower intensity than required on Earth (± 1 g) are sufficient to lift an unrestrained rider from a vehicle seat, or shake objects loose from stowage. On the Moon, for example, vertical vibration with an acceleration-amplitude of only 0.11 g_{rms} will be intense enough to cause such an effect. The phenomenon has a bearing on the design of suspension and restraint systems for surface vehicles intended to ride on bodies lighter than the Earth, and on the stowage of loose objects likely to "walk" due to vibration from nearby running equipment.

Reentry and recovery. Vibration during return to Earth does not appear to be a problem with

current techniques, although the superimposition of severe, if short-lived oscillations upon the deceleration pulse has been anticipated in the case of flight instability developing during reentry of a ballistic vehicle [66]. This may be a renewed problem in some circumstances during reentry and descent of winged aerospace vehicles of the space shuttle type, which, after ballistic reentry, are flown to the ground as aircraft under the guidance of a human pilot.

One problem after landing is seasickness, peculiar to recoveries at sea—currently the practice in the US manned spaceflight program. This can trouble an astronaut left floating in the spacecraft in a choppy sea for too long before being extricated; for this reason, anti-motion sickness remedies are customarily carried. However, the problem would appear to be lessening with the increasing precision and speed of recovery procedures.

Vibration of ground and buildings during space operations. Heavy groundborne vibration, in addition to intense broadband noise, can be radiated over great distances when a large space vehicle is launched or when giant rocket engines are tested in captive-firing installations. Other installations and buildings in the surrounding area, up to several kilometers away, are set into low-frequency vibration by the combustion and exhaust noise of the rocket engines, which shakes the ground directly and is propagated acoustically as intense atmospheric waves. Buildings and exposed personnel can be affected by both routes of transmission. Attenuation by distance is the principal means of dealing with the problem.

Effects of Vibration on Man: Biodynamics

The physiologic and psychologic effects of vibration in man are caused by vibratory deformation or displacement of the organs and tissues of the body, so as to disturb their normal function and excite the distributed mechanoreceptors which mediate the vibration sense [47, 50]. Vibration also acts in a purely mechanical way to force differential motion to take place between man and his points of contact with tasks or his points of reference in the external world. The body is a complex vibrating system capable of resonance, so that many biologic actions of vibration are strongly frequency-dependent. From a biodynamic viewpoint, the frequency spectrum of mechanical vibration affecting man can be divided into two main regions: low-frequency and high-frequency responses [41, 49, 50].

Low-frequency response: body resonance phenomena. Human body resonance may be defined as the condition where a forcing vibration is applied to the body at such a frequency that some anatomic structure, part, or organ is set into measurable or subjectively noticeable oscillation of greater amplitude than that of related structures [50]. It may be studied by direct observation and by mechanical impedance and transmissibility techniques [27, 35, 50]. The body can be visualized, and modeled analogically, as a complex vibrating system with many degrees of freedom (Fig. 19). A lumped-parameter approach is appropriate to its modeling at frequencies below 50 Hz [36, 41, 109]. The excitation of particular modes of vibration in man by continuous vibration or by impact forces depends to a great extent upon the direction of vibration and upon such other physical factors as the person's size, build, posture, and degree of tension in the skeletal musculature [50]. Body resonance can also be influenced by external restraints and loads applied to the person and by dynamic interactions between the body and resilient supports, such as a springy seat.

Extensive work in the US and elsewhere has established that the principal resonance of the seated, standing, or recumbent human body vibrated in the z-axis occurs at a frequency of 4–5 Hz, and that this response is reflected in the frequency-dependence of many physiologic and psychologic human reactions to whole-body vibration [27, 35, 50, 61]. The same response is also a major factor governing the frequency-dependence of human voluntary tolerance of severe z-axis vibration [89]. The anatomical basis of the resonance is complex and not yet entirely clear. At least two major anatomical systems may be involved (depending on the degree of restraint)—the thoraco-abdominal system (the principal controlling element) and the pectoral girdle.

A second important resonance in man subjected to z-axis vibration or impact occurs in the region of 12 Hz, which can be demonstrated as a local impedance maximum (see Fig. 20) or as a phase resonance [27, 50]. This resonance appears to be associated with axial compression of the torso and to be controlled by the elastic properties of the spinal column and its associated musculature. It is of significance mainly in relation to human tolerance of severe z-axis impacts and cumulative long-term exposure to z-axis vibration such as in rough-riding vehicles. Other resonances of smaller structures are excited by vibration at higher frequencies, some of which are illustrated in Figure 19.

When man is vibrated in the x- or y-axis, typically by horizontal vibration of a seat or of a floor upon which he is sitting or standing, the principal resonance occurs in a new mode—a body-bending mode at 1–2 Hz. Accordingly, x- or y-axis vibration is most disturbing at such frequencies, in contrast to z-axis vibration, which is most disturbing at about 5 Hz. These differences in the human dynamic response are reflected in the subjective response and in the effects of vibration upon performance. The influence of vibration direction upon the human frequency-response to vibration is, in general, of sufficient magnitude to require different exposure limits [50, 61].

Nonlinearity and biasing accelerations. The amplitude response of the body to z-axis vibration at frequencies around the principal resonance (5 Hz) appears to be fairly constant up to acceleration amplitudes of the order of 0.5 g [49] but somewhat reduced at higher acceleration levels for both z- [26] and y-axis vibration [59]. Some nonlinearity may be accounted for by involuntary muscular tensing during severe vibration at low frequencies.

In certain circumstances, men are vibrated while simultaneously being subjected to acceleration or altered gravitational conditions. During space flight, body weight is altered by the forces of launch and reentry; weightlessness supervenes during orbital and interplanetary flight. Reduced gravity acts when the astronaut is standing or riding upon a lighter body such as the Moon or in the synthetic gravitational field of a rotating space station. Most studies of the human biodynamic response to vibration have, of course, been carried out in Earthbound laboratories, where the body responds under the normal force of gravity. Some recent work, however, has shown that, when man is subjected to accelerations greater than gravity, his biodynamic response to vibrations applied simultaneously in the same direction (the z-axis) is altered. Under accelerations of up to $+4\ G_z$, impedence measurements during z-axis vibration in the range 2.5–20 Hz have shown that the acceleration compresses and stiffens the body so as to raise the resonant frequencies of man and possibly introduce new resonances [133, 134].

High-frequency response: wave propagation in the human body. At frequencies above about 50 Hz, the response of the human body to impressed vibration can be visualized as that of a continuous viscoelastic medium of propagation rather than as a lumped-parameter system [41]. As the frequency rises into the kilohertz range, the propagation of vibration within the body tissues progressively becomes increasingly acoustical in nature, i.e., at high frequencies, most of the vibratory energy entering through the body surface is propagated through the tissues as compressional waves.

Physiologic Effects of Vibration

Physiologic effects of vibration fall into two broad categories [49, 50]. In the first are those responses attributable directly to the differential vibratory motion or deformation of the organs or tissues of the body. Such responses are mainly frequency-dependent and can be related to body resonance phenomena. In the second category of response to vibration are nonspecific generalized reactions, i.e., reactions to stress in general, not specific to the physical nature of vibration. The latter reactions are not markedly frequency-dependent, and appear to be related predominantly to the overall severity of the vibration exposure and its cumulative duration.

Systemic Effects of Whole-Body Vibration

Cardiopulmonary responses. Whole-body vibration of moderate intensity (above about 0.1 g_{rms})

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induces the vegetative manifestations of alarm or mild exercise, with increases in heart and respiratory rates, pulmonary ventilation, and oxygen uptake [49, 50]. Such changes are associated with raised metabolic activity due to increased activity in the skeletal musculature in maintaining the posture during vibration, but other reactions are evident during severe vibration. Under certain conditions, strong whole-body vibration can induce hyperventilation, which is probably due to a centrally mediated reflex response to the widespread vibratory stimulation of somatic mechanoreceptors, including those in lung and the respiratory passages [30, 50, 77]. The response exhibits features of a classical (Pavlovian) conditioned reflex response to a strong environmental influence; it can be blocked in man by light general anesthesia [77]. A pronounced hyperventilatory effect in man, with symptoms and signs of hypocapnia, can be produced by a few minutes of z-axis vibration at acceleration-amplitudes above 0.5 g in the range 1–10 Hz [31].

Cardiovascular responses during vibration. Increases in heart rate are commonly observed in animals and man during whole-body vibration at infrasonic frequencies, but the magnitude and time course of the response are highly variable between subjects and with the prevailing heart rate before vibration [50, 57, 112]. Heart rate changes during vibration are not necessarily correlated with changes in blood pressure [24, 57]. As a rule, however, increases in heart rate, cardiac output, and arterial blood pressure which are observed resemble those in response to moderate exercise [57] or alarm [34]. Local vibration of hands or feet can induce peripheral vasoconstriction, with restriction of blood flow in the extremity. A Soviet investigation [67] has shown that this action can be opposed or abolished by warming the same part.

Metabolic and endocrinological effects. Various changes in cellular and biochemical constituents of urine and blood have been observed in animals and in man in response to sustained low-frequency, whole-body vibration. In general, these changes appear to reflect a nonspecific response to the stress [11, 49]. Certain endocrinological changes in animals, involving the adrenal, thyroid, and other endocrine glands [108] appear also to be a generalized stress response. The question of protein and carbohydrate metabolism and metabolism of certain vitamins has attracted considerable interest in the Soviet Union and elsewhere. Animal and human studies have revealed mild disorders or abnormalities of various metabolic indices in response to occupational-type vibration stress [10, 18, 67, 75, 84, 108, 110, 130, 139, 140].

Sensory and Neuromuscular Effects of Vibration

Sensory mechanisms. Mechanical vibration is perceived over a much wider range of frequency than is occupied by the sensation of hearing; more than one kind of receptor organ is involved [47, 49, 50]. Mechanoreceptors of the body respond to vibration in various overlapping frequency ranges, differing both in the effective bandwidth of their response and the degree of temporal integration of information they transmit to the brain. The principal vibration-sensing organs in man are the cutaneous receptors subserving the vibrotactile sense [93, 98], the mechanoreceptors distributed in deeper structures (especially muscles, tendons, joints, and the visceral organs and their attachments) [50, 93], and the vestibular organs [14, 50].

Effects of vibration on muscular and postural mechanisms. Several studies have related increases in manual or digital tremor or postural sway of the standing person to heavy regional or whole-body vibration in the 1–100 Hz range [50, 80, 81, 94]. Some workers have postulated that such effects are due to vibratory overstimulation of the receptors and to competition in the neural pathways subserving both postural regulation and the low-frequency somatic and vestibular vibration sense. However, similar responses (especially increased digital tremor) are observed under other conditions, and the effects are not necessarily specific to vibratory stimulation. Increases in sway and tremor can be observed in states of high arousal and in fatigue associated with sustained, high workload and environmental stress not accompanied by strong motion stimuli [102].

Mechanical vibration of the whole body or of individual postural muscles or their tendons elicits tonic reflex contraction, while phasic spinal reflexes (e.g., tendon jerks) sometimes appear to be depressed or inhibited. These phenomena, observable over a wide range of vibration frequency from around 10 to over 200 Hz, have been studied in man as well as in animals (including decerebrate preparations) [50]. The tonic reflex contraction is mediated by vibration-sensitive receptors in muscle itself, chiefly (but not solely) the primary spindle endings [92]. The response, apparently mediated by a polysynaptic pathway involving higher centers including the cerebellum, can be influenced by various factors operating supraspinally. Moreover, some degree of voluntary inhibition can be achieved [91].

Local low-frequency vibration of postural muscles in man does not appear to alter the reflex excitability of the muscle, nor the character or strength of the maximal volitional response [52], at least in short-term exposures. Soviet work, however, in examining the occupational hazard of prolonged exposure to the vibration of hand-held power tools, indicates that some kinds of vibration exposure may lead to alterations in peripheral neuromuscular function in the long term [22, 76, 88, 127].

Effects of vibration on the central nervous system (CNS). Qualitative observations suggest that vibration can alter the level of arousal in various ways (as can noise), depending upon the physical characteristics of the vibration and nature of the subject's activity at the time of exposure. Low-frequency (1–2 Hz) oscillations at moderate intensities can be soporific in man, while stronger vibrations, higher frequencies, and inconstancy of the stimulus are arousing. A considerable degree of adaptation or habituation to steady-state vibration (e.g., the drone of aircraft or shipboard vibration) can be achieved, provided the stimulus is not changed or interrupted. Habituation to vibration is probably a central phenomenon, although some adaptation may occur at the receptor level. Central factors appear to play a role in the reactions of animals to extreme vibration stress. The lethality of intense whole-body vibration (±10 g at 25 Hz) in mice is enhanced by centrally acting stimulants (dextroamphetamine) and reduced by central depressants (chlordiazepoxide; reserpine; barbiturates) [12]. Animal studies conducted in the Soviet Union showed that vibration stress responses include fluctuations in the oxygen uptake of cerebral tissue [85]. In man, industrial vibration stress may be associated with nonspecific alterations in function of the CNS, possibly contributing to industrial fatigue and affecting occupational health [9, 95, 124]. Soviet work has also indicated possible synergistic effects between the actions of vibration and other physical agents on the nervous and endocrine systems. Such agents acting in combination with vibration include noise [9, 90] and ionizing radiation [79].

Motion sickness. Motion sickness (kinetosis) is primarily a response to varying acceleration or to oscillations in the frequency range 0.1–1 Hz [50], but the response depends heavily upon conditioning in man. Motion sickness associated with space flight is dealt with in Volume II, Part 2, Chapter 4, and will not be considered further here.

The electroencephalogram (EEG) and other electrophysiological recordings during vibration. The EEG [4, 101], electrocardiogram (ECG) [111], and electromyogram (EMG) [52] can all be recorded in man during vibration. Sufficient care must be taken however, in the selection and placement of instrumentation in order to guard against vibratory motion artifacts in the recording. The nature of the synchronous activity recordable at frequencies related to that of vibration in the EEG remains an open question [50, 101]; it has been contended that vibration evokes synchronous neuronal activity in certain brain structures [4] but such activity is difficult to distinguish from recording artifacts. Abnormal EEG recordings can be observed during vibration stress as the result of indirect physiologic mechanisms, such as hyperventilation or fluctuations in the oxygen metabolism of the cerebrum [85]. Ursoniu et al [131] have reported EEG changes of uncertain significance, following occupational exposure to hand-transmitted vibration in workers using pneumatic hammers.

Psychologic Effects of Vibration

Several substantial reviews of the subjective and performance effects of vibration have been published in recent years [49, 50, 58, 115, 121]. Accordingly, only a brief summary of the principal psychologic effects of vibration on the organism will be given here.

Subjective Reactions

Subjective reactions to vibration depend greatly upon individual sensitivity and upon the circumstances in which the vibration is felt [54]. While vibrations just above the threshold of perception may be objectionable in some situations (e.g., in an orbiting observatory), quite severe levels may be tolerated for a short time when the motion is, so to speak, *natural* to the situation (e.g., during the launch phase of a space mission). It is therefore very difficult, if not practically impossible, to establish simple or universally applicable limits of vibration according to subjective criteria, even in so restricted a field as astronaut comfort. Nevertheless, extensions of the concept of *reduced comfort* [61], and the tentative limits which have been drawn up according to that criterion, will serve as a guide in this connection.

Subjective rating and psychophysical estimation of vibration. Numerous attempts have been made since early in the 20th century to establish sets of curves of equal disturbance or discomfort due to vibration for the purposes of ride engineering in various branches of transportation [20, 47, 49, 50, 53]. These attempts have made use mostly of empirical, verbally structured rating scales. Such methods have important drawbacks, such as difficulty of standardizing meaning (even in the same language) and hierarchical relationships of such terms as "disturbing," "disagreeable," "uncomfortable," "alarming," and so on. Moreover, there has been little agreement between investigators regarding the end point of human acceptance of vibration in subjective experiments [50]. End points have, for example, included the appearance of physical symptoms, reluctance to continue vibration for unspecified reasons, and interference with a specific activity such as reading.

Psychophysical methods using such techniques as vibration magnitude estimation and intensity matching have, in recent years, shown considerable promise, enabling the construction of equal-sensation contours for vibration analogous to equal-loudness contours for noise [50, 96, 123]. This approach assumes that the growth of vibration sensation magnitude obeys a power law of stimulus intensity of the same general type that Stevens has demonstrated for other modalities of sensation. Thus, Stevens' scaling methods accordingly are assumed appropriate to whole-body vibration intensity judgments—as indeed they have been shown for cutaneous vibrotactile sensitivity [132].

Figure 22 shows a comparison between data obtained by Shoenberger and Harris [123] using intensity matching and magnitude estimation techniques during z-axis whole-body vibration of men in the frequency range 3.5–20 Hz. There is satisfactory agreement between the results from each method, which show the de-

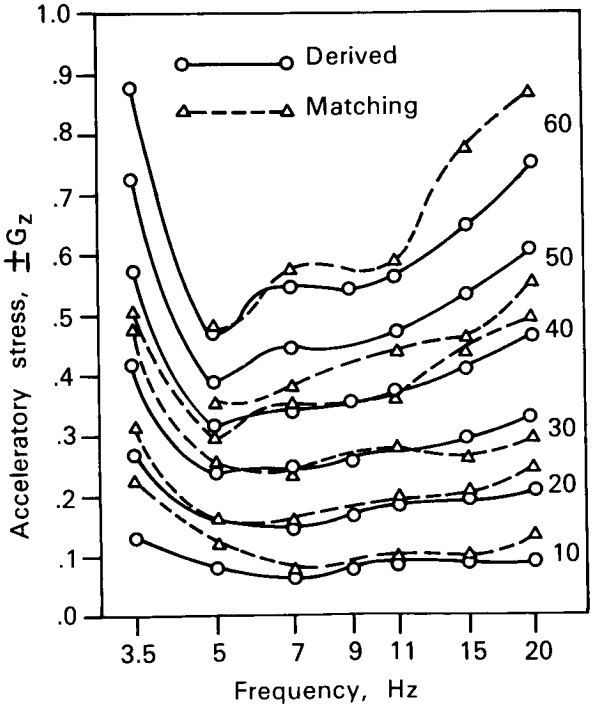

FIGURE 22.—Intensity matching and equal subjective magnitude curves for z-axis whole-body vibration of seated man [123].

pression of thresholds at frequencies in the region of 5 to 10 Hz. This phenomenon becomes more pronounced as the level of vibration is increased and at high intensities (about 0.5 Gz and above), these data accord well with earlier work [89] on the limits of voluntary tolerance of *z*-axis vibration.

There has been little work so far on dual frequency or other composite vibrations [50, 61], but from recent studies of subjective responses to low-frequency compound harmonic vibration, it appears that a form of sensory masking can occur [21, 82] where the presence of one sinusoidal component can alter the threshold for another.

In the dynamic range of human sensitivity to vibration, again, there have been few reliable determinations of human thresholds of sensation for oscillatory motion. These determinations are rather difficult to make, since it is technically difficult to achieve acceptably pure vibration of the whole body at threshold levels and to screen the subject from sensory cues to motion other than the vibration sense in question. Various observational and experimental evidence, however, shows that the human threshold of perception for rectilinear whole-body vibration in the range of 0.1–10 Hz is remarkably low—of the order of 0.01 m/s^2 (or about 1/1000 g) [47, 50]. The threshold for rotational oscillations at frequencies below 1 Hz is approximately $1\,°/s^2$ for motion about the z-axis and may be substantially lower in some subjects [23].

At the other extreme of the range of vibratory sensation, the threshold of pain or gross bodily discomfort during short-term human exposure to whole-body vibration in the 1–10 Hz range is approximately 10 m/s^2 (about ± 1 g) [89]. Thus, the dynamic range of normal human sensation of whole-body vibration in the most sensitive frequency range is approximately 60 dB, which contrasts with a range of some 130 dB for audible sound perceived by the ear.

Effects of Vibration on Performance of Tasks

Heavy vibration or oscillatory motion of man can affect the performance of tasks in several ways [42, 43, 50, 58, 115, 121]. First, vibration of man or of the elements of his task makes it more difficult to comprehend visually presented information; second, vibration disrupts precise movements, particularly of the arm and hand. Flight experience [50], as well as some laboratory experiments, show that heavy low-frequency vibration can also degrade performance centrally, acting in a nonspecific way as a distracting and fatiguing agent, as does noise [48], but such a mechanism is not easily demonstrated by experiment. Moreover, caution should be exercized when interpreting experimental results that appear to show central or time-dependent effects of vibration upon performance, for the effects in question may not be the result of mechanical influences alone. The effect of environmental stressors such as vibration and noise is governed by numerous psychologic factors not necessarily related to the nature of the agent; when stressors are acting in combination, which is frequent in aerospace operations, the effect is not necessarily simply additive—some combinations may act synergistically, others antagonistically upon performance [42, 50, 55, 63, 137].

Experience from flight tests and flight simulation. A substantial amount of insight into the effects of turbulence encounters and aircraft vibration upon performance of tasks by aircrew has been gained from flight experience and experiments in dynamic flight simulators [50, 78]. In summary, aircraft motions in response to external sources of vibration occur mainly at frequencies below about 2 Hz, and are associated by aircrew with:

- discomfort and progressive fatigue
- increased effort by pilots to avoid or correct inadvertent control movements
- difficulty in using navigation instruments
- difficulty in interpreting flight instrument information
- disorientation, occasionally.

Higher frequency (2–10 Hz) airframe vibrations are associated with:

- difficulty in reading instruments or carrying out other tasks calling for final visual discrimination (e.g., visual search, reading CRT display)

interference with some manipulative tasks (e.g., writing, setting cursors on hand-held navigation aids)
general discomfort and progressively worsening fatigue on long missions.

Kindred problems may be anticipated in certain phases of space flight, such as descent through the atmosphere of space shuttle-type vehicles which are flown as aircraft.

Laboratory studies of performance during vibration. Current guidelines for preserving human operational efficiency during whole-body vibration [61] are based largely upon studies of human performance decrements measured during exposure to vibration on laboratory machines. These experiments have been mainly short-term studies showing strongly frequency-dependent effects of low-frequency (1–30 Hz) vibration upon the performance of visual and psychomotor tasks. In relation to manned space flight, these effects are most likely to be important during a mission's launch and reentry phases. Laboratory research into the effects of vibration on visual and psychomotor performance (the threshold for impairment of which is an acceleration-amplitude of the order of 1 m/s^2 (± 0.1 g) in the 1–10 Hz range) has been reviewed extensively in many other publications [42, 50, 58, 60, 115, 116, 121, 122, 128].

Effects of vibration on verbal communication. Human speech can be markedly distorted or interrupted by heavy vibration or jolting of the speaker. This can add to communication difficulties in some phases of space flight, particularly when high levels of masking noise are also present.

Whole-body vibration of speakers at frequencies below 20 Hz, and especially in the range 4–10 Hz, degrades the quality and alters the pattern of human speech, depending upon the speaker's posture and the direction, intensity, and periodicity of the vibration [103, 104, 105]. Within the critical range of frequency, intelligible speech becomes increasingly difficult to maintain as the level of whole-body vibration is increased above about 0.3 g_{rms}. Intelligibility under such conditions can be helped somewhat by maintaining an adequate speech level (speech/noise ratio), by training speakers and listeners to communicate in the presence of vibration-modulation of the speech, and, possibly, by the use of restricted vocabularies for such communication. Whole-body vibration at infrasonic frequencies, even at severe levels, does not appear to have a significant effect upon hearing [51].

Pathologic Effects of Vibration

Intense vibration can cause pain and injury in the living body [50]. Acute traumatic effects, dependent primarily upon the intensity and the frequency of the vibration, are most likely to occur when severe vibration is applied to the unprotected body at frequencies related to the principal system and organ resonances. Long-term or repeated exposure to moderately severe but not immediately damaging levels of vibration can also be a hazard in certain pursuits and occupations, such as driving rough-riding vehicles [114] or flying strongly vibrating helicopters [119]. In such situations, the effect or cumulative duration of exposure to the stress appears to be a primary factor governing the development of injury or disease.

Severe acute whole-body vibration exposure. Animal studies on the lethality of severe whole-body vibration (in the range 1–20 g at 1–50 Hz) have shown that intense shaking causes hemorrhagic injury to many of the soft organs in the body. Roman [113] has shown that in mice, the lethality of whole-body vibration is strongly frequency-dependent (Fig. 23), being greatest at frequencies associated with the main thoraco-abdominal resonance. The most common pathologic changes in small animals killed by vibration are hemorrhagic damage to lung parenchyma and myocardium and bleeding into the gastrointestinal tract. Superficial hemorrhage of the brain and kidneys has been less common. There is some evidence that endocrinologic factors (particularly the level of male hormones) may predispose animals to lethal vibration stress [117, 118]. Lethality may also be influenced by other physical agents acting at the same time as the vibration, such as ionizing radiation and hypoxia [86]. Based on animal experiments, the pattern of injury with acute

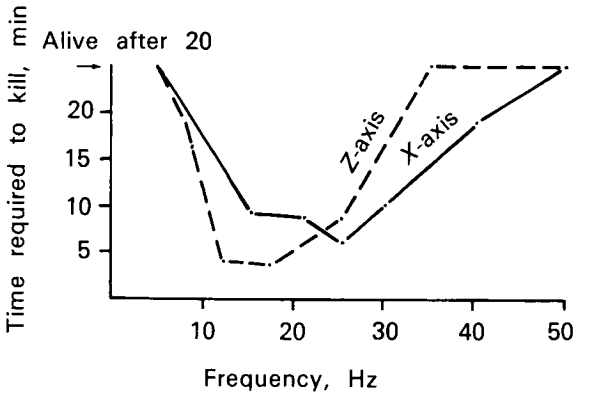

FIGURE 23.—Effect of frequency of vibration on average time required to kill mice [113].

human exposure to injurious levels of whole-body vibration would resemble that resulting from impact accelerations of comparable severity. The probable mechanisms of injury include tearing of the suspensory ligaments and integuments of organs violently displaced at their resonance frequencies within the body and, during severe z-axis oscillation, compressional injury to the spine.

Chronic human exposure to vehicle vibration. Occupational disorders involving the spine and internal systems have been associated clinically with continued exposure to the rough motion of certain types of vehicles, including agricultural tractors and some kinds of aircraft (helicopters) [50, 114, 119]. The etiology of these disorders is not yet clear and may be complex. Certain factors in addition to the vibration exposure, for example, climatically adverse working conditions and bad ergonomic factors in the design and construction of the vehicle, may be equally important. The extent to which chronic exposure to moderate levels of whole-body vibration can injure the otherwise healthy body remains an open question. Disease due to such chronic exposure is not likely to be a problem for the astronaut, because injurious levels of vibration, if occurring at all, are not maintained in space vehicles for prolonged periods.

Although hand-transmitted vibration is an occupational hazard to workers with power-driven tools in industry [9, 50, 90], it is not a serious problem in space flight at present.

Criteria and Limits of Human Exposure to Vibration

Setting limits of safe or acceptable human exposure to vibration has been attempted many times. Until very recently, however, guidance for the engineer in this area has been confusing and frequently conflicting, because of the multiplicity of guidelines published for different purposes and widely varied criteria of protection [20, 50, 53, 58]. The International Organization for Standardization (ISO) has therefore attempted to unify guidelines for criteria, methods of physical evaluation, and acceptable limits of human exposure to vibration. Their recent work [4] has led to formulation of an international standard on evaluation of human exposure to whole-body vibration in the range 1–80 Hz [61]. Their standard is currently in process of adoption as a national standard in several countries, including the US. Previously, only the Soviet Union [87] had adopted a national standard or regulation governing human vibration exposure in workplaces.

The ISO recommendation [61] recognizes three basic criteria for limiting human exposure to vibration and gives advisory limits accordingly. The criteria (and corresponding limits) are:

Preservation of health or safety ("Exposure Limit")

Preservation of working efficiency or performance ("Fatigue-decreased Proficiency Boundary")

Preservation of comfort ("Reduced Comfort Boundary").

Certain values of the Fatigue-decreased Proficiency Boundary for x-, y-, and z-axis vibration are shown in Figures 24 and 25. Corresponding values for the Exposure Limit are obtained by a multiplication of 2 (doubling the values in Figs. 24 and 25) and for the Reduced Comfort Boundary by dividing the values for the Fatigue-decreased Proficiency Boundary by 3.15 (equivalent to a reduction in acceptable vibration level of 10 dB). Figures 24 and 25 also illustrate the

[4] ISO Technical Committee 108 (Mechanical Vibration and Shock), Subcommittee 4 (Human Exposure to Mechanical Vibration and Shock).

allowance made for daily duration of exposure in the evaluation of vibration affecting man. These limits are tentative, remaining subject to revision and refinement of the standard pending new and better data available on the human response to vibration in the future [37, 46, 61].

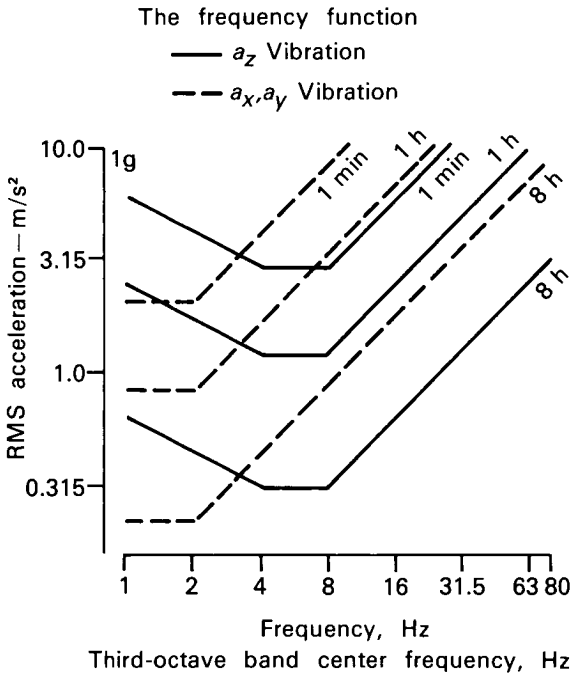

FIGURE 24.—Proposed ISO "Fatigue-decreased proficiency" boundaries (the frequency function) [61].

The ISO vibration exposure standards provide appropriate guidance for average routine vibration exposures of the general population and for normal occupational exposures. The guidelines must be modified for space operations, however, for several reasons:

a special supine (couch) position is used in space flight for the advantages that it tends to provide in sustained acceleration tolerance;

an optimized support and restraint system is provided for astronauts;

astronauts are a special population, selected specifically for their physical fitness and training to undergo the stresses of space flight, and their exposure to severe vibrations is limited to a brief period during their infrequent space missions (i.e., it is not a prolonged, daily occupational hazard);

human vibration tolerance is modified by simultaneous, sustained acceleration exposure.

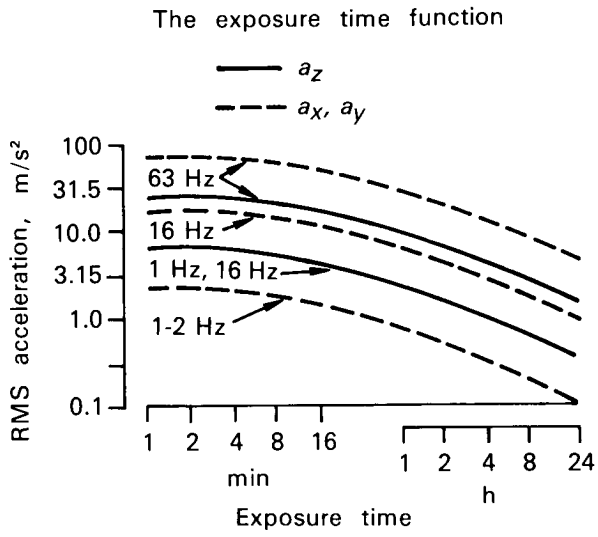

FIGURE 25.—Proposed ISO "Fatigue-decreased proficiency" boundaries (the time function) [61].

The first two of these factors have been studied in specific tests under realistic conditions (Fig. 26). Such tests clearly show that the supine couch position is less favorable in regard to human vibration tolerance than the upright sitting position.

The reason is that the direct transmission of vibratory energy from the couch to the astronaut's head in the supine position results in head symptoms limiting physiologic and subjective tolerance and leads to performance decrements at relatively low-vibration magnitudes [25, 122, 128, 129]. In the supine position, the vibration transmitted to the head is not attenuated by the intervening body structure as it is in the upright position. Depending on the helmet design and degree of restraint [38, 128], vibration of the helmeted head can affect tolerance as well as speech and visual capability.

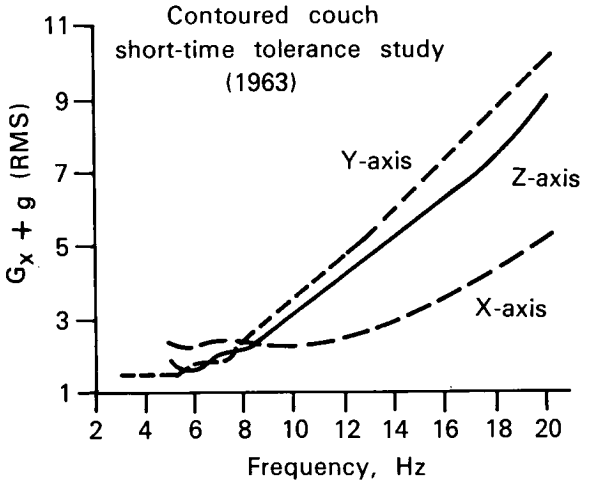

FIGURE 26.—Acceleration tolerance in three directions of vibration in a contoured couch [129].

Exposure limits for space operations have been generally accepted as the tolerance limits for healthy young subjects undergoing the stress for the maximum vibration exposure time (a matter of minutes) for the particular mission. It is logical in space flight not to apply the additional safety factor of 2 (or 6 dB) which was incorporated in the ISO Exposure Limits [61]. Those limits were intended to cover safely the case of repeated vibration exposure of general populations. (The same consideration can usually be applied to military or other occasional or nonroutine vibration exposures.)

The influence of sustained acceleration upon vibration tolerance is of considerable interest. In space operations severe vibrations almost always occur simultaneously with high acceleration loads. Based on limited experimental data and theoretical considerations, vibration stress and sustained acceleration stress do not appear to be synergistic [42, 45, 99]. Thus, the safety and performance limits established separately for each of these stressors could be safely adopted. The experimental evidence has shown that typical space rocket vibration (11 Hz at ± 3 G_x) in combination with moderate sustained acceleration (3.8 G_x) results in slightly increased vibration tolerance [25]. This paradoxical finding can be explained by the "restraining" effect of the sustained acceleration (with decreased transmissibility of low-frequency vibration to the body) which provides some protection (Fig. 21).

Principles of Protecting Man Against Vibration

In the classical approach to vibration control in engineering, four essential steps are taken:

1. Measure or predict the adverse environment.
2. Select and apply an appropriate criterion of control and a corresponding limit of exposure.
3. Determine the kind and amount of vibration control (usually reduction) required.
4. Select and apply the most economical and effective means of control.

These principles can be applied to protect man from aerospace vibration as well as to control vibration affecting engineering structures and equipment. Again, adopting the classical engineering approach in step 4, three main points can be distinguished at which to attack vibration disturbing to man:

at the source,
in the transmission pathway between source and man,
at the receiving point, i.e., in man himself.

Vibration Control at Source

The reduction of inputs from external sources remains largely a theoretical option in space operations.

Reduction of vibration from internal sources in space vehicles. There is scope for improvement (preferably at the design stage rather than by retrospective treatment of troublesome sources of spacecraft vibration) in the engineering of secondary sources of troublesome vibration and noise in spacecraft equipment.

Longitudinal ("pogo-stick") vibration of space boosters excited by the main propulsion units had to be reduced substantially (at considerable expense) during the development of the launching vehicles used in the US manned spaceflight program. The requirement for reducing vibration

levels in those vehicles was dictated by both equipment and human tolerance limits.

Control of Vibration in Transmission from Source to Man

Minimizing the response of structures. Vibration disturbing to the astronaut can be reduced by preventing structural resonances in the vehicle and its internal equipment wherever possible. This can be achieved frequently by the use of high-damping materials in the construction of equipment and vehicle components and, where it proves to be practicable, by damping treatments.

Isolation. Among the various ways of isolating man from vehicle vibrations, an important one is the interposition of springing or some resilient element between the man and the source of vibration [50]. There are rather strict limitations to the results that can be achieved by this device when the man is necessarily coupled closely to the vehicle structure, e.g., when the astronaut is restrained in his couch during launch. Perfect isolation is achieved, of course, when the astronaut floats freely in the weightless state. Attention should be given to possible sources of flanking transmission of vibration (e.g., stiff or rigid personal equipment connectors).

Minimizing Adverse Effects of Vibration Reaching Man

Where it is operationally feasible to minimize exposure to vibration, it is always worth considering the extent to which the duration or frequency of human exposure to vibration can be reduced. The opportunities for practicing this principle in space flight are limited.

Ergonomics of crewplaces and of displays and controls. Flight instruments and other equipment to be used in spacecraft during phases of the mission when there is severe vibration should be designed specifically for use in that condition. The legibility of flight instruments is one area where this principle may be applied [50]; another is the design and placement of manual controls such as console switches and control sticks. Tolerance of vibration and disturbing oscillatory motion in general is improved also when crewplaces are well-designed, comfortable, and pleasantly conditioned.

Training and experience. Individuals who must live and work in vibration and other abnormal states of motion (including weightlessness) show considerable and continuing habituation to the stress; with experience, they develop specific skills enabling them to carry out tasks in spite of the disturbance. Experience in both US and Soviet manned spaceflight programs has proved the importance of training and meticulous rehearsal of all phases of a space mission to the greatest extent possible in Earth-bound simulation, including simulation of vehicle vibration in phases where that condition is important in the spacecraft environment.

Physical fitness and freedom from undue fatigue are clearly of importance to the astronaut in all respects, including his tolerance of vibration and unusual motion. With the exception of remedies for motion sickness (see Volume II, Part 2, Chapter 4), no pharmacologic agents are known to increase human tolerance of vibration.

Summary

The vibration environments associated with space propulsion units and space maneuvers were carefully researched at an early stage in the development of manned space flight; it was not expected that vibrations would pose a major problem in space operations. Available guidance in regard to human safety and performance limits allowed dictating proper engineering specifications to forestall serious adverse effects upon the astronauts. Through careful research and testing of human and equipment capabilities in simulated space environments and mission, vibration has not been a seriously stressful factor in any USSR or US manned space missions carried out so far.

Human vibration research has added significantly to our understanding of the effects of biodynamic environments in general upon aerospace crews. This is particularly effective with regard to human protection against mechanical shock or impact, the field in which human vibration research has proved an indispensable key to

the understanding and mathematical description of all manner of force and pressure environments. Research begun initially to support space programs has enhanced the development of biodynamics as a distinct discipline, which is contributing not only to aerospace medicine but also to occupational and general medicine and physiology.

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