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SPACE SCIENCE BOARD

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Charles A. Berry, M.D.
Director for Life Sciences
National Aeronautics and
Space Administration
Washington, D.C. 20546

Dear Chuck:

Enclosed for your information and review is a preliminary draft of the Life Sciences section of the report of the recent Board study on Scientific Uses of the Space Shuttle. We would appreciate any comments and suggestions you care to make. As you know, this document is privileged while in draft form and is not for attribution prior to publication by the Academy.

If it would be possible for you to let us have your comments within the next 10 days or so, that would be very helpful in meeting our deadlines.

With best wishes,

Sincerely,

Ann Grahn/m
Ann Grahn
Executive Secretary
Committee on Space Biology
and Medicine

Encl

LIFE SCIENCES

The shuttle era will provide the first opportunity to carry out a thorough experimental program in the life sciences in space under conditions approximating those of ground-based laboratories. The Skylab experience has already demonstrated the feasibility of performing many kinds of general experimental manipulations under weightless conditions and has provided considerable support for the concept of a manned space laboratory in which sophisticated biological and biomedical experiments can be done. The ability to manipulate experimental material directly rather than by automated remote control alone is essential in the life sciences, and the capability for immediate follow-up of new experimental findings is an important facet of any effective biological experimentation. Having these attributes the pressurized laboratory concept constitutes a major advance in capability for definitive life sciences investigations in space. In addition to biomedical investigations relevant to man's well being in space, basic principles of biology and medicine can be examined using the 0-g environment as a research tool. The laboratory will provide the operational conditions necessary for the evaluation of components of advanced life support systems and of man-machine integration technology.

In the following sections are outlined examples of investigations in life sciences that are necessary to assure man's safety and to define further the conditions in which he can take part in spaceflight, or which utilize the space environment to learn more of basic biological processes on earth. Shuttle capabilities and requirements in these studies are discussed. Studies relative to life elsewhere in the universe (exobiology) are not discussed because shuttle capabilities here, other than as a launching or collecting platform, are minimal. Observations of the terrestrial environment (e.g., ecology, agriculture) are omitted as earth applications were excluded from the Study's charge. It is recognized that the scientific questions asked are based on 1973 concepts and technology and that maximum flexibility must be maintained in restructuring the questions and protocols with the development of new knowledge.

Cellular and Molecular Biology

Theoretical and experimental grounds for predicting detectable effects of zero gravity at the cellular, subcellular, and molecular level are still fragmentary. The experiments of Biosatellite 2 and other early flights have given some clues to potentially significant effects of weightlessness at the cellular level, and early shuttle flights should include well-designed and well-controlled experiments to confirm and consolidate potential problems identified by observations in these early experiments.

The weakness of the gravitational force relative to other physical and chemical forces operating over molecular dimensions suggests that 0 g is not likely to affect directly kinetic properties of biochemical reactions *in vitro* in a detectable or physiologically significant way. Similarly, the small size of procaryotic microorganisms would be expected to minimize potential gravitational effects. It has been suggested that bacteria might be used as models for eucaryotic systems, but major differences between bacteria and higher forms in size, cellular organization, and mechanisms of fundamental processes such as cell division, contraindicate this plan.

It seems more likely that gravity may significantly influence complex intra- or intercellular processes involving oriented supra-molecular structures such as the mitotic apparatus. Indeed, both U.S. and Soviet studies have suggested a slight increase in random chromosome aberrations and mitotic abnormalities in response to spaceflight conditions. Significant perturbation of the process of cellular replication in the absence of gravity would be of clear importance to the ultimate understanding of fundamental mechanisms; it could also have serious consequences as a source of potential disturbance in normal processes of cellular proliferation and turnover during long-duration spaceflight. Studies of the kinetics of cell growth and cell division in plant and animal tissue culture and in rapidly proliferating tissues _in vivo_ (e.g., bone marrow, skin, intestinal epithelium) will be required to assess quantitative and qualitative effects of the space environment and 0 g on cell replication and turnover time, including parameters such as chromosome replication, function of the mitotic apparatus, and cytokinesis. It would be of interest to test responses to mitogens such as phyto-hemagglutinin as a probe for potential alterations in control of the division cycle. Wound repair involves another sort of proliferative system appropriate for study in 0 g: the rate of repair of a cored skin wound has been very carefully analyzed under conditions of normal gravity as has the repair of mechanical injury to bone marrow. Investigations of embryonic development under 0 g (see section on Organismic Biology) may also give information pertinent to the cell division question.

An on-board centrifuge providing variable g in the range of 0 to 1.5 g and capable of handling both tissue culture and small animals of the size of mice or rats will be essential for these studies.

The spacelab environment would not seem to offer any special opportunity for genetic studies other than those concerned with cell division and chromosome replication. The suggestion of synergism between radiation mutagenesis and weightlessness is probably neither a genetic nor a radiation problem, but a problem in molecular and/or cellular reactions to 0 g. It is not certain at this time that a better understanding of such 0-g effects would have any importance for molecular or cellular genetics per se, but the possibility should be kept in mind for long-range planning.

It is not clear to what extent gravity may influence processes involving cellular and intracellular movement such as cytoplasmic streaming, rapid axonal flow, and amoeboid locomotion. Phase-contrast microscopy and photomicrography provide simple experimental means for investigating these questions.

The intriguing possibility of gravitational effects on membrane-mediated processes deserves careful consideration. At the present time there seems little reason to anticipate significant gravitational effects on carrier-mediated solute transport across biological membranes. Current information suggests that convectional forces are not important to the mechanism of biological membrane transport systems and that gravitational effects on the molecular organization of biological membranes should be negligible. For these reasons, investigation of possible effects of 0 g on the kinetics of carrier-mediated transport does not appear to offer a particularly fruitful area of study. However, study of electrolyte and water transport in model systems such as the toad bladder may be appropriate in relation to the problem of redistribution of fluid volume and electrolyte balance in man.

It may be of interest to examine effects of weightlessness on phenomena involving specific cell-cell interactions, such as cell sorting in sponge and embryonic tissue and differentiation in the cellular slime mold. Possible effects on density-dependent (contact) inhibition of growth in tissue culture would also be of interest.

Organismic Biology

In considering the potential effects of the space environment on the organism as a whole, a central scientific question is the long-term influence of weightlessness on growth, development, maturation, and reproduction. This question is conceptually the same for both plants and animals but for convenience is discussed sequentially below. Other major questions -- effects on individual body systems of the mature organism and effects of radiation -- are treated in the section on Biomedicine.

Plant Biology. The classic picture of the influence of gravity on plants is that of the positive and negative geotropism exhibited by stem and root tissue. Obvious questions have arisen as to what is the receptor mechanism by which plants perceive gravity and what are the mechanism(s) which mediate the tropic response. Although numerous ground-based experiments have been performed, no single hypothesis has been formulated that explains or clarified the phenomenon to the satisfaction of a majority of scientists. Studies carried out on Biosatellite 2, although providing rather uncertain results, indicated that ground-based control experiments employing the clinostat gave results comparable to those carried out at 0 g. We agree in general with the concensus of earlier study groups that future experimentation should be largely limited to precise ground-based experiments aided by clinostat studies to mimic weightlessness. However, it should be emphasized that the validity of the clinostat as an adequate model of 0 g conditions for plant studies must be unequivocally demonstrated. A variable-g centrifuge in the pressurized laboratory would strongly aid in this evaluation.

Geotropic experiments should be performed only as part of other experiments designed to examine additional aspects of plant and cell development that are thought to be influenced by gravity. Only those experiments that have had the most thorough exploration under 1-g conditions should be considered for analysis at 0 g. As part of this evaluation, it is important that thorough analysis and review of any potential flight experiment by a good cross-section of the concerned section of the scientific community be obtained.

Equal attention should be directed toward growth and development of plant cells in 0 g. For example, does the absence of gravity influence the morphogenesis of plant cells and affect chromosome replication to alter the mechanism of cell division? Previous flight studies have indicated that chromosomal aberrations do occur, and clinostat data suggest alteration of certain enzyme activity (glutamine synthetase) and of tracheid formation. Additional information as to the cause of such effects might contribute to a more tenable explanation for the ability of plants to respond to a gravitational field.

In preparation for shuttle experiments, a thorough study should be made of the types of plants that would provide the most useful information concerning the wide range of phenomena expressed by plants as a function of gravitational field.

Many of the experiments proposed for 0-g conditions encountered in spaceflight are directed toward short-term responses of organisms because of the limited duration of available flights. Although results from short-term 0-g experiments will augment thinking about possible effects produced by longer exposure, the obvious question, derived from extrapolation of the possible effects of weightlessness on chromosome replications, is whether plants can grow and develop normally in long-duration spaceflight. For example, can a microalgae population continue in a normal fashion after several generations at 0 g? Such information would be essential if one were to propose plant systems as secondary life support systems in long-duration spaceflights. If malfunction of cell division is induced by extended 0 g, populations of microalgae and higher plants would diminish, photosynthetic capacity decrease, and the support systems ultimately fail. Long-duration growth and development experiments might also provide important evidence for the possible evolutionary mechanisms of terrestrial plants. Plants which are able to complete one or more life cycles, such as Aribidopsis, or which are easily grown in tissue culture (carrot, tobacco), or that produce extensive xylem proliferation (sunflower) would be typical objects for experimentation.

Animal Biology. Thirty-day shuttle flights and recoverable free-flier flights of six months or more provide an excellent opportunity for long-term 0-g experiments with animal systems. Results of complete life-cycle studies on small mammals such as mice and rats should provide important information, transferrable to man in many cases, on physiological effects of weightlessness.

A unique feature of the 0-g conditions in the pressurized laboratory will be the opportunity to determine in aqueous medium the morphogenetic characteristics of protozoa and some simple metazoans (hydra or perhaps copepods). The purpose of this type of experiment would be to evaluate whether the terrestrial aqueous environment is truly 0 g in its morphogenic effects. Similar studies on the fine structure of various diatoms would represent an alternative way to examine this interesting aspect of possible gravitational effects on the development of aquatic organisms.

The placental mammal in utero might also be considered as developing in a generally omnidirectional force field. If so, then gestation in a weightless environment should have little or no effect on the developmental processes of organogenesis and fetal growth. However, the suggestion is speculative and should be tested. For example, do blastocyst formation and implantation have any dependence on external force fields? To what extent might critical delineations of organ systems be so dependent? Is parturition at all gravity-dependent? Postnatal growth and development in 0 g should then identify the adaptive sequence to which we are committed by our terrestrial confinement. For example, if cardiac "deconditioning" is solely a function of 0 g, then a mammal brought from birth to young adulthood (~25-30 days for the mouse) in the absence of gravity might be irreparably "deconditioned." Aspects of mineral metabolism and concurrent musculoskeletal development might be clarified by studies of early postnatal growth in 0 g.

To carry out these studies, animal-holding facilities are required for small mammals and selected avian species. An onboard centrifuge with a range of 0.1 to 1.5 g should be available for the smaller species to define effects of fractional g. Dissection and preliminary fixation of tissue samples would be required. Mission duration should be no less than 25 days, and a polar orbit, with concomitantly higher levels of radiation, should be avoided.

Study of the behavioral patterns of lower vertebrates, perhaps small fish such as goldfish or guppies when exposed to 0 g in an aquatic environment would provide additional information on the ability of such organisms to maintain themselves in the appropriate pressure/buoyancy gradient. This type of study would give insight into the mechanism of function of the swim bladder and possible other position-orienting sensors in aquatic vertebrates.

Rhythmicity in biological phenomena has fundamental importance in all life sciences disciplines. Processes that are cyclic in their time response (circadian rhythm) are found over a broad spectrum of responses, i.e., from nucleic acid synthesis to complicated stress reactions in plants, animals, and birds, and have had extensive study in biological systems on earth. They should be studied under the unique circumstances provided by spaceflight. This topic was covered in depth by the Santa Cruz Study in 1969*, and some of the experiments proposed will be flown on Skylab 3. This aspect of space biology should be carefully considered in light of the Skylab findings. If the data indicate any obvious positive effect of 0 g on circadian rhythms, a continuation of further studies would be recommended. Barring such observations, a lowering of priority of this type of biological experimentation would be recommended.

*Space Biology, NAS, 1970, Chapter 2

Biomedicine

The space environment offers new experimental approaches to analysis of mechanisms of a variety of fundamental physiological control systems. In addition, certain human (and mammalian) functions have become deranged in space, and corrective or preventive measures must be sought in order that man may perform adequately. Other functions offer special advantages for investigation of the 0-g condition.

Cardiovascular System. Prolonged spaceflight may be accompanied by complex physiological changes, and evidence to date suggests that these changes may be manifest most in the cardiovascular system. Disturbances that can be related to the cardiovascular system have consistently occurred in astronauts and cosmonauts and have been primarily evident as a decreased tolerance to the burden of gravity after reentry to earth. The regulatory pathways that normally maintain arterial blood pressure and peripheral blood flow on earth necessarily are still present at 0 g, and some adaptation has apparently taken place, rendering compensation for 1 g less effective.

The essential responses of heart rate, strength of contraction of the heart muscle, and peripheral vascular resistance are the result of complex reflex interactions among (a) the mechanoreceptors in the heart, lungs, aortic arch, and carotid sinus, (b) the central nervous system, and autonomic nerve outflow, and (c) the smooth muscle of the blood vessels and the heart, all reacting to maintain blood flow to the vital organs. Experiments in both animals and humans will be needed to determine which parameters must be monitored inflight to detect functional changes in the cardiovascular control system and what procedures are effective in combatting or preventing these changes. Examples of pertinent experiments that could be carried out in the pressurized laboratory are: measurement of peripheral blood flow by venous occlusion plethysmograph during lower body negative pressure (LBNP) or during a deep breath; and determination if exercise, isometric exercise, or LBNP prevent the abnormal cardiovascular regulatory responses that are seen after exposure to weightlessness.

It is presumed (see section on Kidney and Metabolism) that substantial loss of sodium and water occurs on entry into 0 g. If so, it may be initiated by the movement of extravascular fluid into the capillaries of the lower body under osmotic forces. Experiments are needed to determine the validity of this hypothesis, particularly in relation to the long-term changes that can be expected.

There are reasons to expect that the pressure-blood-volume-flow workload on the right heart might be reduced in space, leading to some decreased efficiency. This could be critical on return to the 1-g environment after prolonged residence at 0 g. Experiments should be designed to study possible atrophy of cardiac and other muscles.

Respiration. There are no apparent reasons to expect any significant alterations in cellular respiration, gas diffusion exchange, or control of respiration as a result of 0 g.

As the atmosphere of the orbiter cabin and pressurized laboratory will be air at sea-level pressure (20% oxygen, 80% nitrogen at 760 mm Hg), with the partial pressure of carbon dioxide maintained at less than 7 ppm, the basic composition of the gas the crew and passengers will inspire presents no difficulty. However, as discussed in the section on Life Support, the atmosphere must be monitored assiduously and excess gases and particulate matter removed.

The absence of gravity will alter the mechanical function of the lungs. Lung function should be studied after a protracted stay in space to determine if there is significant deterioration of muscles and supporting structures. The lack of hydrostatic pressure in the pulmonary circulation may alter the distribution of capillary blood flow/alveolar ventilation through the lungs and decrease the effective pulmonary vascular resistance. Spaceflight provides a unique opportunity to study these effects. Ciliary transport, lymphatic drainage, and phagocytic functions may become abnormal after exposure to 0 g. These mechanisms are of great importance in protecting the lung from infection and are deserving of study.

Kidney and Metabolism. It is our present hypothesis that, with the entry of man into a weightless environment, there occurs a rapid translocation of interstitial fluid into the intravascular space with an attendant activation of volume control mechanisms leading to an increased rate of renal excretion of sodium, chloride, and water. With the net contraction of extracellular fluid volume, there may follow an increase in the rate of aldosterone secretion leading to an increase in the renal excretion of potassium. If the excretion of potassium exceeds the concurrent rate of intake, total body potassium depletion will ensue. The latter could have widespread physiological effects on the cardiovascular system (as may have occurred in Apollo 15) and on the rate of secretion and effects of certain hormones such as insulin and growth hormone. The perturbation of volume regulation imposed by the weightless state offers the opportunity to examine the component parts of this complex control system in a manner that is not possible on earth.

The astronauts have shown a negative calcium balance in space, presumably analogous to that seen in prolonged bedrest at 1 g. Although the calcium loss has not been accompanied by signs of general demineralization of the bones, it is important to determine if it will continue for as long as man is at 0 g, or whether it levels off or can be made to do so. It may be possible to obtain information about calcium metabolism as well as about any perturbations in the rate of bone formation in 0 g by monitoring the repair of minute mechanical injuries made to the bone marrow of small animals. The rate of repair on earth has been very carefully timed. It provides a useful model because it involves the deposition and resorption of cancellus bone.

The absence of gravitational force may reduce the total basal energy requirements of the body, which would produce a lower metabolic rate, or qualitatively altered metabolism, detectable for example as a decreased food intake or lower body temperature.

Hematology. There has been a consistent decrease in red blood cell mass in the astronauts produced by increased destruction of red blood cells as well as a suppression of the bone marrow's normal compensatory response. It has been generally assumed that the basic cause was the hyperoxic atmosphere breathed by the astronauts because ground studies in similar atmospheres were able to duplicate the effect. However, an anemia appeared in the first Skylab mission despite a normal inspired O_2 tension, suggesting the influence of other factors. It is important to uncover the cause of this decrease in red cell mass, and to determine whether it plateaus or progresses with the stay in space. Studies should be done to learn if the rate of turnover is changed and also to learn the rate of granulocytic response to inflammatory stimuli.

Neurology. It was anticipated that 0 g would affect the vestibular apparatus. Astronauts have indeed had some difficulty with "motion sickness," but it has been relatively transient; susceptibility is not predictable from ground-based tests. Recent results from Skylab 1 indicate that the otolith organ is functionally denervated in 0 g because moving the head forward and sideways while rotating in a chair (a maneuver which leads to symptoms of motion illness at 1 g) produced no effect. Advantage should be taken of the 0-g environment to study vestibular functions in man and animals.

No other significant dysfunctions are anticipated in man. Animals raised from conception in a 0-g environment might show important neurophysiological defects at 1 g, because development of the nervous system is critically dependent on the presence of the relevant stimuli at certain stages.

Microbiology. Microbiological problems in spaceflight divide themselves into two major categories: those concerned with interactions of microbial flora within an enclosed system including possible alterations in host resistance, and problems arising from the possibility of mutation during flight leading to the emergence of additional pathogenic microorganisms.

The possibilities of mutation leading to new pathogens have been explored and, although this must always be considered, the risks do not seem much greater than they would be on earth. It seems likely that alterations in host resistance attendant upon prolonged spaceflight and the spread of microorganisms within an enclosed space will be more important considerations.

Although there is a tendency to equate host resistance with antibody formation, function of phagocytes, and activity of immunocytes, it is often forgotten that the first lines of defense consist of relatively nonspecific reactions, such as the intact integument, rinsing mechanisms such as tears and other secretions, the motility of the gut, and extremely active capacity of the alveolar macrophage system to kill inhaled bacteria in aerosols, and the antibacterial mechanisms in mucous membranes. It is still not clear whether 0 g will have a deleterious effect on some of these defenses, such as rinsing mechanisms, or the capacity of the lungs to clear inhaled bacteria because of altered deposition of aerosols in the lungs. A major potential problem is gastrointestinal disturbance. It is known that the motility of the gastrointestinal tract is a major factor in keeping the duodenum and jejunum relatively free of bacteria. The degree to which such motility and the movement of bacteria will be influenced by 0 g remains unexplored. There is increasing evidence that prevention of and recovery from disease are dependent on cell-cell interactions and cellular immunity. Study of the effect of 0 g on these cellular functions relative to host resistance is thus very important.

Specific immune responses to spaceflight have been monitored in previous flights and do not seem to have been greatly disturbed. However, we must remain alert to this problem.

Preflight isolation of astronauts and immunization procedures have reduced almost to zero the incidence of inflight illnesses, and it is mandatory that precautions of this nature be continued in shuttle flights. They will require continuous review and adjustment in accordance with changing knowledge and increasing experience. Epidemiological study of the environments of the flight personnel and their families during the preflight period would also appear to be essential. Conditions favoring the exchange of microorganisms among individuals are not yet well understood on earth let alone in space, and further work is needed so that control measures can be fashioned if such exchange proves harmful. The life support systems should remove viable microorganisms from the shuttle atmosphere or kill them as the most practical way of reducing this potential hazard. Finally, the possibility of replacing the usual earth flora in the microbial environment with relatively innocuous organisms should be given much more attention than it has received so far.

Behavior

Although much indirect evidence has been accumulated about man's ability to perform in spaceflight, there is a need to quantify man's performance in order to plan properly for his effective utilization in all modes of spaceflight activity. Most of the planned shuttle missions have tasks that might be used to investigate and quantify the human operator's visual, mental, and psychomotor performance. The development of precise tests which are able to discern subtle decrements in performance, and perhaps changes in behavior, will be necessary in preparation for longer flights when the ability to predict decrements will be important. Study of existing tapes of communications during flight should yield detailed observations on the interchanges among personnel and permit the study of interpersonal interactions and relationships. The data should identify reaction patterns between colleagues under these unique conditions and perhaps suggest improved personnel screening techniques.

Preliminary findings indicate that quality of sleep is not significantly altered in spaceflight, whereas there may be an alteration in sleep quantity. Regardless of what may be learned concerning sleep during Skylab missions, the question of mental state, i.e., alertness, and performance in relation to sleep, will not have been answered. The shuttle flights provide an excellent opportunity to investigate this relationship.

The participation of a scientist-passenger population with professional astronauts in the shuttle flights will require modification of selection criteria and screening procedures, and finally assessment of the techniques for evaluating the performance of those individuals ultimately selected. The results of such investigations would serve the dual purpose of validating the selection criteria and providing insight for improving subsequent screening methods for future participants in spaceflight missions. In addition, studies should be made to determine how much and what kinds of training are necessary to enable the scientist-passenger to tolerate and perform well under the unusual environmental conditions in space.

Radiobiology

The radiations encountered in spaceflight can present a hazard to man during long-duration flights where flight trajectories forbid quick return. There are no unique radiations in space, with the exception of the heavy-ion or HZE-particle component. Thus, present understanding of radiation effects is quite adequate to permit accurate prediction of the consequences of space-radiation exposure and to prepare countermeasures as needed or appropriate.

There are two areas of possible exception; the biological effects of HZE-particle irradiation and the possibility of synergisms between radiation and other elements of the space environment. The first is a matter of ascertaining if randomly located microlesions, induced by HZE particles being stopped in deep tissue, might cause sufficient cumulative damage to nonproliferating cells that pathological consequences might ultimately result. Could HZE-particle hits, for example, induce a detectable loss of retinal function?

For both scientific and practical reasons HZE-particle effects are best studied initially in ground-based laboratories. The studies required and the methods of study are described in detail in the recently issued Space Science Board report "HZE-Particle Effects in Manned Spaceflight." One strong recommendation has been made in that and other related reports: basic studies on radiation effects should not be attempted in flight laboratories.

Ground-based studies with accelerator-produced heavy ions are thus the first requirement. NASA has the operational problem of assesing the potential hazard of HZE particles to man during long-duration space missions and should therefore take full advantage of the ground-based facilities that are becoming available. Flight studies can then be designed for proof-of-principle.

If flight experiments on HZE-particle effects do develop sufficient priority as a result of the earth-based work, then a polar orbit should be sought. With minimal shielding, about 3 iron nuclei might be stopped per day in each gram of tissue. At lower orbital inclinations, the geomagnetic cutoff would reduce the expected number of hits by a factor of 10 or more.

The exposure of biological specimens to the ambient flux of heavy particles should not be encouraged on the assumption that the HZE-particle microlesions will be readily observable in deep tissue and their pathologic consequences then identified. In fact, it is forbiddingly difficult to detect such lesions because of their minute size and random location. All significant HZE events (thindowns or stopped particles) impinging on the biological target must be recorded and geometrically correlated with the target so that the precise location of the microlesion can be anticipated. The Biostack and Biocore experiments of the Apollo program are examples of two methods for correlating physical and biological events. Additional techniques should be sought, especially for lesions in deep tissue.

The question of synergism between radiation injury and weightlessness, or other flight-related factors, largely raised by some of the uncertain results of the Biosatellite 2 experiments, cannot logically be resolved by immediately embarking upon a series of flight experiments. There seems to be evidence accruing from both U.S. and USSR studies that 0 g has an impact on cell division. The evidence is seen in the form of small increases in certain chromosome aberrations, spindle misorientation, and cell lethality (of chromosomal origin?), but the mechanism that might produce these findings is not clear. The molecular basis of 0-g perturbations of cell division should first be thoroughly studied (see section on Cellular and Molecular Biology) before studies of synergism are undertaken. Some critical studies might be possible on molecular aspects of radiation target theory and the many associated concepts of genetic and cellular radiation injury. These, too, must be preceded by more complete evaluation of strictly 0-g effects upon cell metabolism and reproduction.

Ultimately, sophisticated multivariate radiobiological experiments could be conceived. These would require onboard radiation sources, both low- and high-LET, the capacity for <u>in vitro</u> and <u>in vivo</u> cell labelling with tritiated and carbon-14 labelled compounds, and the use of both cell cultures and small mammals. While such studies would best be done in orbits of about 30° inclination to avoid the cosmic radiations as much as possible, studies on heavy-ion effects, as noted above, will require a polar orbit. The latter, however, may also best be designed not to require any complex inflight manipulation, but to allow a maximum buildup of particle hits for later evaluation on the ground.

On all flights dosimetric devices and materials should be positioned to accumulate data on the flux and energy of the several radiations in space, and the shielding effect of spacecraft components on their intensity and scattering. While the influence of these components on the actual radiation levels in different parts of the spacecraft can be predicted to some degree, it is necessary to test these expectations against observations.

Life Support Technology

Requirements for atmospheric control in spacecraft are: (a) to supply oxygen in the amounts needed to sustain life, (b) to maintain appropriate temperature, pressure, and relative humidity, (c) to remove carbon dioxide and water produced by metabolism, and (d) to monitor and remove trace contaminants and particulate matter.

With the present state of the art, for the short-duration missions presently planned for the shuttle, open-loop systems, in which oxygen is supplied and wastes are removed and stored, weigh less and use less energy than closed-loop systems in which wastes are recycled. From the standpoint of weight and power requirements, the present breakeven point between open-loop and closed-loop systems is about 30 days.

If development of recycling systems proceeds, there is a high probability that in a very few years such systems will be able to compete with open-loop systems for missions of two weeks or even less. A wide variety of systems have been proposed for the recovery of oxygen from both carbon dioxide and water under the conditions prevailing in space. Examples of such systems include chemical conversion (e.g., Bosch, Sabatier), electrochemical (e.g., fused carbonate, solid electrolyte), electrolysis cells, and bioregenerative systems. None of these systems is yet at the point of acceptability in space from the standpoint of weight, energy requirement, or reliability, although substantial progress has been made.

It has been suggested that the lack of gravitational force would affect transport through artificial membranes, an important process in many proposed life support systems. The rate of transport of a molecular species across a membrane system can be dependent on gravity only if gravitational forces affect concentration gradients in the system. This might occur, for example, if gravity-dependent convection is required to prevent the development of concentration gradients in the boundary layer adjacent to the membrane. However, it is presently possible, within the current state of the art, to design out any adverse effects caused by 0 g. Forced convection and the use of capillary action in porous structures are presently utilized to minimize adverse 0-g effects on ionic and nonionic solute rejection, concentration gradients at the membrane surface, absorption phenomena, etc., in such devices as batteries and fuel cells designed for operation at 0 g.

The orbiter cabin and pressurized laboratory should provide facilities for the testing of components of closed-loop life support systems developed on the ground on a competing basis, so that efficient and reliable systems can be developed. In particular, appropriate space, power, and access to the main atmospheric circulation loop should be provided for at least two prototype component units to be tested simultaneously.

The closed environment of the shuttle will undoubtedly produce a wide variety of trace contaminants, some of which will be dangerous or distressful. Many of these contaminants have synergistic effects on body function. For example, trace amounts of ozone in the atmosphere produce lung tissue damage and also have a profound effect on the ability of the lungs to clear microorganisms. Man and other animals also produce a variety of chemicals which are eliminated into the ambient in trace amounts. The rates of their buildup in a closed system have not been studied adequately, nor have their possible deleterious effects on man, animals, or plants. Plants, for example, are exquisitely sensitive to ethylene. Apparently the only contaminant-monitoring systems currently being contemplated are a rudimentary carbon monoxide sensor and, possibly, a hydrogen leak detector. The only contaminant-scavenging systems now being planned include the use of LiOH for carbon dioxide removal, filters for particulate matter, and activated carbon for removal of material for which it has an affinity, such as high molecular weight matter. Clearly a better system to remove trace contaminants will be required, such as a catalytic burner or a rechargeable absorbing system. It should be pointed out that rather sophisticated systems for sensing and scavenging contaminants are currently available and in commercial use. Both for crew health and safety and for the success of scientific experiments, a substantial improvement in the contaminant control system over what is presently contemplated will be necessary.

For safety reasons it is mandatory that the air in the orbiter cabin be monitored continuously for oxygen and hydrogen, the first to guard against a significant reduction in oxygen for breathing and the second, as an index of a fuel leak, to prevent fire. In addition, it is most important that the atmosphere be monitored periodically (several times a day) for trace contaminants such as carbon monoxide, ozone, amines, sulfides, mercaptans, and hydrocarbon. The particulate content of the cabin air must also be sampled and measured periodically and the number of viable microorganisms determined. There will need to be a mechanism for removing this particulate matter, as by filters, and possibly for sterilizing the air stream, as by ultraviolet radiation. Trace contaminants and particulate matter, including microorganisms, must be removed to levels consistent with standards recommended in reports of the NRC Committee on Toxicology and the Space Science Board.*

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*See: "Atmospheric Contaminants in Spacecraft" (SSB, 1968), Physiology in the Space Environment: 2, Respiration (NAS 1967), Infectious Disease in Manned Spaceflight: Probabilities and Countermeasures (NAS, 1970).

Computers and Teleoperators. Recent developments in the computer sciences indicate that, by the 1980's, shuttle users can expect that their needs for inflight computation will not be limited by size and weight considerations. One important potential use for this improved onboard computer capability will be in the teleoperator, or remote manipulator, system. Projected developments in teleoperators, particularly improved hand geometry and use of tactile- and force-feedback, make it probable that many of the presently contemplated needs for extravehicular activity in the shuttle-spacelab can be handled remotely. Accordingly, new and improved designs of teleoperators should be field-tested in the shuttle-spacelab to determine their suitability for general use in space, and facilities for such field-testing should be provided.

Laboratory Operations

The wide spectrum of experimental approaches employed by the various biological and biomedical disciplines will require a pressurized laboratory module of the maximum size possible and with maximum flexibility as a major design principle. Requirements for specific experiments will vary greatly among different investigators, and from flight to flight. However, certain common requirements can be identified; these include light, water, electricity, thermal control within ±2°F, suction, laboratory refuse disposal (solid, liquid, gaseous), and such generalized equipment as a small multipurpose centrifuge, refrigerator, and freezer. It is impossible to identify or enumerate all types of specialized instrumentation required for individual missions, but it is likely that major classes of equipment used in many types of investigation would include, for example, radioisotope-handling apparatus, constant-temperature incubators, plant-growth and tissue-culture facilities, aquaria, photographic instrumentation, microscopes, and animal-holding and -handling facilities. We do not anticipate special requirements or problems with respect to data handling and storage. However, need for an onboard centrifuge to provide gravity control and to test responses to fractional g forces has been emphasized by several disciplines. A variable-speed centrifuge is required. It should have a radius not less than 4 to 5 feet and be capable of generating accelerations up to 1.5 g and handling tissue cultures, plants, and small animals up to 0.5 kg. This centrifuge will not be required for all experiments and should therefore be removable from the laboratory module in order to conserve weight and space.

The above, very incomplete enumeration implies two important points. The first is that there can be no such thing as the "ideal space laboratory" for all biomedical work: there are too many different sets of equipment that will be needed at one time and not another. The design of the pressurized laboratory should therefore be based on modular concepts and interchangeable components. This will furthermore reduce lead times necessary for experimental work as the investigator will be responsible for furnishing his specialized equipment which can be plugged into the basic laboratory facility. The second point is the need to assure, insofar as possible, that the basic laboratory facilities (power, atmosphere control, etc.) will in fact accommodate the requirements of the majority of potential users. This will require further contract study.

A prime requirement of the life sciences laboratory is the ability to carry out investigations on the intact animal. The exact species that might be employed cannot be set out other than to identify the familiar vertebrates used in experimental biology and medicine. Among the mammals this would include mice, rats, Chinese hamsters, rabbits, and possibly dogs and small primates. Among the nonmammalian species, needs might arise for avian species up to the size of chickens, and fish, frogs, and diverse amphibia and reptiles.

Adequate atmospheric and thermal control of the animal-holding facilities is essential. Ambient temperature should be held to about 72 ±2°F and about 40 to 60% relative humidity for most mammals and birds. Lower or higher temperatures may be required for some reptiles, amphibia, and fish. We would prefer that a separate air input system be provided for the animal facility in order to avoid mixing of the two atmospheres except when animal handling is required, but there is no reason why the two atmospheres should not vent into a common exhaust and revitalization system. Isolation, however, defeats the purpose of the facility; full access to the animals must be available throughout flight. In addition to simple access, provision should also be made for some rather detailed manipulations including dissection and removal of selected organs and tissues. An especially difficult problem might arise when the gastrointestinal tract will have to be sampled, as may well be required in certain studies on cell proliferation. As micro-organisms comprise the major component of intestinal contents, these contents, as well as other body fluids, hair, and dander will have to be safely contained without inhibiting the investigator's manual or instrumental access.

Additional presently foreseeable requirements involving animals are the capability for radiologically safe use of radioisotope-labelled compounds for injection and on-board tissue or fluid sampling, counting, and disposal; artificial insemination of small mammals; small mammal nesting, parturition, and litter-rearing; avian egg incubation; and sampling of tissues and fluids and their storage for postflight chemical analysis. Small, live-in compartments may also be needed on the centrifuge for those species upon which the critical tests of weightlessness are made.

While certain of the projected experiments in the life sciences can be accomplished within the span of 7-day missions, others, such as those concerned with embryonic and fetal development, wound healing and other aspects of cellular proliferation (e.g., marrow, skin, and gut), will require the full capability of the 30-day mission. In general, we anticipate that the longer missions will be of particular value to the life sciences. In some cases, free-flying unmanned satellites, recoverable after 6 months or so, will be necessary. For most purposes, orbital attitude and inclination will not be critical. Polar orbits may be required occasionally for radiobiological experiments.

Experimental and Administrative Approaches

If the potential of the shuttle for life sciences research is to be realized to any meaningful extent, certain experimental and administrative approaches must be accepted and followed.

All persons on all missions should be available for routine biomedical tests and monitoring. In view of the critical need for information about the adaptation of humans to 0 g, necessary to assure the safety of manned flight, means it would be wasteful not to obtain physiological data on all crew members and other personnel in addition to any life sciences experimenters. Many of the shuttle flights will not have the pressurized laboratory or life scientists on board, so the type of measurements obtained would necessarily be relatively unsophisticated. For example, at this time there is an identifiable need for metabolic balance studies, requiring collection and preservation of urine and fecal samples. This demands that the feeding and waste management systems of the orbiter be designed to permit such tests and that space be allotted for the samples obtained. Measurement protocols should be designed not to interfere with mission tasks.

The degree to which nonastronaut scientists of all disciplines are able to participate in shuttle flights will have a strong impact on the amount of research that can be done in the shuttle. Medical and psychological screening should therefore be as lenient as possible, within safety limitations. The initial period of conservatism in selection should be as short as possible, its end hastened by continuing tests to warrant lowering of criteria.

As a general principle, biomedical experiments should be conducted in humans first, where feasible, and supplemented by animal studies. Experiments should not overload the test subjects by trying to obtain many different kinds of data in one protocol: early experiments at least are likely to be more successful if they are quite simple in design and execution.

A cardinal rule is that all flight experiments should be preceded by adequate and thorough ground-based preparation. The responses of the test materials must be completely familiar under 1 g and the other experimental conditions. In no other way can the quality of the experiment and the legitimacy of any flight results be assured. The above implies that financial support for ground-based preparatory work will be necessary in some cases. Such support is justified, but it must not be abused or allocated without careful review.

Peer review of the entire structure of space life sciences programs, both supporting research and technology (SR&T) and flight experiments, both proposed and on-going, is essential. The reviews should be made at regular intervals, systematically, by formal panels appointed for fixed terms and consisting of members of the national - and international - scientific community. This procedure should be initiated promptly because out of the current SR&T programs will doubtless come many of the shuttle flight experiments.

It is imperative that the base of life scientists participating in space research be broadened. Similarly, communication between life scientists and the space program must be improved. Broad dissemination of information on flight opportunities should be helpful, as should appointment of a wider circle of scientists to review panels. Nevertheless, the most important influence to bring about a lasting, satisfactory participation of the scientific community is the continuing execution of high-quality work.

At present there is no formal representation for the life sciences within the administrative structure of ESRO. If the European community proceeds with the space laboratory, this situation will almost inevitably have an adverse impact on the quality of the biomedical laboratory. Appointment of staff and panels, as appropriate, would seem essential to this work and to increasing the participation of European life scientists in the shuttle program.

Recommendations

1. For life sciences work in space, within the shuttle concept, a pressurized biomedical laboratory that is as large as feasible is necessary. The laboratory will be used for a broad array of biological and medical experiments and must have flexibility as an intrinsic characteristic of design. We can identify some general requirements that will have to be built in, for example, that about 3 to 4 kW, or about 3000 kW hr, of power will be needed for a 30-day mission. In addition, many special requirements will be dictated by specific experiments that will differ from flight to flight. Thus

modularity of equipment and facilities is important to permit interchange within common spatial dimensions and consequent saving of weight and space.

2. We foresee a requirement for recoverable unmanned free-flying satellites, or bioresearch modules, for experiments requiring long periods (~6 months) in orbit. A typical example would be the long-term effects of weightlessness on small mammals over several generations, including hematological effects.

3. On all missions all shuttle personnel should be available as possible subjects for routine medical and performance monitoring inflight. Facilities must therefore be available on the orbiter to conduct metabolic balance studies and to measure, sample, and preserve medical specimens, including urine and feces. This will place requirements on the feeding and waste management systems of the orbiter cabin and on space in the orbiter cabin.

4. The composition of the atmosphere of the orbiter cabin and pressurized laboratory must be monitored continuously for oxygen and hydrogen and periodically for trace contaminants (e.g., CO, hydrocarbons, particularly ethylene, Freons, O_3, sulfides, mercaptans, and amines) and viable microorganisms. Trace contaminants and particulate matter, including microorganisms, must be removed to levels consistent with standards recommended in reports of the NRC Committee on Toxicology and the Space Science Board.*

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*See: "Atmospheric Contaminants in Spacecraft" (SSB, 1968), Physiology in the Space Environment: 2, Respiration (NAS, 1967), Infectious Disease in Manned Spaceflight: Probabilities and Countermeasures (NAS, 1970).

5. It will be necessary to conduct onboard control experiments for the gravity component and to generate gravity-level response curves for many biological studies. This will require a variable-speed centrifuge with a radius not less than 4 to 5 feet, capable of producing accelerations up to 1.5 g, and handling plants, tissue cultures, and animals up to 0.5 kg. Since the centrifuge will not be required for every life science experiment, it should be detachable from the laboratory.

6. In order to capitalize on the laboratory's potential for animal experimentation, easy access to the animals, for direct manipulation such as for surgery, must be provided. Although an entirely isolated (sterile) environment is unnecessary and impractical. The gas outflow from the animal-holding area should not be discharged directly into the atmosphere inspired by the crew. The animals can be maintained in a closed compartment with intrinsic environmental control, that could be opened as required.

7. To permit certain biological studies which are time-dependent, late access to the payload is essential. We have been informed that access up to 2 hours prelaunch is feasible, and at the present time this would seem to be sufficient.

8. Dosimetric devices and materials should be positioned in the orbiter cabin on all flights to accumulate data on radiation fluxes and energies and on the effect of diverse spacecraft components on intensities and scattering. While some

predictions can be made about the influence of spacecraft materials on the actual radiation exposure parameters, it is necessary to test these expectations against the observed radiation environment.

9. In order to test new or redesigned components of life support systems at 0 g in the course of their development, there should be access to the gas-flow loops in the pressurized laboratory.

10. Recent developments in remote manipulation using force-reflecting master-slave servomechanisms and stand-alone force- and tactile-sensitive manipulators have great potential for shuttle operations and should be applied and encouraged. If this instrumentation is properly developed, remote manipulation can be at least partly substituted for EVA, with concomitant increases in payload efficiency.

11. In order to permit maximal participation by the research community, criteria for selection of scientific participants should be no more stringent than is absolutely necessary to protect the health and safety of the passengers themselves and the crew.

12. There is need for a standardized procedure to inform and to attract potential scientific users of the shuttle. In addition to the Announcement of Flight Opportunities (AFO), there should be announcements in major relevant scientific publications. All proposals for flight experiments and SR&T should be subject to peer review by panels drawn from the international scientific community. Similarly, peer review of ongoing flight and SR&T projects should be made at regular intervals. After a proposal has been accepted, ground-based research specific to the flight experiment will normally be required and should be supported.

13. If ESRO proceeds with the Space Laboratory, we hold it essential that life sciences should be formally represented in the ESRO management structure.