NASA-CR-3487

NASA Contractor Report 3487

Biomedical Research

CONTRACT NASW-3469
NOVEMBER 1981

NASA

NF02155

NASA Contractor Report 3487

Biomedical Research

NASA

National Aeronautics
and Space Administration

**Scientific and Technical
Information Branch**

1981

FOREWORD

This report presents the results of a survey of the biomedical research program of the National Aeronautics and Space Administration. The survey covers the research activities of biomedical scientists working at NASA Centers, academic institutions, and industrial facilities. The purpose is to describe the principal problem areas faced by NASA in support of manned space flight and to present an overview of current efforts addressing each problem.

This survey was requested by the Life Sciences Division of the National Aeronautics and Space Administration and was conducted under Contract NASW-3469 with BioTechnology, Inc.

CONTENTS

1. MAN IN SPACE

"My condition is good."

This statement, made by Astronaut Alan Shepard during his suborbital flight on 5 May 1961, was the first medical report from an American in space. Since then there have been many such reports, all carrying the same message: Humans can live and work in space rather well. However, as we now know, we do experience a number of physiological changes.

The fact that humans must adjust physiologically to residence in space should come as no surprise. By Earth's standards, space is a most unusual place. The normal day-night circadian cycle is gone; radiation levels are much different; the familiar force of gravity, to which our bodies are physiologically adapted, is replaced by weightlessness.

The many environmental differences between space and Earth led to pessimistic predictions during the early days of preparing for the first manned flights. Some scientists felt there would be functional difficulties, such as an inability to sleep, urinate, or reach properly for distant objects. Others saw the possibility of more dramatic physiological problems, such as heart irregularities and gastrointestinal disturbances. Little wonder that there was considerable relief when the Project Mercury flights, including one which extended for 22 orbits of the Earth, showed that man could, in fact, live in space and do the tasks required of him.

The first opportunity to examine in detail the effects of space flight on man was in the Gemini Program. The Gemini 7 flight, launched on 4 December 1965, lasted for 14 days and was dedicated for the most part to biomedical research. Astronauts James Lovell and Frank Borman made 206 revolutions of the Earth in a capsule with a habitable interior of less than one and one-half cubic meters—about the size of the front seat in a Volkswagen Beetle. Their mission provided the first opportunity to study the extended effects of weightlessness on human physiology and to determine the response of astronauts to long-term confinement in a space vehicle. The results of the Gemini studies began to spell out the dimensions of man's adjustment to residence in space.

The Apollo missions had a very specific goal: To reach the moon, explore its surface, and return safely. Although biomedical studies were limited, new findings were made. For the first time in the U.S. manned space program, disturbances of the inner ear, the organ primarily responsible for maintaining balance, were noted. In the Apollo 8 and 9 flights alone, five of the six crewmen developed some degree of space motion sickness, leading to vomiting in two of the instances. Although the problem was generally confined to the first day, in some cases it disrupted planned flight activities.


Significant Biomedical Findings in the Gemini Program

Moderate loss of red cell mass
Moderate postflight orthostatic intolerance
Moderate postflight loss of exercise capacity
Minimal reduction in bone density
Minimal loss of bone calcium and muscle nitrogen
High metabolic cost of extravehicular activity

The three Skylab missions, lasting for 28, 59, and 84 days, allowed in-depth studies of man as he adapts to life in space. Many detailed medical experiments were conducted. Changes which had been seen in Gemini and Apollo mission astronauts were studied more rigorously.
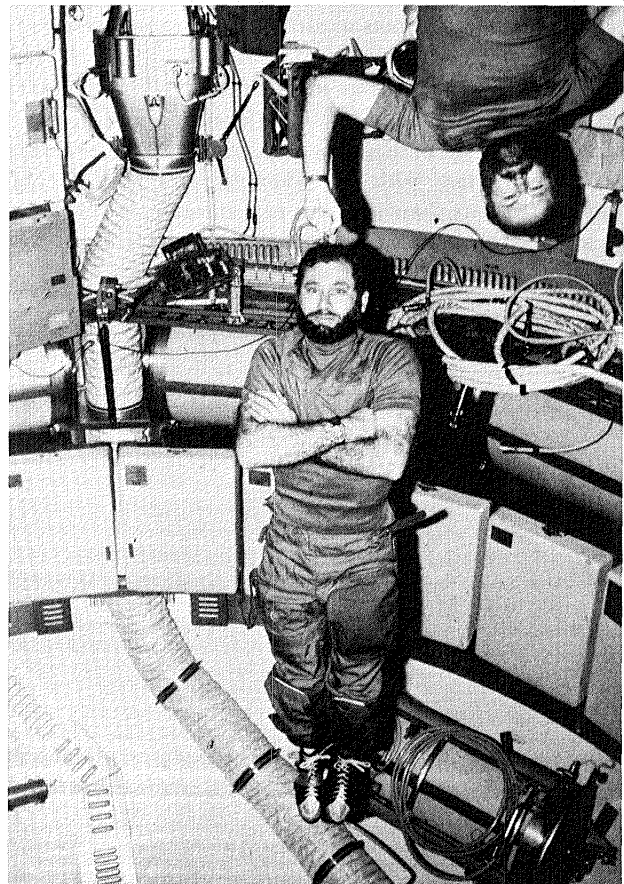
Astronauts William R. Pogue and Gerald P. Carr demonstrate weightless effects during the 84-day Skylab 4 flight.
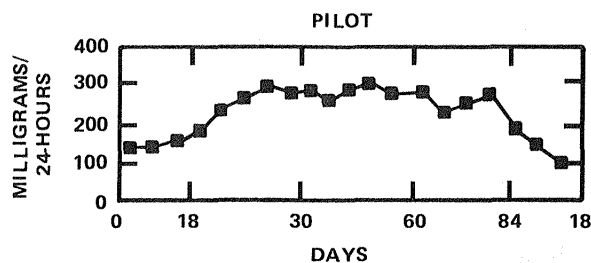
PILOT

*Continuing urinary calcium excretion by the Skylab 4 pilot over an 84-day period (From **Biomedical Results from Skylab**).*

The Skylab investigations identified three types of space effects. The first type includes acute disturbances, temporary in nature, but important nonetheless. The occurrence of space motion sickness was observed more frequently in Skylab than during earlier programs. Three astronauts had episodes of motion sickness when they first entered the large-volume workshop of Skylab, even though they had the opportunity to adapt to orbital conditions before transferring to the workshop. Although not life-threatening in a medical sense, space motion sickness is a problem if it reduces the effectiveness of astronauts at times when precise performance is critical.

A second type of change includes those which represent adaptation of the body to weightlessness. Fluid loss and cardiovascular deconditioning appear to be such responses. In general, but with considerable variability among astronauts, tests show that loss of cardiovascular tolerance to an erect posture under the influence of gravity (orthostatic intolerance) develops after four to six days of flight, with greatest instability and intolerance during the first three weeks. After this, there seems to be a stabilization of response at a level considerably different than the preflight measure. The cardiovascular system has made an accommodation to a new biological state.

There is every reason to believe that these responses are normal and pose no risk for an astronaut—as long as he remains in space. But what happens when, sometime later, this deconditioned system must withstand the sudden deceleration forces of reentry into the Earth's atmosphere?

The third class of change seen in space flight is progressive, at least for flights of up to three months. One problem is the loss of bone mineral, which could be symptomatic of a disturbance in the metabolism of the musculoskeletal system. Inasmuch as weightlessness removes the normal weightbearing stress from the long bones of the legs and spine, some change in bone composition is to be expected. Skylab results, which show a continuing loss of calcium throughout flight, do not suggest any self-limiting feature, although longer Soviet flights do show some attenuation of the process. Some measures will have to be devised to prevent serious musculoskeletal problems during these long flights.

The alterations in the human body just discussed represent man's response to the stresses of space and illustrate the range of biomedical problems needing attention as plans are made for more extensive manned space missions. The problems are difficult but not insurmountable. Through the work of a team of biomedical scientists and engineers, NASA is achieving new medical understandings of these problems and is developing countermeasures which will alleviate the physiological stresses imposed by travel in space.

2. THE SPACE SHUTTLE

The first orbital flight of the Space Shuttle in April 1981 has been acclaimed for its remarkable success. This flight, which achieved every engineering design goal, represents a real step toward a larger goal of changing the nature of the American space program. In the past, the development of spacecraft systems and the exploration of near space have been themes. In the 1980's, these themes will be expanded and will emphasize the benefits of practical work in space.

The Space Shuttle is the first reusable spacecraft, lifting off like a rocket and landing as an airplane. It consists of the Orbiter, two recoverable Solid Rocket Boosters, and an expendable External Tank. The Orbiter is built to last for at least 100 flights. Its crew consists of two pilots and as many as five scientists or technicians to manage the payloads. Payload capacity is impressive. The Orbiter can deliver single or mixed payloads of up to 65,000 pounds (29,500 kilograms) into near-Earth orbit. Following a nominal mission of seven days, the Orbiter can return to Earth with a payload of 32,000 pounds (14,515 kilograms).

One of the payloads to be carried into orbit by the Space Shuttle is the Spacelab. Built by the European Space Agency, the Spacelab is a large module, capable of being assembled into many different configurations depending upon the use desired of it. One configuration of the Spacelab will be a pressurized module where experimenters can work in a shirt-sleeve environment. A connecting tunnel will allow movement from the Shuttle's crew compartment into the Spacelab. Instruments can be mounted on a pallet outside the rear of this module, if direct exposure to space is required. The tending of these instruments and experiments will require extravehicular activity by crewmembers while wearing pressure suits.

Certain of the Spacelab missions will be dedicated to life sciences research. These flights present an opportunity for investigators to conduct experiments on living organisms, including man, in the space environment. The effects of weightlessness, in particular, and of gravitational forces of less than one-g can be studied in detail during these investigations. Experimentation aboard Spacelab represents a logical next step to the ground-based research conducted under NASA's Biomedical Research Program.

3. NASA BIOMEDICAL RESEARCH

The Biomedical Research Program in NASA was established to investigate the major physiological and psychologial problems encountered by man during space flight. There are several areas of interest. These areas address specific physiological problems that have either been encountered in previous manned space flights or are anticipated to occur as space flights become longer and otherwise differ from earlier missions. The next sections describe each of these areas of investigation.

The research efforts within the Biomedical Research Program are for the most part ground-based although they include the use of aircraft flying parabolic trajectories and other specialized procedures for simulating weightlessness. The program is intended to develop new knowledge relevant to issues of man in space, to solve problems encountered during space missions, and to establish a framework within which later experimentation in space can be conducted. Many of the experiments now selected or being considered for flight in the Space Shuttle were conceived and nurtured by this ground-based program.

Considerable program attention is directed toward the motion sickness problem because of its relevance to Space Shuttle operations. Cardiovascular and musculoskeletal studies are being pursued since we recognize that fundamental knowledge must be acquired in these areas if effective countermeasures are to be devised against the effects of long-term flight or of repetitive shorter flights. Increased awareness and understanding of the radiation hazard has resulted in more emphasis being placed on the biological effects of high energy, heavy particulate radiation and upon radiation protection. Major new avenues of research will deal with the psychological factors influencing performance effectiveness during space flight. There also are efforts to develop mathematical models of physiological systems which will describe the response of these systems to stresses found in space.

Research is conducted in both intramural and extramural laboratories. The intramural laboratories are primarily those at the Ames Research Center, Moffett Field, California, and the Lyndon B. Johnson Space Center, Houston, Texas. Additional work is conducted at the Langley Research Center, the Kennedy Space Center, and the Jet Propulsion Laboratory. Extramural research is pursued throughout the United States in universities, other Government laboratories, and occasionally at industrial facilities.

The Biomedical Research Program supports scientific investigations by over one-hundred principal investigators. These individuals are conducting research which has been judged to have scientific merit and to be related to the broad goals of the National Aeronautics and Space Administration. Through their efforts, progress is being made towards understanding and solving the physiological problems of sustaining human life and productivity during future U.S. space missions.

Individuals wishing to conduct research directed toward the problems of NASA should request a copy of the brochure "The NASA-University Program: A Guide to Policies and Procedures," obtainable from the University Affairs Office, Washington, D.C. 20546.

Space Motion Sickness

Space motion sickness was not recognized as a problem on early Mercury and Gemini missions. It was not until the Apollo and Skylab flights that a significant number of astronauts began experiencing motion sickness-type symptoms, perhaps because the larger cabin volume permitted greater movement. The symptoms range from queasiness and nausea to actual vomiting. Anti-motion sickness drugs that are useful on Earth were not very effective in dealing with the problem. The symptoms disappear after three to five days in space and most crews apparently are quite resistant to this ailment for the remainder of a mission. Post-flight, however, symptoms that seem to be related to motion sickness have reappeared in some crewmembers, particularly in those who showed inflight symptoms.

The problem of space motion sickness has not proved troublesome in long duration missions, but it may be quite important for the shorter flights of the Space Shuttle. Three to five days of sickness would seriously hamper the performance of susceptible astronauts and could greatly impact the success of a mission lasting only a week.

The most probable hypothesis to explain the occurrence
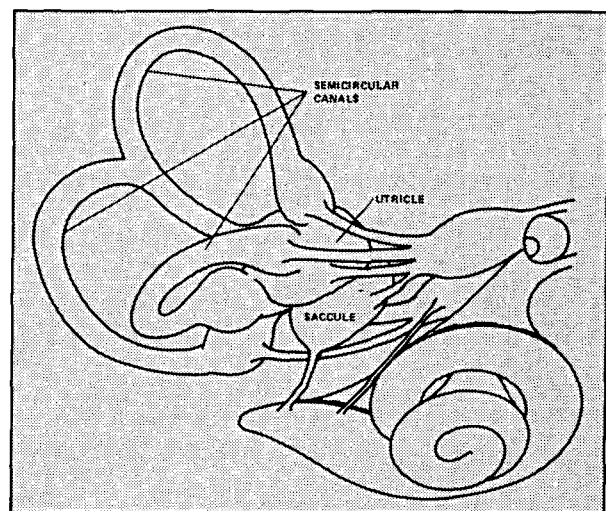
The inner ear, showing the principal components used for balance and for detecting change of position.

4

of motion sickness in space implicates the vestibular organ, located in the inner ear. This organ contains sensory receptors that detect head movement and the direction of gravity and send this information to areas of the brain that control movement, coordination, equilibrium, and balance. Normally, visual signals and other information from muscle and joint receptors are integrated with the vestibular signals, resulting in accurate balance, smooth movement, and eye-hand coordination. In space, the part of the vestibular organ that detects gravity undoubtedly sends unusual neural signals to the brain. Many scientists hypothesize that the "sensory conflict," the conflict between the vestibular, visual, and kinesthetic information, is the primary cause of space motion sickness. Although other theories have been advanced, none appears more consistent with the observations that have been made.

A major objective of the Biomedical Research Program is to determine the cause of space motion sickness. The belief that sensory conflict underlies this affliction serves as a starting point for many investigations dealing with the anatomy and physiology of the vestibular organs and their response to stimuli. A number of experiments currently are underway involving a variety of organisms including rodents, small mammals, and man himself. There are many objectives of these studies. The mode of operation of the vestibular nerve, how sensory information is received and processed, the interaction of the vestibular system with what is visually perceived, the reaction of the organs of the inner ear when the body is suddenly or forcibly moved or reoriented, and the brain's role in controlling the system are just a few of the areas presently under study. As a means of integrating the results of these many studies, mathematical models to describe the entire system are being developed. Manipulation of these models is expected to lead to new and fruitful research approaches.

Much current research deals with the neuroanatomy and physiology of vestibular action. Scientists at the NASA Ames Research Center in California are working on visual-vestibular interaction in the vestibular nuclei of the cat, an animal whose susceptibility to motion sickness is apparently quite similar to that of man. These studies will provide new insights into the neural crossovers of the two sensory modalities.

Although more and more information on the workings of the vestibular system is being gained, predicting the susceptibility of an individual to space motion sickness has so far proved elusive. Astronauts who show no symptoms during vigorous aerobatic maneuvers may well suffer motion sickness in space. Pre-flight ground tests of susceptibility have not yet been fully successful in predicting symptoms in space, but new approaches are being investigated. One promising avenue emphasizes not just an individual's initial resistance, but also his capacity to adapt to a motion stimulus after several exposures. Tests measuring tolerance to the weightlessness induced by parabolic aircraft flight play an important role here.

Since it is not yet possible to predict an individual's response, countermeasures to space motion sickness are of paramount importance. In addition to the orally-administered drugs that normally are effective for motion sickness in the Earth environment, other pharmaceutical preparations and modes of administration that might prove effective in space are being studied. Such drugs may one day be used routinely to stem the symptoms of motion sickness in those first few days of space flight while the body adapts to its new environment.

One potentially effective countermeasure is prior adaptation to the types of movement that might be encountered in flight. After several exposures to an environment that produces motion sickness, most individuals become somewhat habituated and more resistant. The effectiveness of this type of prevention procedure, used immediately prior to a space mission, is being actively explored.

A novel approach to the problem of space motion sickness involves the use of biofeedback. Subjects learn to control their own heart rate, skin temperature, and other physiological functions by observing changes in these functions on monitors. When they are exposed to unusual motions, they appear to be able to use biofeedback training to suppress the initial symptoms of motion sickness.

While space motion sickness may not be life threatening, it might well affect the performance of an astronaut during a critical part of a mission. The development of procedures for the prediction and control of space motion sickness is a high priority effort in the Biomedical Research Program. Research to date has shown that solutions will come only as we solve some very complex problems in neurophysiology.

Cardiovascular Deconditioning

The cardiovascular system undergoes a deconditioning process in space, apparently in response to the absence of gravity. In the weightless environment of space, body fluids are not forced toward the lower extremities as would be the case under the pull of gravity. Consequently, when one first enters space, there is a headward shift of fluids. Body receptors interpret this as an increase and the body adjusts by lowering the total blood volume, with a net loss of plasma. The heart now does not have to work quite as hard to circulate the blood. This results in a number of changes. Comparisons of X-rays taken before and after flight show a slight decrease in heart size, and measurements of cardiac electrical activity reveal subtle alterations. Studies on experimental animals returning from space flight show slight changes in heart muscle. Although most changes appear to stabilize within a few weeks, there is concern that exposure to space flight, particularly in long duration missions, might result in changes in cardiac function such that reentry to Earth, and return to a one-gravity field, might cause serious problems.

An important phenomenon associated with decondi-
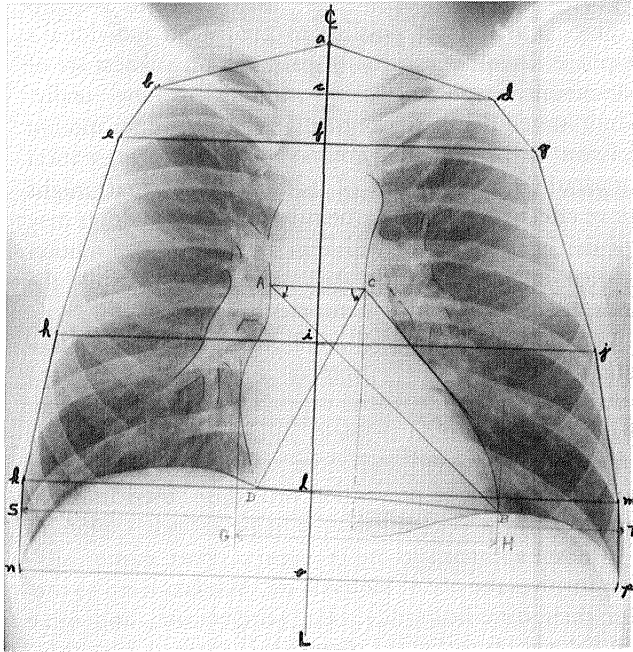
Geometrical measurements were taken from pre- and postflight X-rays to determine whether there were any changes in cardiac size. Most astronauts show slight decreases in heart size on the day of recovery.

tioning of the cardiovascular system in weightlessness is orthostatic intolerance—an inability to stand erect under the influence of gravity and maintain that posture without feeling faint or actually fainting. Pronounced orthostatic intolerance frequently is found during postflight examinations. In general, a test of the extent of orthostatic intolerance has come to be considered one of the best measures of the extent of the deconditioning process.

One technique that has been used both to measure orthostatic intolerance and to counteract its effect is the lower body negative pressure (LBNP) test. In the LBNP, an astronaut is encased in a container from the waist down, while the pressure within the container is lowered. This produces a shift of body fluids towards the legs, much like the change in posture when one stands. One advantage of the LBNP test is that it can be used to assess cardiovascular status in the weightless environment and thus measure the development of deconditioning effects as a space mission progresses.

While experiments conducted on earlier U.S. missions defined the major cardiovascular alterations, scientists require the controlled conditions of ground-based research to further understand how these changes develop. Several types of simulation can produce effects very similar to those observed in weightlessness. These simulations serve as analogs for the weightless state and allow direct measurements to be made of circulatory physiology. Equally important, the simulation can be conducted using individuals with a range of ages and backgrounds who may differ from the astronauts of earlier flights, but who are

more representative of the scientists and technicians who will fly aboard the Space Shuttle in coming years.

Extended bed rest, in either the horizontal position or with the head tilted slightly down to accentuate headward fluid shifts, is one of the most widely used models for studying deconditioning with human subjects. Studies with animals also are being undertaken, using immobilization in body casts as the analogous model. Water immersion also results in headward fluid shifts. This latter technique is especially appropriate for studies of the more acute changes associated with exposure to zero gravity. Unfortunately, experiments cannot be conducted for as long a period as with the bedrest model.

Studies using analog systems as described above, not only in the United States but also in the Soviet Union and in Europe, are attempting to understand the basic mechanisms underlying cardiovascular deconditioning. Basic studies are underway to determine why simulated weightlessness affects cardiac dynamics, myocardial ultrastructure, peripheral circulation, vessel tone, hormone production, and blood pressure and volume. To facilitate this effort, instrumentation is under development that will provide more accurate and detailed information about cardiovascular changes. For example, a method of imaging cardiac dynamics using radionuclides is being tested, and a simpler technique to measure cardiac outputs is being developed. An ultrasonic device for use with primates has been designed to detect flow patterns in major blood vessels. These and other instruments will help to provide researchers the data necessary to understand the changes as the cardiovascular structure undergoes deconditioning.

Measures taken after space flight show the effects of cardiovascular deconditioning in all astronauts. However,

SHUTTLE-ORBITER ENTRY PROFILE
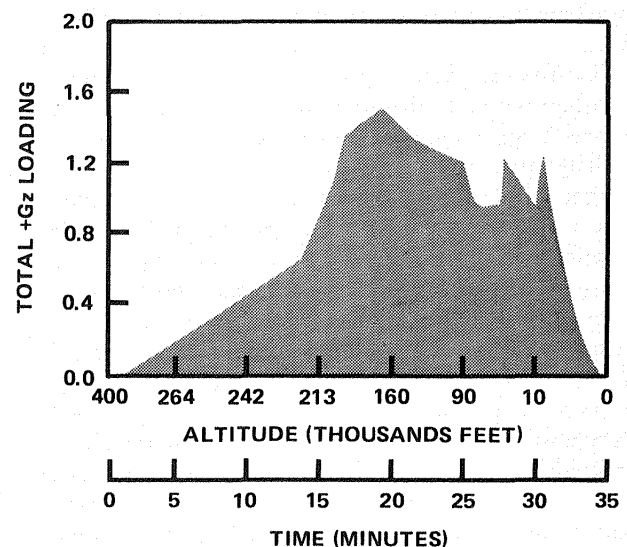
Shuttle Orbiter entry acceleration profile.

there is considerable variability among crewmembers. Everyone is not affected equally. Therefore it is desirable to be able to predict an individual's susceptibility to cardiovascular disturbances and to estimate tolerance to the deceleration forces of reentry. Procedures for measuring susceptibility are being developed. The most promising approach involves the use of a doppler meter that monitors the flow of blood to the head as posture changes. The ability to use systems such as this to assess the likely impact of deconditioning becomes quite important as the population of future space travelers expands to include scientists and researchers who will not have the same physical qualifications as earlier astronauts and who will be even more variable.

Perhaps the most urgent problem is to design effective countermeasures to prevent, or at least minimize, the effects of deconditioning. Countermeasures now being tested in zero gravity simulation studies include antigravity suits, abdominal pressure devices, fluid replacement techniques, body cooling, and a novel procedure involving whole-body oscillation to modify blood flow and distribution. A number of drugs are being evaluated, and the beneficial effects of exercise are being examined. The experience of Skylab and Salyut crewmembers suggests that intensive inflight exercise reduces the amount of deconditioning and hastens the recovery process post flight. Exercise may also be valuable as a countermeasure for the muscular atrophy and skeletal alterations associated with long duration space flight.

Bone Alterations

The weightless environment of space produces important changes in the skeleton, particularly in those bones that normally bear weight. Pre- and postflight measurements of bone density have shown that bones lose minerals approximately in proportion to the length of time spent in space. Studies of calcium balance have demonstrated net urinary and fecal losses and have suggested a diminished gastrointestinal absorption. Skylab crewmembers showed losses of calcium, phosphorus, and nitrogen, with a rate of loss for calcium of about six grams per month or 5/10th percent of total body calcium per month. While bone demineralization at this rate will not be significant on short missions of the Space Shuttle, on longer flights or perhaps on repetitive short flights these bone alterations might lead to an increased incidence of fracture, bone deterioration, or kidney stones.

NASA scientists conducted experiments in the Soviet Cosmos missions to examine changes in the metabolism and mechanical properties of bone. Rats exposed to weightlessness during an 18-day flight showed a decrease of about 45 percent in the rate of formation of certain bones.

Research is underway on the basic processes of bone formation and resorption and on calcium metabolism in

= INFLIGHT
= POSTFLIGHT
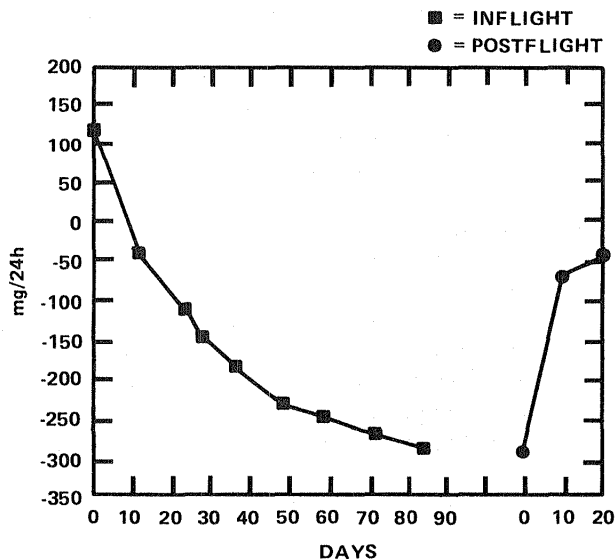
Change in nitrogen balance in space flight.

general. Investigations are planned to assess the roles of several hormones and proteins, including parathyroid hormone, calcitonin, and dihydroxy vitamin D. Animal studies are investigating the importance of local factors such as blood flow and neural input in bone formation. The role of the mechanical stress of gravity on bone metabolism is largely unknown at present, and researchers are taking advantage of zero-gravity simulations to investigate this phenomenon.

Prolonged bed rest is a useful tool to simulate zero gravity in research with human subjects. A number of other techniques, based on physical restraint, also are being explored using primates, rats, and dogs. Immobilization in body or limb casts is widely used for primate
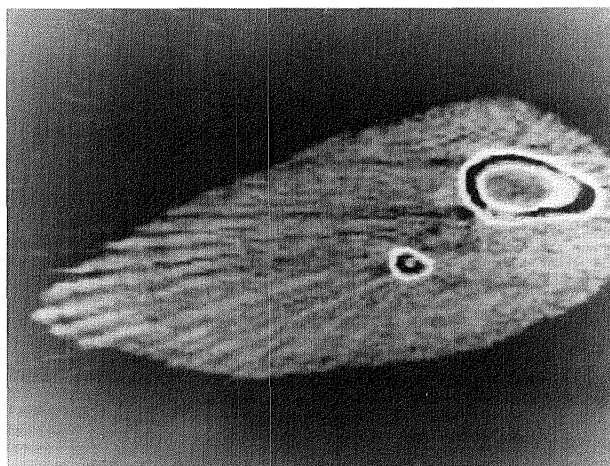
Dimensional display of the cross section of a monkey tibia, taken at the level of the tibial tuberosity. Anterior tibia is shown to the right; the smaller fibula is shown below and to the left.

studies, and a harness that removes the weight load from the legs is employed for rats.

Recent investigations have kept healthy human subjects in complete bed rest for as long as 36 weeks. Results appear to parallel those found during long space missions. However, since gravity is always present even during the inactivity of bed rest, there remains a need to conduct research in weightlessness. The Spacelab missions provide opportunities for such research.

A major thrust of current NASA-supported research is toward improved procedures for measuring bone mineral content. One such technique has been developed to measure the mineral content of the spongy interior of vertebrae using computer-assisted tomography. With this procedure, vertebral mineral loss in healthy bedrested subjects was found to be approximately 2.5 percent per month. This rate of loss, if occurring in astronauts during long-term space flight, could have serious clinical consequences.

Since exercise regimes tested thus far have not been shown to be particularly effective in preventing mineral loss, the action of various drugs is under investigation. Promising results have been obtained in preventing an increase in urinary calcium in immobilized subjects using a diphosphonate compound. The success of other individual drugs is encouraging and points to the possibility of developing a combination of therapeutic agents which will maintain bone integrity through long-duration space missions.

In order to integrate the results of the different research efforts and to further our understanding of bone alterations, scientists at the NASA Johnson Space Center are attempting to develop a mathematical model of calcium metabolism. The model is a compartmental feedback model consisting of four major sections: an input/output system, a distributing system, a storage system, and a regulatory system.

Muscle Atrophy

Movement during the weightlessness of orbital space flight is a simple matter. Very little muscular effort is involved—a slight push by one's arm is sufficient to begin a move from one place in the spacecraft to another. There is almost no real requirement for leg movement.

There are definite consequences of the reduced requirement for muscular activity in space. There is a loss of muscle strength and mass, just as has been found in studies of extended bed rest and limb immobilization. These studies show a consistent atrophy of muscle during disuse, with a breakdown of muscle protein, and changes in the balance of hormonal substances which regulate muscle metabolism. These studies also indicate that after only six weeks of use a recovery period of up to eight weeks may be required before peak muscle output can again be achieved.
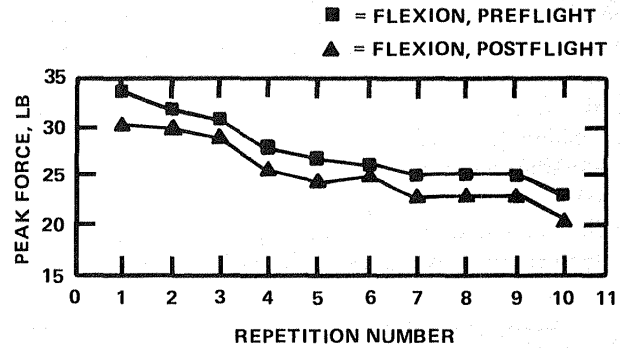
Consistent loss in peak arm forces measured by dynamometer preflight and 9 days postflight for Skylab 3 Commander (From *Biomedical Results from Skylab*).
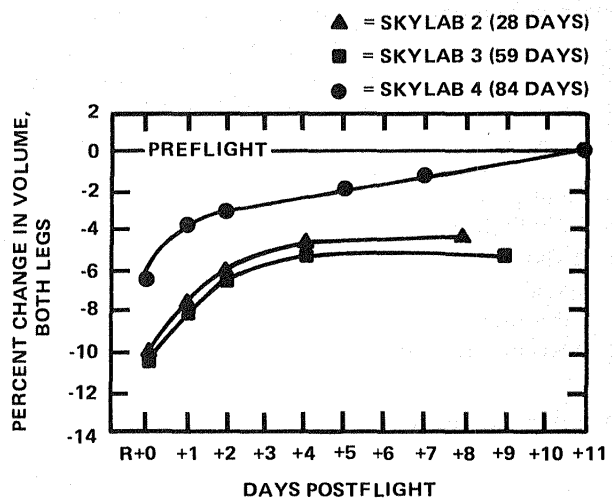
Loss in average leg volume for Skylab crewmembers. The decreased loss for Skylab 4 is attributed to increased exercise during the mission (From *Biomedical Results from Skylab*).

Observations made following extended space flight reflect the findings of laboratory investigations. Astronauts show a loss of strength in both arms and legs, with legs being more affected. There also is a decrease in leg volume, part of which is explained by a headward shift in circulating blood volume, with the remaining loss probably attributable to a loss of muscle tissue.

The Biomedical Research Program supports scientists who are studying the nature of muscle loss during space flight. An understanding of the biochemistry and time-course of this loss is necessary for the development of effective countermeasures. This research deals with the two principal types of fiber which make up skeletal muscles. *Fast fibers* contract rapidly and fatigue easily. These are the fibers used in quick, forceful movements. *Slow fibers* contract slowly and are more resistant to fatigue. These fibers are used in maintaining posture in a gravity field.

8

To study muscle changes under spaceflight conditions, U.S. investigators have flown experiments in the Soviet Cosmos series, with weightless exposures in the order of 20 days. Both muscle loss and changes in muscle structure were found. Weight loss in the soleus muscle of rats ranges from 25 to 38 percent when compared with control animals on the ground.

Laboratory studies have shown that simulating weightlessness through limb immobilization of the rat produces a greater degree of atrophy in the slow soleus muscle than in any of the fast muscles. The atrophied slow muscle has an impaired ability to utilize intracellular calcium, possibly leading to muscle breakdown. Other evidence, however, suggests that the muscle atrophy may be due more to a decrease in the formation of muscle tissue than an increase in muscle breakdown. This research found that insulin, a growth-promoting hormone, does not affect muscles of immobilized limbs as it does normal skeletal muscles. This is a step toward understanding the biochemistry of muscle loss during space flight.

The ongoing laboratory research will be aided through use of new analytic techniques recently developed in the Medical Image Analysis Facility at NASA's Jet Propulsion Laboratory in California. This technique uses a microscope-mounted television camera which converts the muscle image into numerical form and feeds it into a computer for analysis. The computer program produces a scatter plot showing the distribution of fibers by type as well as by diameter and optical density.

At this time, the best countermeasure for muscle atrophy appears to be a program of rigorous physical exercise. Researchers are testing specific exercises that stimulate the anti-gravity muscles in particular. The use of pharmacological agents and nutritional supplements also is being evaluated as a means of controlling muscle fiber change during prolonged weightlessness.

Fluid and Electrolyte Loss

The initial entry of an astronaut into weightlessness is accompanied by significant loss of fluids and electrolytes. The fluid loss is reflected by a rapid decrease in body mass, most of which is water. Sodium and potassium are excreted in unusually high amounts in the urine as well. Although the decline in body fluids does not appear to be hazardous while the astronaut is in space, it may reduce tolerance to the stresses of reentry.

Many of these biochemical and fluid alterations reflect adjustments resulting from headward fluid shifts. This shifting of body fluids results in a puffiness of the face and a feeling of fullness of the head which lasts for many days into a mission. The redistribution of fluids produces at least a transient increase in central blood volume, which is interpreted by the body as an increase in total blood volume. Neural, hormonal, and direct hydraulic mecha-
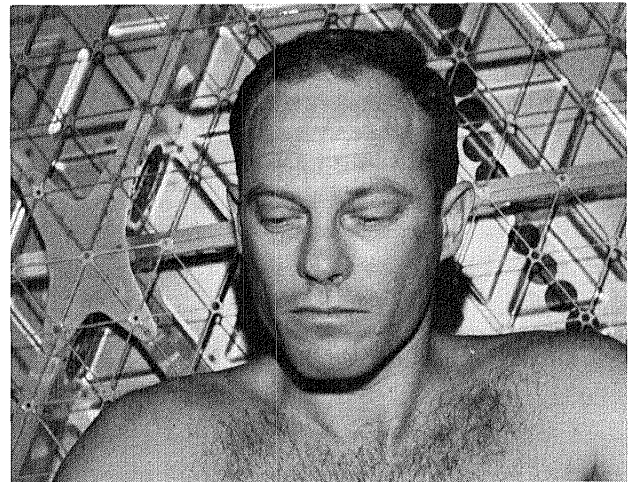

Inflight photograph of the Skylab 4 Pilot showing the facial puffiness attributed to headward fluid shifts.

nisms are triggered that result in a compensatory loss of water and salts from the kidney tubules. Eventually, fluid balance is re-established at a new lower level of fluid volume, more appropriate to the weightless environment.

Several innovative approaches are being utilized in NASA's research program to simulate the weightlessness which produces fluid and electrolyte loss. Once again the bedrest model is widely used since many of the early physiological events observed in astronauts are known to occur during the first days of bed rest. Headward fluid shifts are even more pronounced in subjects exposed to bed rest with six-degree head-down tilt. This model of weightlessness appears to reproduce more faithfully the signs and symptoms of space flight than horizontal bed rest.

Head-out water immersion is a simulation model that results in changes in fluid volume and renal function similar to those that occur in space. This model has been used with both animal and human subjects.

Another technique used to produce fluid shifts and trigger neural and hormonal compensatory mechanisms in-
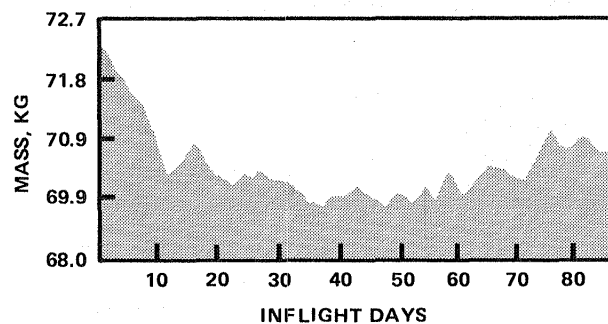
Loss of body mass measured for the Skylab 4 Scientist Pilot. The rapid initial drop is due mostly to fluid loss (From Biomedical Results from Skylab).
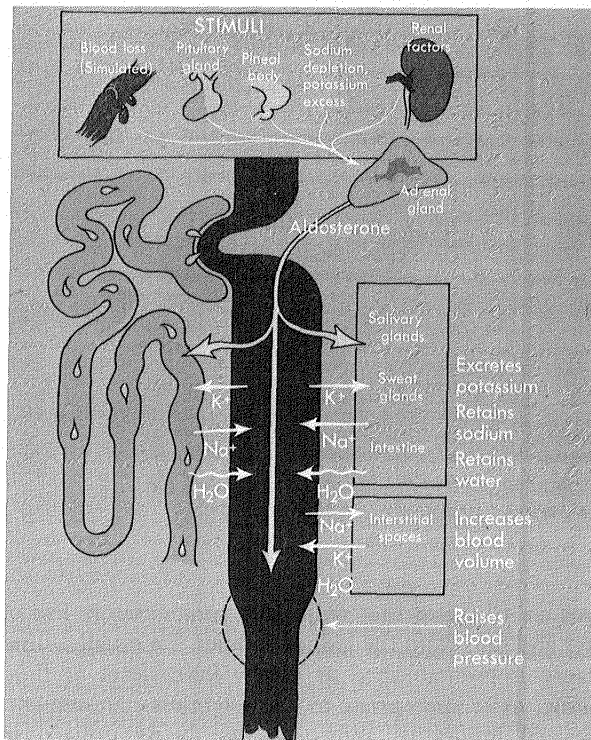
Hormonal control of electrolyte excretion (Aldosterone).

volves using lower body positive pressure. Raising the atmospheric pressure around the lower body of squirrel monkeys has been found to produce an increase in central venous pressure, elevated blood pressure and heart rate, and subsequent increased urine output and loss of electrolytes, including a significant decrease in plasma potassium concentration in the first 12 hours.

One of the primary goals of NASA's research program is to clarify the homeostatic mechanisms responsible for maintaining fluid and salt balance and to ascertain how these mechanisms are disturbed in the weightless environment. A number of hormones and enzymes appear to be involved. Antidiuretic hormone, for example, is released by the pituitary gland and results in increased fluid retention. Aldosterone, secreted by the adrenal cortex, influences the excretion of sodium by the kidneys. Other hormones also are involved, including cortisol, renin, angiotensin, prolactin, and the prostaglandins.

More sensitive assays are under development for a number of the hormones and enzymes so that it will be possible to measure very small changes with time. Scientists are also exploring the possibility that space flight might not only affect the output of hormones; it may also change the sensitivity of target tissues to the hormones that the body normally releases. Studies such as these are consistently demonstrating how the removal of gravity as a constant force disturbs the balance of a finely-tuned biochemical regulatory system within the body.

Blood Alterations

Astronauts returning from space missions have been observed to have a kind of "anemia," the major signs of which are a reduction in red blood cell mass, alterations in cell shape, and a decrease in plasma volume. Postflight alterations also have been found in white blood cells and certain blood proteins, important components of the body's immune system. The full implications of these changes are as yet unclear. Skylab results suggest that these alterations represent a self-limiting adaptation to the stresses of space flight. There may even be a return to normal over a period of many months. Astronauts in the three Skylab flights, lasting for 28, 59, and 84 days, showed mean red cell losses of 9.4, 8.6, and 5.9 percent, respectively, a consistent improvement with flight duration.

The cause for the red blood cell mass reduction has not been identified completely. It was first thought that the oxygen-enriched spacecraft atmosphere might be responsible, but this theory was discarded when crews on Apollo and Skylab missions, with lower concentrations of oxygen, showed similar blood alterations.

It is now believed that the reduction in red cell mass is triggered by headward fluid shifts in weightlessness. Renal receptors may sense the local concentration of red blood cells and cause a decrease in the production of erythropoietin, a protein secreted by the kidneys which stimulates the early formation of red blood cells. Skylab studies indicate red cell mass loss apparently is related to a suppression of production, since little evidence was found to support increased cell destruction.

A number of investigators are studying the mechanisms of blood alteration as certain conditions of space flight are simulated in the laboratory. Lower body positive pressure is being used to induce a headward shift of body fluids in squirrel monkeys as a basis for studying the dynamics of red blood cell production. Studies have shown that external influences, such as might be present in prolonged space missions (oxidants, drugs, alterations in acid-base balance) have profound effects on the red blood cell mem-
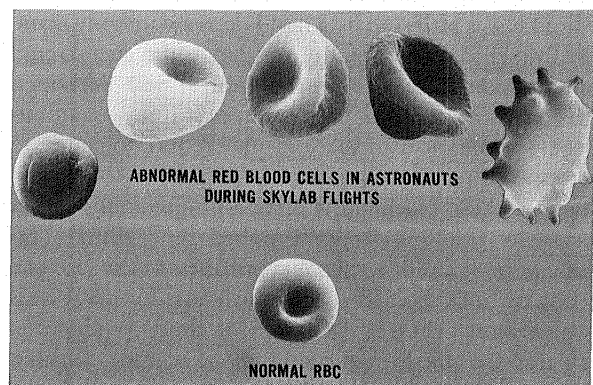
Photo of red blood cells (abnormal and normal).
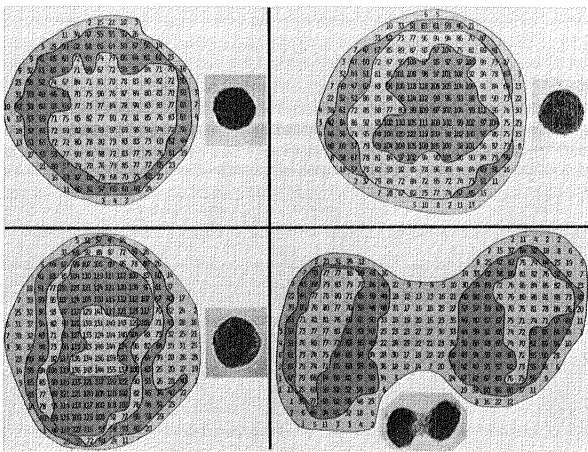
Computer digital image analysis showing form and density variations in white blood cells.

brane, causing a "stiffening" and decreased ability to deform within the circulation. Such cells then are trapped and destroyed in the spleen. Since it is known that red blood cells show some alteration in form during space flight, this work would indicate that there is in fact some cell destruction which, together with reduced production, may account for the total cell loss.

The effects of space flight on the body's immune system also are important and work is underway to develop techniques for precise measurement of white blood cell number and form under the stresses of space flight. Several NASA facilities are working, in a program coordinated by the Jet Propulsion Laboratory, to develop specialized equipment including a microscope, video camera, and computer capable of providing a visual image showing both qualitative and quantitative features of lymphocytes (white cells). The visual image of the cell is converted into a digital matrix which provides a numerical data form for rapid computer processing and storage. Scientists at the Johnson Space Center are using this system to study thymus dependent (T) and thymus independent (B) cells as they respond to immunological challenge as might be encountered by astronauts.

In other work on immunologic defense, scientists are studying interferon, Type II, and its relation to disease resistance. Initial investigations with humans indicate that alterations in interferon production may prove useful as an indicator of infection. Further, there seems to be a genetic base for individual response to interferon. Such information could be of some value in screening future candidates for space flight on the basis of inherent resistance to infectious disease.

Radiation Effects and Protection

The unique nature of ionizing radiation in space presents a special hazard, particularly for long duration flight. The space environment contains electrons, protons, X-rays, neutrons, and high energy heavy ions called HZE particles. In the past, NASA's Biomedical Research Program emphasized the biological effects of acute exposures to such radiation, particularly as appropriate to the development of guidelines for exposure limits on short-term missions. The research plan has recently been restructured to address the question of chronic exposures and to prepare for longer duration flights planned for the future.

Radiation exposure on previous space missions has not been excessive. Mission planners try to avoid periods of solar flares, known to produce sudden increases in the amount of radiation. The orbits and trajectories of previous missions have also avoided the Van Allen Belts of trapped radiation as much as possible, and Shuttle missions will do the same.

The biological effects of HZE particles represent the most uncertain radiation hazard for future flights, particularly those planned for geosynchronous orbitor for deep space. Several research programs are underway to examine the long term effects of HZE exposure in animals and in mammalian cell cultures.

Scientists are closely watching physiological and behavioral changes in animal subjects exposed to low doses of HZE particle radiation to determine the effects of this unique hazard. An increase in the incidence of cancer is one potential danger of chronic exposure. Damage to non-regenerating tissue in the central nervous system and the eye may be another. Changes in performance are being measured in trained animals to determine whether this kind of radiation might produce behavioral alterations in space crews. The reproductive system is of particular interest because radiation is known to have specific effects on DNA and on reproductive cells.

The measurement of radiation exposure in space is an important issue for NASA's Biomedical Research Program. The radiation research of NASA is done in concert with the rest of the Federal establishment through the Interagency Radiation Research Committee. This allows information developed elsewhere to be incorporated in the NASA program.

A prototype universal dosimeter has been developed that is capable of measuring the accumulated dose from all types of space radiation in real time. Other instruments focus on measurement for specific kinds of radiation. About one-half of the total radiation exposure in space is from neutrons, and a device that passively measures neutron dose is being tested. Methods to measure the amount of HZE particle exposure are also in the test stage, using materials that detect particle tracks. These devices can be attached to astronauts' garments to measure human dose levels, and can also be used to measure radiation dose in different areas of the space cabin.

The University of California is using its Bevalac accelerator to produce HZE particle beams, simulating space radiation, to develop risk estimates based on exposure of

mice and mammalian cell cultures. This same facility is being used to study heavy particle radiation effects on nerve cell synapses and certain neurological cells.

The design of a spacecraft necessitates certain constraints on the amount of shielding that can be used to protect the crew. Mathematical models are being developed to describe the interaction of space radiation with biological systems and with potential shielding materials. Shield designs are under test that will ensure adequate protection against radiation without imposing too great a weight penalty on the vehicle. The results of these efforts will impact the development of career guidelines for radiation exposure, and may permit astronauts to travel safely in space more frequently and for longer periods.

Behavior and Performance

The crew of a spacecraft is exposed to a number of unique stresses not normally encountered on Earth. Among these are confinement, isolation, crowding, circadian rhythm disruptions, unusual work/rest cycles, monotony, and the ever-present danger of life-threatening emergencies. Unusual conditions such as these are known to produce performance decrements in laboratory and field studies on Earth. Research is needed to determine the extent to which extended exposure to such conditions might also affect the performance of astronauts.

The experience of Apollo 13 illustrates the need for superior performance during emergencies in space and also that human problem solving may suddenly become urgently required even during passive phases of a space flight. About 56 hours into the mission, the rupture of an oxygen tank set off a series of malfunctions that resulted in rapid depletion of oxygen supplies. Fortunately, both the ground and space crews were able to formulate creative solutions to the problem, and the spacecraft returned safely to Earth.

Characterizing the effects of different types of spaceflight stressors on human behavior is an important goal of the NASA Biomedical Research Program. Studies are attempting to isolate psychological factors which might affect performance and adjustment during space missions. In these studies, commercial airlines are cooperating with scientists examining problems of crew performance. The conditions in the cockpit of an airplane represent a reasonable analog to those in the Space Shuttle, particularly for investigations into the behavioral coordination of team members and the social-psychological aspects of small-group dynamics in a work setting.

The confinement and isolation inherent in space travel may present particular psychological hazards, especially on longer missions. Measures therefore are being obtained of social interactions, endocrine response patterns, and behavioral decrements in small groups of individuals during continuous residence in a programmed laboratory.

A major goal in NASA's research on human behavior is
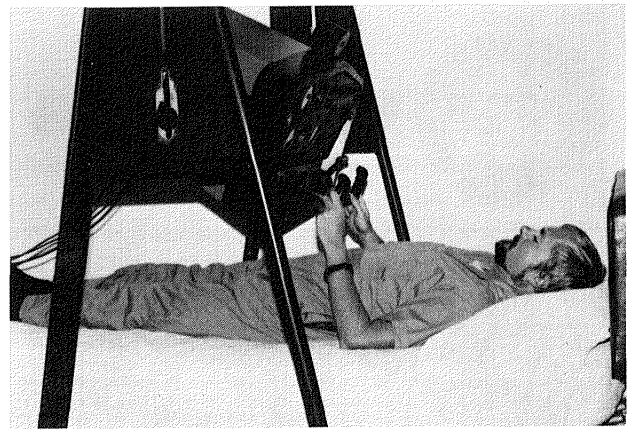
Testing the aircraft control performance of a subject during a bedrest study.

to be able to design appropriate countermeasures to prevent performance decrement during space travel. Previous missions have primarily attempted to solve the engineering and basic biological problems associated with space flight, but as solutions to these problems are acquired, more attention will be focused on psychological factors. Issues such as spacecraft habitability, individual motivation, crew compatibility, and maintenance of skilled performance over long durations will be emphasized in order to ensure that humans continue to perform effectively in space.

An interesting approach to the development of behavioral countermeasures is found in research dealing with the nutritional control of neurotransmitters. Here, the investigator is studying the effects of dietary factors on intellectual function, alertness, and performance. Strict dietary control might prove to be an important factor in maintaining desired behavior during long missions.

General Biomedical Problems

The Biomedical Research Program encompasses a number of approaches to the problem of maintaining the health and performance of space crews. The prevention and early detection of disease is an issue of obvious concern. Profiling techniques are being developed for the analysis of organic volatile metabolites in biological fluids so that such profiles can be used to identify chemical markers characteristic of viral infection. With this technique, which is based on high-resolution capillary gas chromotography, considerable success has been achieved in analyzing serum samples to diagnose virus infection as well as to predict virus susceptibility in a normal population prior to exposure.

Changes in the immune system also are being evaluated as early indicators of disease. Techniques are being developed for the differentiation of the subpopulations of one of the two major classes of lymphocytes, T cells. It is known that these subpopulations perform different functions

within the immune system. An antibody-producing hybridoma, Tumor 1-50, has been constructed which interacts with one subclass of T cells and not at all with B cells, thus providing a means for analyzing cell structure, function, and role in immunological defense.

Decompression sickness remains a hazard for space crews, since the use of the space suit during extravehicular activity requires a change from a sea level atmosphere (14.7 psi) to a much lower atmospheric pressure (4 psi). The Johnson Space Center is developing a quantitative index of individual susceptibility to decompression sickness based on physiological correlates including age, sex, lean-to-fat ratio, exercise, and effectiveness of inert gas elimination.

This index will prove useful in establishing the type and extent of protection required by astronauts as they move outside a spacecraft for maintenance activities.

Proper nutrition is a major concern of NASA. Ground-based investigations are in progress to assess metabolic changes and to measure the effects of zero gravity simulation on insulin production, triglyceride levels, and other features of carbohydrate and fat metabolism. Mathematical modeling of these metabolic changes is aiding in understanding the interactions among the many biochemical factors. This research is a key element in our growing capability to sustain astronaut health during long-term missions.

4. RECOMMENDED READING LIST

General References

Calvin, M., & Gazenko, O. (General Eds.). *Foundations of space biology and medicine* (Joint USA/USSR publication in three volumes). Washington, DC: U.S. Government Printing Office, 1975.

Johnston, R. S., Dietlein, L. F., & Berry, C. A. (Managing Eds.). *Biomedical results of Apollo* (NASA SP-368). Washington, DC: U.S. Government Printing Office, 1975.

Johnston, R. S. & Dietlein, L. F. (Eds.). *Biomedical results from Skylab* (NASA SP-377). Washington, DC: U.S. Government Printing Office, 1977.

Nicogossian, A. E. (Ed.). *The Apollo-Soyuz Test Project medical report* (NASA SP-411). Springfield, VA: National Technical Information, 1977.

Space Motion Sickness

Homick, J. L. Space motion sickness. *Acta Astronautica*, 1979, *6*, 1259–1272.

Parker, D. E. The vestibular apparatus. *Scientific American*, 1980, *234*(5), 118–135.

Reason, J. T., & Brand, J. J. *Motion sickness*. London: Academic Press, 1975.

Von Baumgarten, R. J., Bardrichi, G., Schillinger, G. L., Jr., Harth, O., & Thuemler, R. Vestibular function in the space environment. *Acta Astronautica*, 1974, *2*, 49–58.

Cardiovascular Deconditioning

Hoffler, G. W. Cardiovascular studies of U.S. space crews: An overview and perspective. In N. H. C. Hwang & N. A. Normann (Eds.) *Cardiovascular flow dynamics and measurements*. Baltimore, MD: University Park Press, 1977.

Sandler, H. Cardiovascular effects of weightlessness. In J. F. Goodwin & P. N. Yu (Eds.), *Progress in cardiology* (Vol. 5). Philadelphia, PA: Lea and Febiger, 1976.

Sandler, H. Effect of bed rest and weightlessness on the heart. In G. H. Bourne (Ed.), *Hearts and heart-like organs* (Vol. 2). New York: Academic Press, 1980.

Bone Alterations

Morey, E. R., & Baylink, D. J. Inhibition of bone formation during space flight. *Science*, 1978, *201*, 1138–1141.

Rambaut, P. C., & Johnston, R. S. Prolonged weightlessness and calcium loss in man. *Acta Astronautica*, 1979, *6*, 1113–1122.

Muscle Atrophy

Fedorov, I. V., & Shurova, I. F. Content of protein and nucleic acids in the tissues of animals during hypokinesia. *Kosmicheskaya biologiya i meditsina*, 1973, *7*, 17–21.

Fluid and Electrolyte Loss

Berry, C. A. Medical legacy of Apollo. *Aerospace Medicine*, 1974, *45*, 1046–1057.

Epstein, M., Denunzio, A. G. & Ramachandran, M. Characterization of renal response to prolonged immersion in normal man. *Journal of Applied Physiology*, 1980, *49*, 184.

Leach, C. S. A review of the consequences of fluid and metabolic shift in weightlessness. *Acta Astronautica*, 1979, *6*, 1123–1135.

Blood Alterations

Kimzey, S. L. The effect of extended space flight on hematologic and immunologic systems. *Journal of the American Medical Women's Association*, 1979, *30*, 218–232.

Kimzey, S. L. A review of hematology studies associated with space flight. *Biorheology*, 1979, *16*, 13–21.

Radiation Effects and Protection

Grahn, D. (Ed.) HZE particle effects in manned space flight. Washington, DC: National Academy of Sciences, 1973.

Ionizing radiation risks to satellite power systems (STS) workers in space (Report No. DOE/ER-0094). Washington, DC: U.S. Department of Energy, 1980.

Behavior and Performance

Cheston, T. S., & Winter, D. L. (Eds.). *Human factors in outer space production*. Sponsored by the American Association for the Advancement of Space. New York: Westview Press, March 1980.

5. THE FUTURE

The Space Shuttle is the key element in American space activities for the near future. As the world's first reusable space vehicle, the Shuttle introduces a new era of economy and utility into the American space program. The real value of the Shuttle, however, lies in the direction it provides this program for more distant days. The Space Shuttle, as the principal component of the Space Transportation System, was built for one purpose—to take things into orbit. All kinds of things—men, tools, building materials, habitats, other spacecraft—in short, anything necessary to further a vigorous and productive program of moving into space. Astronauts will be involved in all phases of this movement. The only change will be that the term "astronaut" probably will come to apply to only a few of those making this move. The rest will be known as "space workers," and there will be a need for large numbers of them.

A possible use for the Space Transportation System is for the transport of materials into space for the construction of a "Solar Power Satellite." Such a system could greatly reduce our dependence on fossil fuel as a national energy source. Under one plan, a chain of 60 satellites will be placed in a 22,000 mile orbit over the equator, requiring approximately 30 years for the delivery of all construction materials to the orbital site. Each satellite, basically a giant grid of solar cells, will measure more than three by six miles and will continuously convert sunlight into electrical energy which then will be transmitted by microwaves to Earth. Such a system could satisfy roughly one-half of the current demand for electrical energy in America.

The construction of any system such as that discussed will require the maintenance of a large labor force, involving hundreds of workers, in an orbital environment. Establishing selection criteria for space workers, meeting life support requirements, maintaining health standards, and providing countermeasures against the stresses imposed by long periods of work in orbital space represent real challenges for biomedical scientists in the future. There will be comparable challenges presented as the nation embarks on long-duration manned missions to explore the planets in our solar system. The current efforts of the Biomedical Research Program are establishing a base of knowledge and technology with which future scientists can meet these challenges.

1. Report No.	2. Government Accession No.	3. Recipient's Catalog No.
NASA CR-3487		

4. Title and Subtitle	5. Report Date
BIOMEDICAL RESEARCH	November 1981
	6. Performing Organization Code

7. Author(s)	8. Performing Organization Report No.
--	
	10. Work Unit No.

9. Performing Organization Name and Address	11. Contract or Grant No.
BioTechnology, Inc. 3027 Rosemary Lane Falls Church, VA 22042	NASW-3469
	13. Type of Report and Period Covered

12. Sponsoring Agency Name and Address	Contractor Report
NASA Headquarters Life Sciences Division Office of Space Science Washington, DC 20546	14. Sponsoring Agency Code

15. Supplementary Notes

Technical Monitor: Gerald A. Soffen, Office of Space Science

16. Abstract

At various laboratories throughout this country, research is conducted into the biomedical problems encountered by man in space. These problems which have been identified as a result of previous experience in simulated or actual spaceflight include cardiovascular deconditioning, motion sickness, bone loss, muscle atrophy, red cell alterations, fluid and electrolyte loss, radiation effects, radiation protection, behavior, and performance. This report reviews the major investigations and some of the findings in each of these areas. It also provides a description of how biomedical research is organized within NASA, how it is funded, and how it is being reoriented to meet the needs of future manned space missions.

17. Key Words (Suggested by Author(s))	18. Distribution Statement
Gravitational physiology Hypogravics Weightlessness Space medicine	Unclassified - Unlimited Star Category 52

19. Security Classif. (of this report)	20. Security Classif. (of this page)	21. No. of Pages	22. Price
Unclassified	Unclassified	19	A02

End of Document