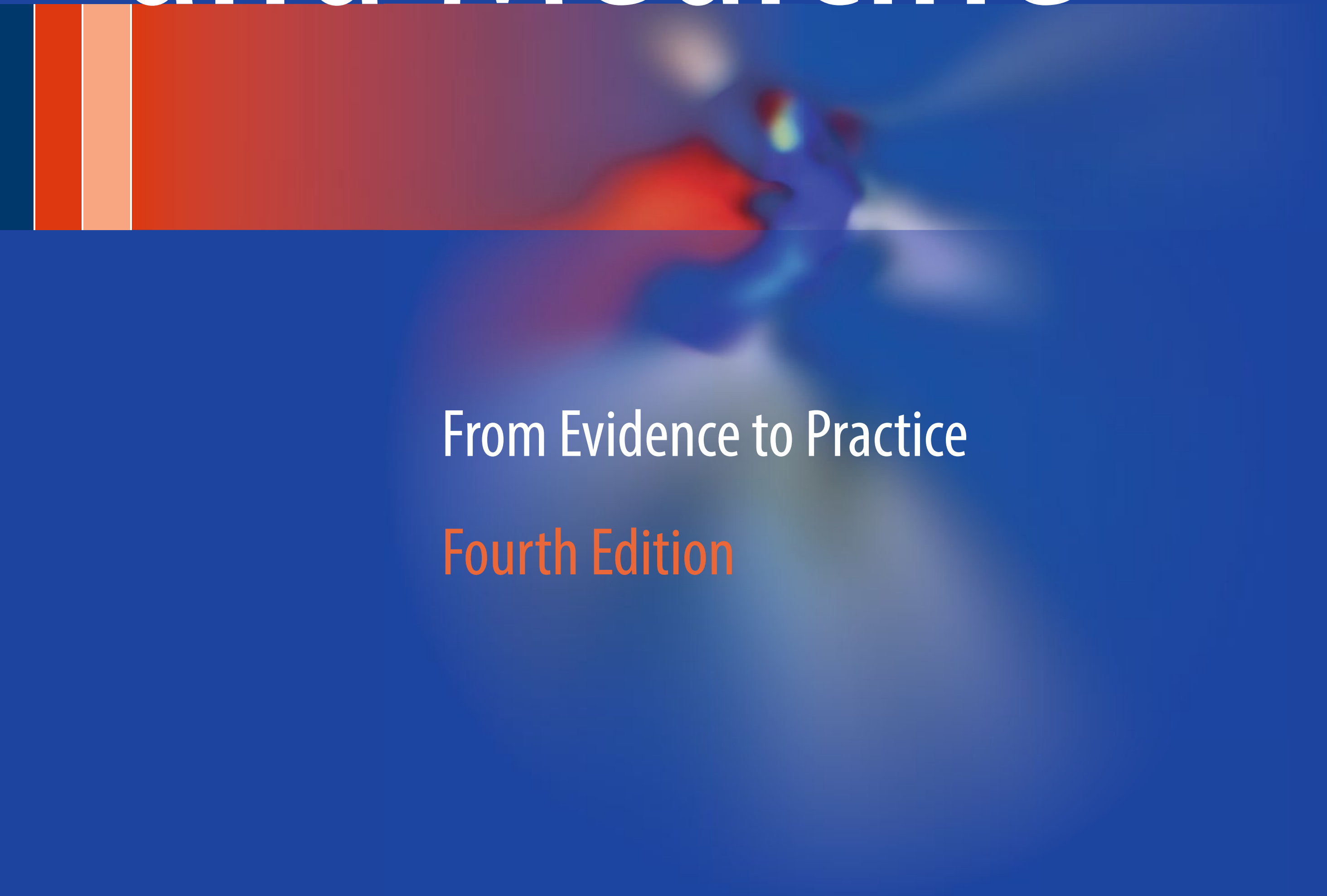
Arnauld E. Nicogossian · Richard S. Williams
Carolyn L. Huntoon · Charles R. Doarn
James D. Polk · Victor S. Schneider *Editors*

Space Physiology and Medicine



From Evidence to Practice

Fourth Edition

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Springer

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We dedicate this book to our families whose encouragements guided us through the writing process. We are grateful to the astronauts and the men and women of NASA whose dedicated work and selfless contributions generated the knowledge used in this book. John Glenn's [1921–2016] encouragements inspired the editors during the preparation of this textbook.

Foreword

This Fourth Edition provides a unique perspective into the principles of the expanding space medicine practice, drawing on the underpinning knowledge gathered over the last six decades of research and clinical practice in support of human space exploration. This textbook serves as a ready reference for space medicine specialists, engineers, and educators alike. Built upon the success of the first three editions, this fourth edition brings to the reader the evidence necessary to plan for human health of future space explorers. Since my last space flight on the Space Shuttle on October 29, 1998, on Discovery mission STS-95: the U.S. Space Shuttles docked with the *Mir* Space Station; the ISS was built using the Space Shuttle, which was retired in 2011; commercial companies began to launch spacecraft for logistic and resupply to the ISS; and China joined the U.S. and Russia as the third nation with piloted space mission capabilities. And last but not least, the exciting discovery of exoplanets and the abundance of water and life building blocks in the universe.

My reason for receiving the assignment to go up again on the Space Shuttle was to investigate the striking similarities between what happens to all astronauts in all extended space flight and how it compares to some of the natural aging processes right here on Earth. If breakthroughs can be made in our knowledge barrier, perhaps we can provide for longer term space flight and cut out or reduce many of the frailties of old age right here on Earth.

The materials presented in this textbook not only unravel in an elegant and understandable manner our current clinical knowledge but also point to the major knowledge gaps to be addressed to ensure future crews' health and safety while launching bold missions into the solar system. The wealth of knowledge gathered from space research and practice has also benefitted the life on Earth. I was instrumental in bringing together the best minds of NIH and NASA to work on the problems of aging. Healthy and productive aging reduces healthcare costs and minimizes disparities in future generations. My two space flights demonstrated that people do survive and work productively in space, but also more importantly age is not a limiting factor to space travel. My experiences do pave the way to future space tourism as the information provided in this textbook will undoubtedly contribute to safe space travel.

I am pleased to introduce this book and commend NASA and its medical community for their contributions to the future of human space travel.

Columbus, OH, USA John Glenn

Preface

Built upon the success of the first three editions, this fourth edition brings to the reader currency of space physiology and medicine. It has been more than 20 years since the publication of the third edition. In that time, U.S. Space Shuttles docked with the *Mir* Space Station, the International Space Station (ISS) was built using the Space Shuttles and Russian launch capabilities, the *Mir* Space Station was deorbited into the Pacific Ocean, the Space Shuttle Program was retired, commercial companies began to launch spacecraft for logistic and resupply to the ISS, and countries such as China and India have initiated programs that launched space assets into low Earth orbit. In the case of China, there have been a number of Chinese crew members who have been launched into space and safely returned to the Earth. The knowledge gained from the third edition (1994) to the fourth edition (2016) has been significant.

The growth in knowledge is attributable to international life sciences' research, significantly more complex space-based systems, technology in medical monitoring as well as computers and telecommunications, and the number of "man" hours in space. The construction of the ISS required an increase in the duration of an individual's time in space, a significant increase in the number of extravehicular activities, as well as advancements in environmental control and life support systems. With each successive program from the Mercury Program in the U.S. and the Voshkod in the Soviet Union to the ISS, our ability to understand the nuances and capabilities of providing healthcare in support of astronauts and cosmonauts during all phases of flight has progressively evolved. The current ISS Program, and the opportunity it provides for research and significantly longer stays in space, concomitant with commercial capabilities, has set the stage for exploration of other celestial bodies such as Mars and our own moon.

This fourth edition provides a foundation for those interested in space physiology and medicine practice and research. It is intended to be a teaching textbook with accompanying teaching materials to help the educator and student alike. Through 19 chapters, it provides a comprehensive review of space medicine, spacecraft environments, adaptation and rehabilitation in response to space flight, occupational health and safety issues, and ground-based testbeds and training of physicians and other personnel to support space medicine. The textbook is unique in distilling currently published clinical evidence for the benefit of the busy practitioner and researcher.

As editors, we are pleased to provide clinicians the needed practice tools at the time of expanding commercial interests in space.

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Introduction

Box Space Medicine and Physiology Textbook Organization

Parts

1. Introduction to Space Medicine
2. Spacecraft Environments
3. Space Flight and Crew Health: Adaptation, Pathophysiology, Rehabilitation, and Countermeasures
4. Occupational Health and Safety Issues in Space Flight
5. Ground-Based and Academic Training Programs
6. Future Perspectives

Chapters Outline

1. Chapter Overview
2. Learning Objectives
3. Key Words/MeSH terms
4. Introduction
5. Topical Knowledge Base and Gaps
6. Ethics and Legislations (as appropriate)
7. Conclusions
8. Cases Studies
9. Self-Study Questions
10. Key Points to Remember
11. References

Optional Teaching Tools (Web-Based)

1. Syllabus
2. Teaching aids

On April 13, 1960, a meeting was held at the Aviation Medical Acceleration Laboratory, WDAC, Johnsville, Pennsylvania, to examine and recommend biomedical information to be collected from astronauts and the Mercury spacecraft.[1] Fifty-six years later the editors and chapter contributors, in cooperation with Springer, are delighted to introduce the fourth edition of *Space Medicine and Physiology*. This revised textbook is intended for teachers, students, and practitioners interested and engaged in this rapidly evolving discipline. The knowledge

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[1] Space medicine in Project Mercury Chap. 7. history.nasa.gov/SP-4003/ch7-3.htm.

gained over the past five decades is reflected in this textbook. A common outline provides the reader with a ready cross-referencing between different chapters. The authors have provided their expertise from a variety of disciplines. Each has contributed in significant ways. All of the authors have been part of the space program in the U.S. over the course of their careers, and their experiences helped shape the narrative of NASA's space medicine activities.

This fourth edition builds on the foundation of the previous three editions, adding new information on relevant legislation, medical policy, and ethics. A syllabus and a set of teaching materials are made available for academic purposes.

The standard chapter outline (see Box) contains Case Studies, which add an important element for the reader to connect the evidence to clinical practice. The information contained in the chapters reflects the evidence in a point of time, which is subject to potential change based on new information obtained from research and observations conducted on the International Space Station (ISS). The Self-Study Questions and Key Points summarize the knowledge underpinning space medicine standards of practice and the remaining uncertainties to be addressed. Supplemental information from biomedical research based on human surrogate subjects and biological specimens are also included as appropriate.

Many of the research findings and publications from the Skylab and Apollo programs remain current and have been retained in this textbook.

Highly cited NASA experts at the forefront of space physiology and medicine contributed to this textbook. This is especially true with Part II, which includes Chaps. 8–14 on a variety of human systems and the impact space flight has on them. Each of the 19 chapters is either new or rewritten to reflect knowledge gained from the 30 years of research conducted in the Space Shuttle Program, the Shuttle/*Mir* Program, and the ISS Program. In addition, ground-based research, a critical component of space flight activities, has also been updated.

This textbook describes space medicine from the U.S. perspective and relies on the peer-reviewed literature and government sources divided into six parts and 19 chapters. A short overview of each part is described as follows:

Part 1, entitled *"Introduction to Space Medicine*,*"* presents a discussion on the evolution of human capabilities and space medicine, the environment of space exploration, and the clinical implications of the adaptation to space flight.

Chapter 1 provides a historical context for the human spacecraft design evolution, robotic tools, and biomedical research intended to protect the crew health and safety. It also dwells on the nascent commercial human space flight initiatives, the evolution of medically relevant legislation, policies, and standards, and ethical dilemma in the conduct of space exploration.

Chapter 2 describes the space exploration environment of Low Earth Orbit (LEO) and beyond. Most recent information on the Solar System and astrobiology, gathered from ground and space telescopes and robotic planetary rovers and probes, is presented. Robotic explorers are pathfinders for future bold human initiatives and provide invaluable information on potential resources, and possible health risks from physical and perhaps biological threats. Life's building blocks, the availability of water and other energy sources, are summarily addressed for individual planets and their satellites, including asteroids and comets. Planetary protection and associated policies are also discussed.

Chapter 3 is an overview of the bioastronautics of space flight and clinical implications to the human living and working in space. This chapter addresses astronaut demographics, epidemiological findings, and crew health maintenance in space and post-flight. The chapter also informs on microgravity as an analog to aging on Earth. Human factors influencing crew performance and the status of current countermeasures are concisely summarized. This chapter sets the stage for Parts II and III.

Part II, entitled *"Spacecraft Environments,"* provides an in-depth review of spacecraft internal environments that impact crew health, including toxicology, microbiology, immunology, acoustics, audition, and radiation. These four chapters provide a thorough review of how spacecraft systems may impact the human in the system. While research continues to be done in these disciplines, the literature, while current, requires additional information to enhance clinical practice, through the development of spacecraft standards and systems.

Chapter 4 provides an overview of spacecraft atmosphere contaminants, particulates, and other chemicals. In addition, monitoring and management of the toxicological threats to crew health and performance are addressed, including the handling of emergency events such as a fire or leaking coolant. This chapter also discusses accepted environmental hazards exposure limits for astronauts living in closed environments in missions in excess of 1 year.

Chapter 5 is focused on microbiology and infectious disease that may result from crew exposures to microorganisms present in the spacecraft environment, including the air, water, and surfaces. Environmental systems of the Space Shuttle, Shuttle/*Mir*, ISS, and management of health risks are discussed.

Chapter 6 describes health problems related to noise onboard the spacecraft. Attributes, characteristics, and mechanisms of acoustics and auditory response are described. Hearing conservation and principles for monitoring hearing thresholds and mitigating impact to crew health and performance are discussed.

Chapter 7 provides a thorough review of radiation exposure, including types and location of spacecraft related to the Earth and the Sun. In addition, acute and chronic effects of radiation exposure on crew members are discussed as well as countermeasures and prevention to minimize impact to crew health and performance. Radiation protection standards and clinical management of radiation-related health risks are presented.

Part III, entitled *"Space Flight and Crew Health: Adaptation, Pathophysiology, Rehabilitation, and Countermeasures,"* covers major body systems and the impact space flight has on them. There are seven comprehensive chapters, including cardiopulmonary, neurology, regulatory, metabolism and nutrition, clinical pharmacology and therapeutics, musculoskeletal, and behavioral health and performance. The chapter authors bring forward highly relevant findings and clinical evidence of the impact to the space traveler and the adaptive response to short-duration and long-duration LEO missions. These chapters have been refined with major updates from the third edition. Thirteen chapters of the third edition were consolidated into seven to minimize duplications.

Chapter 8 reviews aeromedical considerations and the cardiopulmonary system's response to space flight. An examination of the evidence supporting cardiopulmonary system function during all phases of flight is provided. This includes a discussion on cardiac physiology, orthostatic tolerance, pulmonary response, and countermeasures to maintain physical fitness and aerobic capacity.

Chapter 9 is a thorough review of the acute and chronic responses of the neurosensory and motor functions during space flight and post-flight health risks. Clinical findings presented include sensation, vision, cerebellar/vestibular function, spatial orientation, space motion sickness, and post-flight control of the circulatory system. Visual changes and risks due to altered cerebrovascular circulation are addressed.

Chapter 10 is focused on regulatory physiology, including health implications of space flight impacts on the endocrine, fluid, electrolyte, and hematological systems. Endocrine and biochemical functions as well as hematologic alterations in plasma volume, red cell mass production, and destruction are discussed. Renal stone formation risks and the impact of the iodine, used as a potable water biocidal treatment, on the thyroid function, and interventions to minimize health risk are presented.

Chapter 11 provides a summary of metabolism and nutrition in human space flight. A historical review of the development of food systems for space is presented as well as a discussion of the current system used on the ISS. Nutritional requirements for crew members are provided, which include palatability and cultural considerations. Food as a countermeasure for mental health and physical deconditioning is discussed.

The authors of Chap. 12 present a review of the clinical pharmacology and therapeutics concerns in human space flight. The principles of space pharmacology are addressed and the use and efficiency of medications in the space environment are discussed. Testbeds for the study of space pharmacokinetics as well as future directions of the use of medication in space flight are presented.

Chapter 13 is focused on the musculoskeletal adaptation to space flight. The mechanisms for musculoskeletal adaptation to microgravity, the health risks association with this adaptation, and effective countermeasures are discussed in detail. The outcomes of the use of animal models both in-flight and ground-based analogs and simulated conditions are provided.

Chapter 14 provides an updated review of behavioral health and performance and how space flight affects them and how these effects can be ameliorated. A discussion on the psychological adaptation factors, human-to-human system interface factors, sleep, and circadian factors is provided. Examples of pre-, in-, and post-flight and ground-based activities are used to illustrate the challenges for exploration missions.

Part IV, entitled *"Occupational Health Safety Issues in Space Flight,"* is focused on crew health monitoring and the international aspects of space medicine. This includes healthcare delivery systems and its challenges, telemedicine, and the development of a multinational approach to health through interaction with international partners and the experience gained between the U.S. and the USSR/Russia beginning in the 1960s.

Chapter 15 explores the principles of crew health monitoring and care. This includes a description of astronaut medical certification, pre-flight, in-flight, and post-flight crew biomedical monitoring, and use of countermeasures, psychosocial support, and in-flight environmental monitoring; and post-flight rehabilitation is discussed. Health and Medical Technical Authority and medical policy development are presented for both NASA and international partners.

Chapter 16 is focused on a number of issues related to the international aspects of space medicine. These include historical perspectives dating back to U.S./USSR relations in the late 1960s and early 1970s, the foundations for multilateral medical operations in support of international initiatives, the development of selection standards for the ISS era, and a look at the future of space medicine in a multicultural and technologically diverse environment.

Part V, entitled *"Ground-Based and Academic Training Programs,"* includes a concise summary of simulations and analogs as well as training in space medicine. Both of these are necessary elements for research and practice in space medicine.

Chapter 17 describes the development and utilization of a wide variety of testbeds and analogs used to conduct clinical supporting research and training. Testbeds discussed range from simulations to analogs that provide geographic and physical similarities to space flight with regard to isolation, limited communications, and time delays in reaching definitive care.

Chapter 18 addresses the current academic and professional skill training offered to space medicine practitioners as these individuals prepare to support human space flight activities with a focus on its development and evolution. In addition to academic training, other modes of training in space medicine are detailed, including international collaborations in preparing flight surgeons for duty. The chapter also highlights training efforts in a number of other space-faring nations.

The book closes out with *"Future Perspectives,"* which provides a conclusion and next steps as space medicine moves forward. Chapter 19 discusses national plans and commercial endeavors as human space flight and the launch systems that support LEO operations are being conducted by nongovernment entities. This includes a summary support for NASA-specific missions and emerging technological designs as well as efforts for commercial tourism. Commercial entities are discussed with regard to their progress and collaboration with NASA and its partners.

The operational necessities of space missions require that the clinical knowledge base is continuously updated to ensure that proper medical policies and standards are incorporated in a timely manner into space medicine practice. Recent reviews of biomedical publications suggest that the volume of research literature has been on the rise, but most of the epidemiological and clinical information is still of a descriptive nature. A scientometric and bibliometric analysis of the space medicine literature from major databases, such as the ISI Thompson Web of

Science, PubMed/Medline, and archives specific or relevant to this textbook, was conducted by the George Mason University faculty,[2] validating high relevance materials are cited in this textbook. When compared to the wealth of the world biomedical literature, the number of clinical publications in space medicine is quite modest. Only 15 % of the space medicine literature provides robust knowledge readily translatable into medical policies, practice, and standards. This does not differ from other biomedical disciplines, and especially in the field of occupational and environmental health [1–4]. It is also worth mentioning that this analysis revealed that while the U.S. remains the leading contributor to the space medicine and physiology knowledge base, the People's Republic of China has an increasing presence in this discipline, primarily in simulations and ground-based research.

This textbook will be updated on a regular basis to reflect new knowledge and challenges as they are made available from the ISS research and clinical observations. This text contains an extensive amount of information, and the editors and authors took utmost care to ensure accuracy and minimize potential errors or omissions. The authors are especially grateful to NASA for the use of the archives, narratives, and illustrations. In many instances those were the only sources of information available at this time as the NASA-supported research continues.

Finally, the editors will be more than happy to consider requests for tutorials on the subject matter.

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[2] Professor Laurie Schintler, Rajendra Kulkarni, Research Instructor, and Kingsley Haynes, Eminent Scholar, University Professor Emeritus at George Mason University (supported by the NASA Research Grant # NNX12AK32G).

Acknowledgements

The editors acknowledge the efforts of a large number of individuals who contributed to this book. The fourth edition of *Space Physiology and Medicine: Evidence and Practice* has been completely revised and covers a wide range of topics that have relevancy to the practice of and research in space medicine. Numerous experts within academia and private organizations, especially the NASA Lyndon B. Johnson Space Center, played a part in early drafts of chapters as well as rewrites and refinement of the text. These contributions, whether small or large, helped the chapter authors develop the evidence and practices reflected in this textbook.

While it would be appropriate to list all the individuals that played some role, we would assuredly omit some. So we choose to acknowledge the men and women who have been associated with NASA over the past 20 years since the release of the third edition. There are two individuals who were selfless in their contributions, Dr. Sam Pool and Dr. Lakshmi Putcha. The space medicine community lost them both in the past few years. Each spent most of their careers conducting medical research and operations at the NASA Lyndon B. Johnson Space Center.

The editors wish to extend their appreciation to the astronauts who contributed so much as researchers and experiment participants to collect the information contained in this book. Special thanks are offered to Professor Laurie Schintler and Mr. Rajendra Kulkarni, Schar School of Policy and Government, George Mason University, who lent their expertise and time to help with the bibliometric analysis of the literature cited in this book.

As editors, we appreciate the dedication of the editorial staff and the publisher for keeping us on our toes and accurate in our summary of space medicine.

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Part IV Occupational Health and Safety Issues in Space Flight

Part V Ground-Based and Academic Training Programs

Part VI Future Perspectives

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Part I

Introduction to Space Medicine

Evolution of Human Capabilities and Space Medicine

1

Arnauld E. Nicogossian, Charles R. Doarn, and Yinyue Hu

Chapter Overview

NASA is the world's largest civilian space and aviation engineering research agency and a showcase of U.S. technological advances. It is the true birthplace of modern space medicine, which continues to be primarily influenced by engineering requirements. This chapter brings together the historical evolution of space medicine and human factors driven by technological development and political imperatives of human space exploration. Sustaining life, minimizing health risks and chances of injury have been and continues to be the primary goals for space medicine practice. In the sixteenth century, Ramazzini (Bernardino Ramazzini. *De Morbis Artificum Diatriba*. Apud Guilielmum van de Water Academiiæ Typographaphum [Publisher]. Geneva, Switzerland. 1703), the father of occupational medicine, observed that sailors on long voyages of exploration did not fare as well as those on land when afflicted by chronic disorders. His observations still apply to modern space medicine practice, which is rooted in the principles of preventive medicine. Thus, space medicine practitioners' primary focus is on life support, food and water production systems, selection of cabin atmosphere and gas composition, hygiene, space habitat toxicology, radiation protection, and preventing infections. The principles of astronaut medical selection are to ensure "healthy" and disease-free candidates, while medical retention standards (annual clinical evaluations) and care ensures career longevity. Depending on the type and length of the space mission, certain medical conditions are considered compatible with the ability to perform assigned mission duties and a medical waiver is issued. Space medicine draws heavily on 50 years of aviation medicine knowledge and continues to be the central focus of today's practice of "personalized medicine." Traditionally, the knowledge underpinning space medicine practice lagged behind operational needs and remained largely empirical, relying on data from terrestrial analogs and simulations. Historically, extremely complex short duration missions to the Moon, followed by long duration low Earth orbit missions, did not permit adequate time for a systematic acquisition of biomedical knowledge base. Clinical and psychological research remained resource constrained for access to space, funding, and sufficient sample size of astronauts (the astronaut community constituted the astronaut sample size. Astronaut exposure to the space environment precluded a meaningful selection of a control group) due to political pressures of the "space race" and mounting costs from unexpected technological challenges. The national debate on the future of the space program, following the Apollo 17 mission, coupled with federal deficits due to the Vietnam War, resulted in significant reduction to NASA budgets, and termination of follow-on missions to the Moon. Excess Apollo program hardware was used to deploy the first U.S. space station (Skylab) and to conduct the first U.S.-Soviet collaboration in space: docking an Apollo and a Soyuz spacecraft. The U.S. investment in Skylab produced an unprecedented amount of data on the human responses to orbital long-duration space flight. The three Skylab missions produced the most comprehensive and fundamental seminal knowledge used by all space-faring nations in designing medical support and habitability systems for human space flight. Despite the many operational and logistic challenges, and occasional in-flight crew illness, no U.S. missions resulted in an unscheduled termination, or loss of life, due to medical conditions. This in itself is a testimonial to the soundness and

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Electronic supplementary material: The online version of this chapter (doi: 10.1007/978-1-4939-6652-3_1) contains supplementary material, which is available to authorized users.

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efficiency of the clinical infrastructure and space medicine skills and expertise evolved since the early 1960s.

Budgetary and political imperatives led to periodic NASA management and programmatic reorganizations often affecting medical staff and projects. The number of NASA space medicine physicians (flight surgeons), remains small, and between 1960 and 1990 reached its peak of 35 individuals (not including astronaut physicians). Today, this small federal workforce is supplemented by military detailees and supported by contractors in the many demanding duties outlined throughout this textbook.

The experimental nature of spacecraft designed by the U.S. and other space-faring nations are briefly detailed in the context of space medicine. The interaction of the environment and spacecraft design, leading to potential health risk(s) are summarily reviewed. Extravehicular systems and robotics, intended to minimize unsafe exposures, while enhancing human performance, are briefly discussed. Space tourism and evolving commercial infrastructure and the potential for space medicine practice expansion are also presented. Finally the socioeconomic, cultural, and health care impacts of space exploration are briefly addressed.

Learning Objectives

1. Review major historical events framing the evolution of space medicine and exploration technology.
2. Discuss international collaboration in space medicine and contributions to the peaceful uses of space exploration by humans.
3. Become familiar with the evolving legislation, policies, and ethics guiding space medicine practice.

Introduction

> "…chronic diseases also attack them (sailors), but they do not suffer from them as long as do those whose occupation is on land, for a ship is not a good place to ministering to chronic diseases…"
>
> Bernardino Ramazzini: *De Morbis Artificum Diatriba* 1703 *[Diseases of the Workers]*

For millennia, humans have watched in awe the unending spectacle of the night skies. Ancient civilizations relied on the sun, moon, planets, and stars for time keeping and navigation, exploring the far horizons of our spaceship Earth. Over time, astronomy became intimately involved with religion, science, health, medicine, politics, philosophy, and war (Box 1.1). Changes in seasons, appearance of floods, and agriculture were predicated on the astronomical observations. These observations were essential to ensure the health security of the communities and mitigate disasters, plagues, and food shortages.

Box 1.1
The roots of space flight can be traced to the introduction of rocketry more than 2000 years ago with the invention of gunpowder in China. By the time of Genghis Khan's reign, gunpowder in the form of firecrackers and rudimentary rockets had become an integral part of Chinese defenses.

Box 1.2
Shortly before World War II, Oberth joined his former pupil, Wernher von Braun, in Germany's secret facility at Peenemünde Army Research Center (Heeresversuchsanstalt Peenemünde in German), located on the northern peninsula of the Baltic Island of Usedom, where they both worked on the development of the V-2 rocket [1]. This weapon was responsible for the death of 9000 civilians and military personnel and more than 12,000 slave laborers used to build them.

In the late nineteenth and beginning of the twentieth centuries, and purportedly inspired by the Jules Verne novel, *From the Earth to the Moon*, theoreticians, Konstantin Tsiolkovsky in Russia and Hermann Oberth in Germany published mathematical theories and calculations of speeds required to escape the Earth's gravitational force (Box 1.2) [1]. Tsiolkovsky was primarily interested in space travel and was the first to describe the concepts of artificial gravity to protect the health of future explorers.

The era of modern rocketry truly began with Goddard's rocket launch on March 16, 1926, followed by an instrumented rocket in 1929. German engineers at the Peenemünde Army Research Center carefully monitored his experiments, and incorporated his discoveries into the design of Germany's offensive weapons. Under the direction of Wernher von Braun, the liquid-fueled *Aggregat-4* (A4) or V-2 became the first offensive ballistic missile of World War II. In 1945, after the defeat of Germany, V2 technology, together with surviving engineering expertise, was absorbed into the U.S. and Soviet Union military and space programs.

The Origins of Space Medicine in the United States

Interest in human space flight grew rapidly among a small circle of talented biomedical scientists—most of whom were initially from military aeromedical research laboratories.

Box 1.3

Since its inception, space medicine developed interdependencies with astronautics, human factors, habitability engineering, and biomedical research. Scientists and physicians soon recognized the need for an organization to coordinate and exchange information concerning space medicine research and practice. In 1951, the *Space Medicine Association* became the first constituent of the *Aerospace Medical Association*. In May 1978, NASA physicians P. Buchanan, J. Buhaine, J. DeGioanni, R. Hessberg, W. Hoffler, and A. Nicogossian established the *Society of NASA Flight Surgeons* as a constituent member of the *Aerospace Medical Association*.

This interest was also fueled in part by concern over the health and safety of pilots involved in supersonic test flights. Many conditions faced by space crews during launch and landing were similar to those encountered by test pilots in supersonic flights.

In 1948, a U.S. Air Force (USAF) physician, Colonel Harry G. Armstrong (1899–1983), organized a meeting at the USAF School of Aviation Medicine to discuss aeromedical problems of space travel [2]. Participants included biologist Hubertus Strughold[1] (1898–1986) and astrophysicist Heinz Haber (1913–1990) [3]. This meeting saw the birth of a new aerospace medicine discipline within the field of preventive medicine (Box 1.3) [2]. Space medicine is considered a product of the Cold War, borrowing applicable standards and knowledge from occupational, environmental, and aviation medicine [4].

Sustaining life and productive human function during space flight presented unique technological challenges requiring innovation in distance health monitoring, medical care, and life support. Concerns with physiological responses to weightlessness led both Soviet and U.S. pioneers in space medicine to use high-altitude balloons, Earth suborbital rockets, and orbital spacecraft carrying a variety of living organisms to study responses to the stresses of flight and validating engineering systems design [5]. In 1957, the Soviets flew invertebrates and vertebrates, including dogs. The *Sputnik 2* carried a dog named Laika into space on a non-retrievable platform [6]. Subsequent missions returned their canine passengers safely back to Earth.

Box 1.4 Early NASA Biomedical Research Partnerships

The newly formed NASA research and operations field centers in Texas and California, as well as select institutes and universities—such as Lovelace and Mayo Clinics, University of New York at Rochester, The Ohio State University in Columbus, the Veterans Administration Hospital in San Francisco, Houston Medical Center in Texas, and others—began accelerated ground-based research and technology development programs in space human factors. These institutions in partnership with the aerospace industry developed a ground-based knowledge and technology base and successfully incorporated this information into future spacecraft development for the exploration of the Moon and low Earth orbit (LEO).

To learn more about how the body would adapt to space flight, the U.S. launched two primates into space on board V-2 rockets by 1950. Although neither animal survived, these early flights demonstrated the need for reliable life-support systems and began the long process of requirements definition for the protection of mammals against the rigors and stresses of flight into space [7]. Early practitioners were trained in aviation medicine by the U.S. Navy (USN) and USAF. Beginning in the 1950s, these two organizations expanded their curricula to include space flight. These developments were reflected by new organizational designations: the Air Force Aviation Medical Facility in San Antonio, Texas became the School of Aerospace Medicine and the Navy's Aviation School at Pensacola, Florida became the Naval Aerospace Medical Institute. The Schools of Public Health at Johns Hopkins University, Harvard University, and The Ohio State University, which cooperated with military organizations in providing residency training, also reflected the changing focus in their curricula (Box 1.4). These training programs eventually led to the development of Aerospace Medicine residencies at Wright State University and the University of Texas Medical Branch (UTMB) (see Chap. 18) [8].

Politics and Space Medicine

The October 4, 1957 launch of the Sputnik marked the Union of Soviet Socialist Republics (USSR) and U.S. engaging in a "space race" that allowed little time for biomedical research and medical practice to conduct a systematic in-depth program of investigations into the health risks of space

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[1] Hubertus Strughold, PhD, was brought from Germany to the U.S. by the U.S. Army, together with other German physicians and researchers. They brought with them results of aeromedical and physiological research conducted in Germany up to the end of World War II. Dr. Strughold continued his research at the USAF Brooks School of Aerospace Medicine, which contributed significantly to the U.S. space medicine successes. Controversy and suspicion surrounding his participation in Nazi medical experiments resulted in several federal investigations and a tarnished reputation [3].

flight. Anecdotal reports, ground-based studies, and clinical observations, together with existing aviation databases became the foundation of the nascent space medicine program. This sense of urgency had a profound impact on the progress of space physiology and medicine, whereas clinical problems were handled empirically and research was conducted addressing issues after they were identified in space missions.

Specialized space biomedical research laboratories, established within the U.S. Air Force (USAF) and the U.S. Navy (USN), supported National Advisory Committee for Aeronautics (NACA) installations (NASA absorbed the NACA installations in 1958) as early as 1955. Some of the needed systems such as the USN's full-pressure suit used for high-altitude flights were adapted for space flight needs. Despite political differences, the U.S. and Soviet space medicine specialists met and exchanged knowledge at scientific meetings. After the Apollo Soyuz Test Project (ASTP), collaboration intensified, and the sides began planning for more ambitious activities using analogs and Soviet/Russian Cosmos missions for joint biological experiments (Box 1.5).

In the 1990s, some of the biomedical experiments using non-human primates came under attack from the People for the Ethical Treatment of Animals (PETA). NASA's use of animal test subjects was an attractive and highly visible target for PETA's goal to eliminate biomedical research using animal test subjects, especially non-human primates, in the U.S. The publicity surrounding the Bion 11 flight resulted in several Congressional hearings and further intensified post-flight with the death of one of the primates, and ultimately led to the cancellation of U.S. funding for the remainder of the program. NASA physicians and biomedical scientists worked with many influential professional and international associations to ensure that ethical and scientific research priorities remained in the domain of the biomedical community and minimized political imperatives. The Bion 11 mission provided valuable inputs into space medicine, but unfortunately it severely impacted the Russian space biomedical community's ability to continue with non-human primate missions, especially at a time of severely constrained funding in the "post-Perestroika" era.

Despite these challenges, space biomedical collaboration between the U.S. and the Soviet Union/Russia continued to flourish, surviving political turmoil. Academicians Oleg G. Gazenko and Anatoli I. Grigoriev remained at the forefront of such collaboration for at least four decades and were joined by other nations.

Box 1.5 NASA's Research Using Non-Human Primates in Space

The U.S. developed a series of biosatellites to initially fly invertebrates and rodents, and later to orbit non-human primates for several days in LEO. The last spacecraft in this series, *Biosatellite III*, was launched on June 28, 1969. On board was a single, male primate, *Macaca nemestrina*, named Bonnie, weighing 6 kg, for a planned 30-day mission. The mission objective was to investigate the effect of long-term space flight on behavior, performance, cardiovascular, and fluid and electrolyte metabolism. Bonnie was over instrumented and became sick after several days on orbit. The mission was terminated short of 9 days. Bonnie died 8 h after recovery from dehydration and other medical complications. The U.S. Congress terminated the program by reducing NASA life sciences funding. A similar Russian-funded research effort *Bion 11* also had issues. One of the primates died on the second post-flight day following anesthesia for tissue, muscle, and bone biopsies.

A NASA/Russian review committee under the chairmanship of Dr. Ronald Merrell found that the post-flight dehydration, cardiovascular compromise, and poor body temperature regulation contributed to the death of the non-human primate. The review committee characterized the immediate post-flight period to a *high risk perioperative category of patients* (American Society of Anesthesiologists [ASA] III/IV Class). NASA dropped out of participation in a planned *Bion 12* mission due to the inability to adhere to the approved study protocols based on the probability of high mortality risks associated with early post-flight procedures. Following several hearings the U.S. Congress disapproved further participation and funding for the Bion 12 mission.

Historical Demographics

The majority of professional space travelers are supported by the space agencies from the U.S., USSR/Russia, European Union, and Peoples Republic of China. Russia was the first country to provide access to paying space tourists. Tables 1.1, 1.2, and 1.3 summarize these human space flight demographics [9]. By October 2016, only 551 individuals (491 men, 60 women) had spent a combined total of more than 135 human years in space missions.[2] Sending humans into space is still the domain of the U.S., Russia, and China, and as of June 2015, with the retirement of the NASA Space Shuttle, the U.S. has been relying on Russian Soyuz spacecrafts to deliver astronauts to the International Space Station (ISS), while developing a new exploration class spacecraft and relying on the private sector to develop a "space taxi" capability for astronauts to travel to and from the ISS.

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[2] This number varies depending on the three existing definitions of astronauts based on altitude reached.

Table 1.1 Number of months logged in space by individual crew members

Months	<1	1	2	3	4	5	6	7	8	9	10	>10
United States	116	147	30	4	3	14	9	12	4	1	0	7
Russia/USSR	27	14	4	4	5	6	12	8	3	1	2	29
China	8	2	0	0	1	0	0	0	0	0	0	0
Europe	21	14	1	0	1	1	1	5	0	0	0	6
Asia	8	3	0	0	0	2	1	1	0	0	0	2
Canada	2	4	0	0	0	1	1	1	0	0	0	0
Other countries	6	1	0	0	0	0	0	0	0	0	0	0
Total men	170	162	31	8	9	22	20	24	7	2	2	41
Total women	18	23	4	0	1	2	4	3	0	0	0	3

Adapted from http://www.astronautix.com/articles/aststics.htm [9]

Table 1.2 Actual number of missions flown by individual crew member and by country of origin

Missions	1	2	3	4	5	6	**7**
United States	102	103	58	58	21	5	2
Russia/USSR	51	29	23	7	3	4	0
China	7	1	0	0	0	0	0
Europe	29	15	5	1	1	0	0
Asia	9	6	1	1	0	0	0
Canada	3	4	2	0	0	0	0
Other countries	7	0	0	0	0	0	0
Total men	188	140	81	60	19	9	2
Total women	19	18	8	7	6	0	0

Adapted from http://www.astronautix.com/articles/aststics.htm [9]

Table 1.3 Space tourists by countries of origin (paying space explorers)

Country of origin	Number of paying tourists	Vehicle	Country of origin
United States	5	Soyuz	One Iranian-American and one Hungarian-American, one British-American
Japan	(1)		Did not fly due to medical reasons
Iran		Soyuz	Iranian-American
Canada	1	Soyuz	
Hungary			Hungarian–American
United Kingdom	1	Soyuz and *Mir*	A woman chemist flew under the project Juno
South Africa	1	Soyuz	South African-British
Total women	2		
Total men	6		

Medical Diplomacy

Medicine is an integral element of all human space missions, both human and robotic. Sustaining humans, searching for habitable planets or extraterrestrial life, is of interest and involves flight surgeons and medical personnel. Humans can present a threat to extraterrestrial life and the reverse is also true. Planning human exploration into the Solar System also requires a good understanding of the operational environments, determining potential health threats and hazards, and devising appropriate tools and countermeasures (Box 1.6 [7]). International collaboration in space is also viewed as a showcase and demonstration of a national scientific capability. Space exploration is considered a contributor to knowledge and a better life on Earth. Most of the international collaborative human space missions are expensive, use unique attributes of space to solve space medicine problems, and offer a promise for potential return on the investment.

NASA medical personnel expertise and innovative practices are routinely sought to address earthbound medical problems. Technological demonstrations such as telemedicine, remote sensing and vector borne infections, natural disaster warnings and mitigations, and miniaturized and compact health care systems for home use were transferred to the private sector by the sponsoring individual space agencies [10]. It is estimated that biomedical space research has contributed significantly to the private sector enterprise [11]. These real and perceived benefits or "spinoffs" are the basis for a vigorous outreach program, often with the participation

Box 1.6

Before the formation of NASA, most of the NACA functions were located at the Langley Research Center in Hampton, Virginia. It is in this location that the majority of the Department of Defense (DoD) detailed medical specialists began their work on Project Mercury [7].

Initially, the Office of Advanced Research and Technology was responsible for both the biotechnology and human research, and institutionally for the biological activities at the NASA Ames Research Center.

NASA followed the military model for its space medicine program. The purpose was, and remains, to ensure crew health and safety and to capitalize on relevant biomedical knowledge gathered by other federal or private agencies and organizations.

With time, a second major activity was developed, mostly under the auspices of the physical sciences, addressing the understanding of the origins, evolution, and destiny of life in the universe—or astrobiology.

Though both programs remained separate for decades, the human exploration of the solar system is bound to bring their research and operational interests together, notably in planetary protection, preventing back contamination and the hazards associated with the search for alien life forms—mostly bacteria (see Chap. 2).

The NASA chief health and medical officer (CHMO) is responsible for coordinating the planetary protection policies with the human solar system planning activities.

of physicians, to ensure the diffusion of space research into terrestrial health programs.

For many years, Dr. Oleg Gazenko, a physician and statesman, and the director of the USSR Institute of Biomedical Problems, led the Soviet delegations to the United Nations (UN) Committee on the Peaceful Uses of Outer Space (COPUOS). He established annual special sessions at the UN to showcase health benefits from applications of space research and technology. He ensured that NASA and other space-faring nations participated in these sessions [12]. NASA routinely testifies to the U.S. Congress on its technology transfer programs, especially in disaster mitigation and humanitarian help, as required by the Space Act of 1958 [13, 14]. Unlike with other U.S. agencies currently, medical diplomacy is not part of the official space medicine training curriculum and is usually acquired over time as part of NASA career opportunities.

Space Medicine in the United States

From NASA's beginning, the responsibilities for life sciences research and space medicine remained diffused and fragmented. NASA's expectation of space medicine is to ensure crew health and mission safety. Most of the knowledge used to plan for the mission was derived from the aviation medicine and ground analogs. The National Research Council Committee on Bioastronautics (1958–1960) was asked to predict possible health risks to astronauts. These risks are detailed in Table 1.4 [15]. The predictions were quite accurate and helped focus the clinical research and development approach [15].

Traditionally, NASA management assigned a high priority to practice and research with relationship to health and safety of the space crews. NASA did seek support for fundamental biological research through cooperation with the international community and especially the U.S. National Institutes of Health (NIH). Flight access was given priority to those activities that were judged to have a direct benefit to human safety, or for the "improvement of life on Earth." This philosophy led to tensions between field centers, clinical (operational) personnel, and academic bioscientists competing for limited funds. In the early 2000s, it became necessary to address these conflicts, real or apparent, by separating organizationally clinical programs from the biomedical research activities within NASA. An office of the Chief Health and Medical Officer (OCHMO) was established, reporting directly to the NASA Administrator. Reorganization of the biomedical programs within NASA continues on a decadal basis and is driven by the availability of resources and human exploration priorities as set by the U.S. president through revisions of the National Space Policy.

NASA has sponsored specific high-priority biomedical research consistent with mission needs during the Gemini, Skylab, and Space Shuttle in anticipation of the ISS program. Such an approach does delay the acquisition of a systematic space medicine knowledge base. Major events shaping the NASA space medicine program, organizations, and relevant policies are outlined in Table 1.5 [16–22].

Project Mercury (May 5, 1961 to May 16, 1963)[3]

In 1960, NASA Administrator T. Keith Glennan established a life sciences program under the direction of Clark T. Randt, a prominent physician and bioscientist. This move was designed to ensure collaboration with the larger community of biologists and clinicians. NASA's intent was to harness the existing

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[3] The dates reflect the launch dates of the first and last missions.

Table 1.4 Predicted and observed medical problems associate with space missions

Predicted by the NRC 1958	Observed as of August 2015
Anorexia	Only in association with space motion sickness
Nausea	With space motion sickness
Disorientation	During initial adaptation to the space environment
Sleepiness	With severe space motion sickness
Sleeplessness	Throughout space mission duration
Fatigue	Poor workload scheduling
Restlessness	None
Euphoria	None
Hallucinations	None
Decreased g tolerance	post-flight
Urinary retention	Affects less than 1 % of crews
Diuresis	None measured
Muscular incoordination	Gait disturbances post mission
Muscle atrophy	Documented
Demineralization of bones	Documented
Renal calculi	Pre-mission increased risk
Motion sickness	In most crew members with varying degree. Repeat exposure, reduces the incidence
Pulmonary atelectasis	None
Tachycardia	Rare and during high metabolic load activities
Hypertension	None
Hypotension	Post-flight and transient
Cardiac arrhythmias	Documented in few instances. Pre-existing rhythm abnormalities not aggravated by space flight
Post-flight syncope	Documented
Decreased exercise capacity	Post-flight
Reduced blood volume	Documented post-flight
Reduced plasma volume	Documented post-flight
Dehydration	Observed post-flight due to decreased fluid intake and mild.
Weight loss	Variable
Infectious illness	Minor infections treated in space. Increased shedding and reactivation of HSV attributed both to stress and possible decrease immune response (see Chap. 5)
Not predicted	Visual changes and pathological findings

NRC National Research Council, *HSV* Herpes simplex virus

knowledge to be applied to the space program needs and not necessarily to spin a major life sciences research enterprise. After 1 year in office, Randt felt that his efforts in establishing a strong medical presence in NASA were blocked, and tendered his resignation. This led to a fragmentation of the life sciences organization in 1962, with the Biosciences Programs, including the Biosatellite Office, being established in the Office of Space Sciences; NASA Ames Research Center, at Moffett Field, California (former Navy Air Station) was designated as the laboratory responsible for biological research including the development of the Biosatellite project to explore the physiological responses of primates, and other living organisms, to extended duration space missions [23]. The space medicine program was transferred to the human space flight organization, to better integrate and address engineering and health safety risk management. The new organizations captured many of these early leaders in space medicine [19]. By 1962, some of the team members were transferred to the Office of Advance Research and Technology, the Space Medicine Directorate, Office of Manned Space Flight, at NASA Headquarters or to the Manned Spacecraft Center (MSC) located in Houston Texas (Box 1.7). These individuals took on the responsibilities at NASA Headquarters and the MSC for developing requirements and systems to support NASA and the nation's program of getting to the Moon and back, including development of the clinical research and designing the Lunar Receiving Operations, following return from the Moon missions.

In the late 1950s, the selection process began with Eisenhower's direction that all astronaut candidates be recruited from the ranks of military test pilots. As a group, military test pilots were required to demonstrate many abilities deemed to be crucial for an astronaut: good judgment, decision making under stress and in threatening situations, quick reaction time, and refined motor skills. Of the first group of applicants, 100 test pilots were given interviews, psychiatric examinations, and a complete medical evaluation that included medical stress tests (Box 1.8) [24, 25]. The main

Table 1.5 Major medical and select policy milestones in the United States space program [16–22]

Programs[a] Elements	Mercury (1958–1963)	Gemini (1961–1966)	Apollo (1961–1972)	Skylab (1973–1974)	Space shuttle/spacelab/spacehab (1981–2011)	NASA*MIR* (1992–1998)	ISS (1995–present)
Clinical Findings	• Medical selection screening focused on psychological, stress, and physical endurance laboratory tests • Six Mercury space missions demonstrated that *man* could function properly and without major untoward deteriorations of body functions for periods up to 34 h of weightless flight	• Second astronaut selection “The New Nine” and the longest mission of 14 days (medical focus), in preparation for the Apollo program • First comprehensive pre- and post-flight medical evaluations documented • Loss of red cell mass (ranging 5–20 % from baseline) • Post-flight orthostatic intolerance in 100 % of crews • Loss of exercise capacity compared with pre-flight baseline • Loss of *os calcis* bone density (7 % from baseline) • Sustained loss of bone calcium and muscle nitrogen • Higher than predicted metabolic cost of extravehicular activity • Sustained performance during the first in space rendezvous and docking	• Vestibular disturbances • Less than optimal food consumption (1260–2903 kcal/day) • Post-flight dehydration and weight loss (recovery within 1 week) • Decreased post-flight orthostatic tolerance (tilt/lower body negative pressure tests) • Reduced post-flight exercise tolerance (first 3 days) • Apollo 15 cardiac arrhythmias (a run of 22 nodal bigemini) attributed to potassium loss) • Decreased red cell mass (2–10 %) and plasma volume (4–9 %)	• First U.S. astronaut physician in space conducting in-flight clinical evaluations. First systematic investigations into man’s physiological responses to flight • Rigorous data collection to meet experimental protocols • Extensive testing of potential countermeasures for post-flight physical deconditioning • Inflation of anti-gravity suits during post-flight landing • Crew schedule overload due to unscheduled ground control requests for scientific experiments • Crew and ground control tensions • Subluxation of a finger corrected by the astronaut physician • Ocular foreign body (pencil lead tip) removed by the astronaut physician • Dry skin and occasional superficial lacerations and boils, responding to antibiotics • Aerobic exercise not sufficient to protect against cardiovascular, bone, and musculoskeletal deconditioning, using the bicycle ergometer • Introduction of the Thornton-Whitmore treadmill on Skylab 4, protected against deconditioning • Dispelled the low caloric requirements in space missions reported during previous missions	• Decreased sensorimotor control at landing; some astronauts unable to walk unaided or make rapid egress • Increased risk of virus shedding (immunocompromised) with increasing flight duration • Simulation of pre-flight sleeping arrangements (bed sack, pillow) helps counter sleeplessness in-flight • Caloric intake improved with wider dietary selections • Fluid loading before deorbiting a promising countermeasure, together with anti-g suit early inflation, for post-flight orthostatic intolerance • Air cooled escape suit increased thermal load, with 33 % incidence of orthostatic intolerance post-flight, reduced to 3 % with liquid cooled garment • Shoulder injuries from the space suit hard torso during underwater training sessions • Risk of renal stone and proposed potassium citrate as a countermeasure • Salt and water drink most effective oral solution • Midodrine potential for preventing orthostatic intolerance • Women more susceptible to orthostatic intolerance post-flight • Injectable promethazine moderately effective for space motion sickness • Transient low back pain • Increased use of analgesics and sleeping medications • Urinary retention relieved by the use of urethral catheters	• Increased cardiac dysrhythmia at >70 days in-flight • Bone and muscle loss continues unabated • Good nutrition necessary for maintaining physical strength • Risk of kidney stones increases with length of flight • Increased neurosensory and neuromotor changes (e.g., posture and gaze control, target acquisition) with long-duration flights • Tilt position counters rapid blood redistribution during deorbit • Recovery post-flight requires three times the length of time spent in orbit for bone and equal length of time following exposure to microgravity for muscles • Increased rest periods, relaxation time, and communication with family and friends improves crew performance and safetyCrew performance improves with the nearing of the mission completion • Radiation levels higher than expected	• Validation of the risk reduction countermeasure for renal stones • Validation of the most effective aerobic and resistive exercise protocols for musculoskeletal deconditioning • 20 % of astronauts (primarily males) suffer from physiological and anatomical visual problems in long duration missions • Some astronauts reaching career limits of radiation exposures

Programs[a]	Mercury (1958–1963)	Gemini (1961–1966)	Apollo (1961–1972)	Skylab (1973–1974)	Space shuttle/spacelab/spacehab (1981–2011)	NASA*MIR* (1992–1998)	ISS (1995–present)
Elements							
Medical Policy, Procedures, Requirements and Major Organizational Changes	• Space Act establishes NASA and a number of the U.S. military aerospace medicine experts transferred to the newly formed Agency's Space Task Group (STG) at the Langley Space Center in Virginia. The STG manages the medical Mercury program • Separate biomedical sciences combined into the Space Life Sciences Office, in 1960 • First medical selection guidelines for screening military test pilots (Mercury 7 astronauts) • First disqualification from flight status for medical reasons in 1962 • Continuous vital signs monitoring in-flight using telemetry	• NASA establishes standard physiological pre- and post-flight data collection protocols • First extensive medical assessments in preparation for Moon landing missions • First metabolic cost of the extravehicular activity (EVA) leading to the formulation of new medical design requirements • In 1969, two biomedical laboratories established at the Ames Research Center for biology, and at the Manned Spacecraft Center for human missions. A Division of Life Sciences created within the Office of Manned Space flight at NASA Headquarters, Washington, DC	• Crew health stabilization program implemented following Apollo 13 concern of exposure to measles • Crew member flight medical disqualification due to suspected exposure to measles • Private medical communications following Apollo 9, guided by medical privacy • Post-flight mobile lunar quarantine of crews eliminated after Apollo 14 (Lunar samples quarantined at the NASA Johnson Space Center)	• Pre-and post-flight crew health stabilization program for medical and research purposes • Crew remains in the Apollo spacecraft until lifted onboard the recovery vessel • Private daily medical conferences • At least one weekly private family medical conference • Medical vital sign monitoring limited to hazardous and high physical demand activities • Life Sciences Division transferred to Space Sciences Directorate and the exobiology program added	• Establishment of NASA Medical Boards • Medical Class I, II and III Standards for Selection and Retention Published • NASA Longitudinal Study/ Surveillance of Astronaut Health Data base initiated • Termination of clinical motion sickness susceptibility vestibular tests pre-fight with testing of motion sickness medication effectiveness • Aerospace Medicine Advisory Committee of the Life Sciences Advisory Board • Introduction of crew transfer vehicle for post-flight crew medical care and testing prior to the "STS walk around" • Ground and flight ethics review boards • Animal subjects ethics review boards • Privacy Act of 1974 applied to the protection of crew medical information and research results • Mandatory pre-landing fluid load and anti-gravity suit inflation • Crew medical information is protected unless the crew member health condition results in significant impact to mission objectives • In 1993, NASA created the Office of Life and Microgravity Sciences and Application (OLMSA) • Exobiology, renamed Astrobiology, with expanded funding, transferred to Space Sciences	• Cultural, language and psychological suitability training • Establishment of the Multilateral Medical Operations Working Group • Integration of medical training and operations for ISS • Institute of Medicine (IOM) Standing Committee on Aerospace Medicine and Medicine of Extreme Environments, established in 1998 to provide space medicine and clinical advice (formally accommodated under the Space Studies Board of NAS/NRC)	• Adoption of the Medical Technical Authority approach to medical requirements development • Process for translating research into the medical practice • Establishment of the multilateral medical boards (MMOP, MSMB, and MMPB) to address and reconcile medical practices based on dissimilar spacecraft design • Space medicine approach based on the occupational model • IOM participates in the capacity of medical issues consultant • Psychological evaluation and care of astronauts • Ethical considerations for space mission astronaut selection in the event of exceeding career limits for radiation (IOM report 2014) • NASA creates an independent office of the Chief Health and Medical Officer • OLMSA downgraded to a division and transferred to the Human Exploration and Operations Office • Space Act amended in 2012 changing "mankind" to 'humankind" • Commercial Space Act of 2004 amended to recognize space tourism, within DOT/ FAA responsible for regulation • Establishment of OCHMO Health and Medical Technical Authority

[a] The program dates refer to the year of authorization (start) and termination

Box 1.7

The Houston MSC was renamed in honor of President Lyndon B. Johnson on February 19, 1973. It is the premier facility for astronaut training, care and preparation for space missions. This NASA facility has and is hosting many international crews, flight surgeons, and biomedical researchers and is the home of the Mission Control Center for space operations. The center also developed and hosts linguistic and cultural suitability training and flight surgeon training programs (see Chap. 16).

Box 1.8

The purpose of these extensive evaluations was to discover any hidden medical problems, to establish baseline levels of physical fitness, and perhaps most important, to compile a medical database for each individual against which any changes brought about by later space missions might be measured and quantified.

goal was to identify individuals in good health and able to withstand extremes of physical stresses, isolation, and sensory deprivation, without psychological or physiological consequences. This type of testing remained in effect until the end of the Apollo era, and was modified over time as new knowledge about health effects of space flight became available.

Following the selection of the Mercury 7 astronauts, Dr. W. Randolph Lovelace, on his own initiative, began the medical evaluation of a group of women aviators who could at a later date fly in space [26, 27]. Unfortunately, Lovelace's vision would not be fulfilled for decades, until the Space Shuttle era. The First Ladies Astronaut Trainees Project fell victim to political and Cold War space race rivalries. The "Women in Space" training was terminated shortly after its initiation. It was the Soviets who launched the first female cosmonaut, Valentina Tereshkova, on the Vostok 6 spacecraft on June 16, 1963.

In 1958, the USAF "Man in Space Soonest" program was transferred to NASA and it became the foundation of the Mercury project. The human requirements for radiation protection, atmospheric pressure and gas composition, food and water, and thermal control had to be established within the constraints on system failure tolerance, size, weight, power, and operation under conditions of thermal extremes, acceleration, and weightlessness [28]. Almost from the onset of human space flight, space medicine physicians and engineers were often at odds on design requirements. The astronauts and physicians insisted that there be a window in the Mercury capsule so the astronaut could look out the window. This addition, notwithstanding the cost and delays, proved a valuable tool for human direct observations of the flight environment, navigation, and Earth observations.

Fig. 1.1 Alan Shephard getting ready for launch (Courtesy of NASA)

The primary goal of Mercury to launch and recover a person was reached with Alan Shepard's flight in May 1961 (Fig. 1.1), and in all, two sub orbital and four orbital Mercury missions were flown, including one that lasted for 34 h and accomplished 22 orbits around the Earth. All 6 Mercury astronauts returned to Earth in satisfactory physical condition [29]. All Mercury astronauts went on to fly on Gemini, Apollo, and Skylab Missions.

However, a seventh astronaut, Donald "Deke" Slayton, was disqualified from flight duties due to cardiac arrhythmia (slow atrial fibrillation), which did not prevent him from flying 20 years later on July 15, 1975 on the first international "détente" mission, Apollo–Soyuz Test Project (ASTP). In the intervening period, Slayton served as the head of the Astronaut Office. He continued to seek reinstatement to flight duties and was seen repeatedly by preeminent cardiologists including Drs. Eugene Braumwald and Dudley White. Through the efforts of Dr. Charles Berry, he was treated with anti-arrhythmia medications, resigned from the USAF, and was put back on aviation duties in the late 1960s.

Box 1.9
Like Yuri Gagarin of the Soviet Union, John Glenn was considered a national hero, and NASA did not allow him to fly again until 1998, following his retirement as a U.S. Senator from Ohio.

Box 1.10
At this time, many U.S. scientists and engineers did not see the value of having the human in the system.

John Glenn became a national hero following his first orbital mission on February 20, 1962. He returned to space on October 29, 1998 as a payload specialist aboard the STS-95 (Box 1.9).

The early space missions were valuable for both dispelling and validating numerous medical concerns (Box 1.10). The principal findings of human adaptation to space flight were weight loss, resulting primarily from dehydration, and some impairment of cardiovascular function. Cardiovascular data from the final and longest Mercury flight showed postflight orthostatic intolerance, dizziness on standing, and hemoconcentration [30]. From a behavioral perspective, astronauts performed well under conditions of weightlessness and stress. The program had succeeded in accomplishing its purposes: to successfully orbit a man in space, to explore human ability of tracking and control, and to learn about microgravity and other biomedical problems associated with space flight.

Gemini Program (March 23, 1965 to November 15, 1966)

Planning for the Gemini Program began in May 1961, just after the successful completion of the first sub-orbital Mercury mission. The 2-man Gemini capsule was based upon the experience of Project Mercury and was designed to demonstrate new capabilities, such as extravehicular activities (EVAs), while providing NASA with the necessary experience in conducting extended space missions. The program also allowed the biomedical community to delineate the physiological limits of astronaut endurance, an essential step for planning future missions of greater complexity.

Box 1.11 Gemini Program Objectives:

1. Demonstrate the feasibility of space flight lasting long enough to complete a lunar landing;
2. Perfect the techniques and procedures for orbital rendezvous and docking of two spacecraft;
3. Achieve precisely controlled Earth reentry and landing;
4. Establish capability for extravehicular activity; and
5. Enhance the flight and ground crew proficiency.

Gemini successfully completed ten manned space missions, with many notable accomplishments (Box 1.11). The program itself was a resounding success in advancing the science of space technology. Fifty-two different experiments were performed during its ten missions. The Gemini achievements were a litany of precedents and records: the first U.S. extravehicular activity during Gemini-4 (Fig. 1.2); the first rendezvous and docking maneuver during Gemini-8; and the 14-day Gemini-7 mission, dedicated to biomedical studies. The question remained, however, whether the observed cardiovascular deconditioning was a self-limiting problem.

For the first time, slow and sustained tumbling was experienced by the crew of Gemini 8 during the docked phase with the Agena spacecraft [31]. Physiological and technical risks led to premature undocking of the two spacecraft. Nevertheless significant knowledge on manual piloting in space under off-nominal conditions was acquired, to be applied during future missions. Once the uncoupling was accomplished, astronaut Neil Armstrong was able to regain control of the tumbling spacecraft and return safely to the Earth.

The Gemini missions reinforced the medical conclusion that humans could live and work in space and could certainly do so for the duration required for the forthcoming Apollo missions (Box 1.12). A number of new responses to the space flight environment, such as bone mineral loss, were noted; however, none were considered of real consequence for missions lasting 2 weeks or less. While bringing new issues and concerns to light, Gemini left other medical questions unresolved [32]. The program's biomedical findings nonetheless served to structure and guide studies to be designed for later, longer missions (Box 1.13) [33, 34]. Such experiments would be needed to determine the basis and time course of the observed physiological changes.

Mercury and Gemini projects attracted new physicians and researchers into the space program. Practitioners in space medicine began the formulation of the operational aeromedical support for space missions and provision of astronaut care. These events led to the expansion of the scientific data base in space physiology: Drs. Craig Fischer and Phillip Johnson were first to describe "space anemia," fluid loss and head ward fluid shifts as a response to exposure to microgravity [30, 35]. Dr. Carolyn Leach described fluid, electrolyte, and endocrine changes [36], while Dr. Steve Kimzey began research into the causes of space anemia,

Fig. 1.2 American astronaut Edward H. White performing the first EVA from Gemini IV (Courtesy of NASA)

Box 1.12
During the Gemini Program, biomedical researchers were able to evaluate in-depth the changes in cardiovascular function noted during the Mercury program. Cardiovascular changes seen in Gemini crew members were regarded as an adaptive response to the intravascular fluid loss resulting from exposure to weightlessness.

immunology, and working together with Dr. Philip Johnson initiated the red blood cell function and bone marrow responses to microgravity using radioisotope labeling techniques [37]. Dr. Robert Johnson together with Dr. Larry Lamb, from the Aerospace Medical Research Laboratory at Brooks Air Force Base, introduced the lower body negative pressure device (LBNPD) for cardiovascular testing of orthostatic tolerance (Box 1.14) [38].

Box 1.13
It is worthwhile to note that President John F. Kennedy made initial overtures to the Soviet Union to undertake the Lunar exploration project together, which was rejected by the USSR, still busy developing their own Moon program [33, 34].

After the disastrous explosion of its N class rocket at the launch pad, the USSR abandoned its plans for lunar manned landings and concentrated on the development of the orbital research space stations and a lunar robotic exploration and sample return program.

Gemini biomedical findings paved the way for future lunar exploration and set the stage for the Apollo Applications Program—the U.S. orbital station Skylab primarily devoted to biomedical research. Dr. Wyck Hoffler introduced

Box 1.14
Under weightlessness, the LBNPD applies negative pressure to the lower part of the body, sealed at the waist, to simulate the effects of Earth's gravity on humans—similar to assuming the upright posture.

vectorcardiography into the cardiovascular research protocol. Dr. Sherman Vinograd at NASA Headquarters began forging ties with the National Academy of Sciences, the National Institute of Health, and the U.S. Navy Pensacola School of Aerospace Medicine. This laid the foundation for collaborations with Drs. G. Donald Whedon from NIH and Ashton Graybiel from Pensacola, leading experts in bone metabolism and neurovestibular physiology, respectively. Dr. Vinograd also set the foundations for the competitive process in space biomedical research. Thus, space medicine was poised to challenge the unknown.

Apollo Program (March 3, 1969 to December 20, 1970)

Kennedy's goal of landing a man on the Moon and returning him safely to Earth before the end of the decade was achieved with Apollo 11 on July 20, 1969. The Apollo missions to the moon included 29 astronauts, 12 of whom spent time on the lunar surface. Apollo is among the greatest human achievements in science, engineering, and exploration of the twentieth century. The unforgettable mesmerizing image of Earth, the "Blue Marble" against the dark background of infinite space represents the most vivid legacy of the Apollo era (Fig. 1.3).

The Apollo Program accomplishments were not without tragedy. In January 1967, during pre-launch testing, an electrical fire in the Apollo 1 capsule killed astronauts Gus Grissom, Ed White, and Roger Chaffee. The program was delayed while the fire was investigated and certain aspects of the Apollo capsule re-engineered (Box 1.15). The hatch, for

Fig. 1.3 Earth rise as seen from the Moon (Courtesy of NASA)

Box 1.15

The Apollo 1 fire also resulted in the removal of the majority of planned in-flight biomedical experiments. Only radiation dosimetry, including the self-contained and externally deployed pocket mouse experiment, and continuous monitoring of the crew's vital signs were preserved on Apollo missions. Extensive pre- and post-flight medical evaluations remained in the program.

Box 1.16

During the pre-flight period of the Apollo 13 mission, NASA's physicians, fearing exposure to measles and potential for in-flight illness, removed Astronaut T. Kenneth Mattingly from the prime crew. He was replaced by John "Jack" Swigert. However, Mattingly did not contract measles and went on to fly on Apollo 16 and STS 4.

instance, was retrofitted with a new escape system to allow the astronauts a quick exit. In addition, the cabin environment was altered from 100 % oxygen at launch to a mixture of oxygen and nitrogen; to reduce the danger of fire. Once in flight, the capsule environment was to convert to pure oxygen and one-third atmospheric pressure. Although an oxygen-only, one-third atmosphere simplified the life support systems design and interface with the extravehicular space suit, removing concerns about dysbarism, it also contributed to the Apollo 1 fire.

Landing in the Pacific Ocean and water recovery, using U.S. Navy (USN) ships, was continued throughout the program. The Apollo spacecraft was also tested for land recovery. However, given the pace of the Space Race and the U.S. belief that the Soviets were still planning a Moon landing, spacecraft systems were designed for maximum simplicity and reliability, bypassing time-consuming complex operational requirements and technological developments.

Apollo incorporated a focused biomedical research effort with three distinct goals [39]:

1. **Ensure the safety and health of crew members**. The Apollo flights highlighted health issues that had not been addressed earlier, foremost among them the potential for in-flight illness. During orbital flight, an astronaut could be recovered relatively quickly in the event of an in-flight emergency; on a lunar mission, circumnavigation of the Moon obviated this option. Therefore, a program was needed to minimize the likelihood of in-flight illness and to allow a reasonable measure of emergency treatment should an illness occur (Box 1.16).
2. **Prevent contamination of Earth by extraterrestrial organisms**. A lunar landing raised for the first time the possibility of contaminating the Moon with terrestrial microorganisms or, of even more concern, the possibility of introducing unknown lunar microorganisms to Earth. To ensure that unwanted microorganisms were not exchanged, strict quarantine and decontamination procedures were implemented before and after each mission. A special Lunar Receiving Laboratory was constructed at the NASA MSC in Houston, Texas to house astronauts and lunar samples for appropriate observation and research.
3. **Study specific effects of exposure to space**. The longer Apollo flights provided an opportunity to study the cardiovascular and bone adaptations observed during the Gemini Program in greater depth and to develop improved measurement techniques. Although the operational complexity and rigorous demands of the Apollo Program limited the time available for biomedical experiments, the studies conducted did provide considerable information concerning cardiovascular function, metabolic balance, and microbial behavior.

Biomedical observations during Apollo missions added vestibular disturbances to the inventory of significant findings pertaining to space flight [39]. Soviet cosmonauts had reported motion sickness symptoms in-flight as early as 1961 (Titov on Vostok-2), yet no symptoms of what would later be called space motion sickness (SMS) was reported by U.S. astronauts before Apollo missions. In the Apollo 8 and 9 flights, however, 5 of 6 crew members suffered some degree of motion sickness, ranging from stomach awareness to actual sickness. In one case, the severity of the vestibular disturbance required postponement of portions of the flight planned activities.

Apollo 13 spacecraft suffered a major systems failure after the explosion of the oxygen tanks. The crew was forced to live in a markedly degraded environment in the Lunar Landing Module, conserving fuel and electric power of the Apollo spacecraft for the circumnavigation of the Moon on the way to a safe return back to Earth. As a result of the poor habitable conditions, and lack of simple preventive health measures, some of the crew developed symptoms of urinary tract infection, successfully treated while still in space (Box 1.17 [33]).

Another Apollo crew member many years after the mission revealed in his book *Carrying the Fire* to have suffered single joint pain, which could be classified as type I bends, during the Gemini 10 and Apollo 11 missions. These symptoms of bends are the only record of dysbarism ever reported in the U.S. or Soviet/Russian space programs [39].

Good mission planning coupled with unusual luck, ensured that all Apollo Lunar landing missions occurred in between significant solar flares, which would have delivered lethal radiation exposures to the crews (see Chap. 7).

Box 1.17
A suspected exposure to measles prompted NASA to develop and adopt a Crew Health Stabilization Program, consisting of isolation (a form of quarantine) of the crew during the last week before launch and routine medical screening of the immediate families and all primary contacts [33]. This program remains in effect up to this date.

Box 1.18
The Apollo Program brought into focus the benefits of portability and miniaturization of medical diagnostic and monitoring equipment, and associated biomedical telemetry and ushered the age of telemedicine and its applications on Earth [6, 10].

Other significant biomedical findings from the Apollo Program confirmed Gemini results and helped further characterize these responses (Table 1.4) [15]. During Apollo 15, a crew member experienced a cardiac arrhythmia on the lunar surface, which brought about serious concerns in the medical community regarding diuresis and excessive loss of potassium. This concern prompted NASA physicians to prescribe potassium supplements (also orange juice) for the remainder of the Apollo missions. Several biomedical tests, using LBNPD to test orthostatic tolerance and submaximal exercise stress testing, a bicycle ergometer, and respiratory mass spectrometry gas analysis, were introduced for pre- and post-flight testing of Apollo crews (Box 1.18 [6, 10]). These research protocols were similar to those used on Skylab missions, which provided for a standardized biomedical data collection, and served as a baseline for future missions.

Post-flight quarantine in specially designed trailers and containers, were implemented for Apollo 11 crew only, and for all Apollo missions returned lunar samples [40]. For Apollo 11, both were transferred from the landing site in the Pacific in specially built isolation trailers, to the Lunar Receiving Laboratory at the NASA MSC, where the Apollo 11 crew completed their 3-week quarantine. The Apollo 11 spacecraft was carefully sampled and also quarantined for several weeks in Hawaii. These precautions were taken to prevent the introduction of alien bacteria into the Earth's environment. Of special interest was the absence of extraterrestrial microorganisms (although Earth microorganisms did survive exposures to the harshness of the lunar environment) in the spacecraft, on the EMUs or the materials returned from the lunar surface. Post-flight crew lunar quarantine was relaxed for subsequent Apollo Lunar Missions.

Box 1.19
A total of 11 Apollo flights were launched between October 1968 and December 1972; 12 astronauts worked on the lunar surface. The Apollo Applications Program (a program of Earth-orbital flights), originally planned to fly concurrently with the lunar program, was reduced in scope during the early 1970s and eventually became the Skylab Program. The Apollo spacecraft was used to transport Skylab and ASTP crews [41].

The Apollo Program provided an opportunity for the biomedical community to display its talent and capacity to excel scientifically and operationally. Recognizing these qualities and contributions to its mission, NASA consolidated all the life sciences elements within one organization at NASA Headquarters, the Life Sciences Division, with its own advisory structure and placed it in the Office of Manned Space Flight, but with direct access to the highest levels of the administration [19]. This was accomplished following advice from several external review groups, chartered by NASA and the White House, and encouraged by the U.S. House of Representatives and the scientific community. Dr. J. W. Humphrey was appointed as its first director. Space medicine became the domain of NASA, and Skylab was largely dedicated to the understanding of human physiology and to test the limits of human endurance in space. The Skylab program was an outgrowth of the Apollo Applications Program (Box 1.19 [41]), using remaining Apollo launch facilities and spacecraft components.

This program was to continue the research and operations in LEO, where the Soviet's ill-fated Salyut 1 expedition (the first space station) left it. By 1973, Humphrey left NASA and Dr. Charles Berry, a former USAF flight surgeon and leader in the space medicine field, was appointed Director for Life Sciences at NASA Headquarters in Washington, DC.

The success of the complex and accelerated Apollo program is a testament to the design integrity of the vehicles and the expertise of the crews and controllers. The knowledge gained from the Apollo Program greatly increased our understanding of how humans systems reacted to the space flight environment.

Skylab Program (1973–1974)

One of the purposes originally envisioned for the Apollo spacecraft was to assist advanced research and studies in Earth orbit. By 1969, plans for an orbital space station, begun under the Apollo Applications Program, had taken definitive shape: a Saturn IVB rocket stage would be outfitted as a workshop, with solar panels for power supply and an

Box 1.20
The interior of the workshop consisted of two major sections: an upper compartment, with two airlocks, for large-scale experiments; and a lower compartment containing areas for food preparation and eating, sleeping, waste management, and an experiment work area.

Box 1.21
The Skylab Program offered the first opportunity to study problems of habitability and physiological adaptation to space flight over extended periods. Composed of multiple components, Skylab was both a space habitat and an orbital laboratory.

external Apollo telescope mount for conducting solar observations. In 1970, as government and congressional support for NASA programs was scaled back, the Apollo Applications Program was renamed Skylab [15].

The Skylab orbital workshop, the heart of the complex had a habitable volume of nearly 275 m^3 (Box 1.20) [15]. Enveloping the workshop structure was a thin, aluminum meteoroid shield intended to absorb impacts from micrometeoroids and protect the workshop from direct solar radiation. This shield broke off during launch, and was later replaced in orbit with an umbrella-like structure.

The Skylab habitable volume had food and waste-management systems, which helped to provide a living environment that simulated terrestrial conditions as closely as possible in space (Box 1.21). The waste-management system included equipment for collecting, measuring, and processing urine and feces, as well as managing garbage. Feces and urine were collected in separate bags with the volume of the bags estimated regularly, and every 24 h were removed and frozen for post-flight analysis. Trash was discarded through an airlock into a holding tank. Other provisions for personal hygiene included a shower contained in a collapsible cloth bag; each crewman showered weekly in this device. Skylab also had a significant medical capability to address in-flight medical events and the crew was linked to the ground for consultation with flight surgeons for managing medical issues during flight.

Three crewed Skylab missions of 28, 59, and 84 day duration, from 1973 to 1974 were conducted (Box 1.22). The third and longest mission set a space flight endurance record that was not broken until 1978 by the Soviet Union. Skylab's orbit eventually decayed, and the station reentered Earth's atmosphere over Western Australia in July 1979. The orbital workshop provided the primary on-orbit living and working quarters for crew members (Box 1.23).

Box 1.22
The first Skylab crew was launched on May 25, 1973, and returned to Earth on June 22, 1973. While in orbit, the crew conducted solar astronomy and Earth resources experiments, medical studies, and five student experiments. During 404 orbits of the Earth, they completed 392 h of experimentation and 3 EVAs, totaling 6 h and 20 min.

Box 1.23
The additional volume allowed astronauts to enjoy a lifestyle somewhat closer to Earth standards, with a radical improvement in freedom of movement. Skylab permitted scientists to engage in detailed biomedical research on the physiological changes first observed in earlier programs.

In order to understand the operational constraints, and test the ability of the first U.S. Space Station to function properly for a minimum of 3 years on orbit, NASA conducted a simulation called the Skylab Medical Experiment Altitude Test (SMEAT). Three astronauts, Robert Crippen, Carrol Bobko, and William Thornton lived and worked for 56 days in a simulated Skylab environment in a specially outfitted hypobaric test chamber at the MSC. All parameters with the exception of microgravity were simulated. In addition, for testing equipment SMEAT brought together all the Skylab science teams, to test integrated research protocols interacting with each other, NASA engineers, and mission control personnel. This simulation and experiment rehearsal proved to be a resounding success, with lessons learned incorporated into the three Skylab missions. In addition, the data collected during SMEAT served as a baseline against which future space data was compared [42].

Each successive Skylab mission increased crew exposure to space flight. In total, nine astronauts occupied the Skylab workshop for 171 days and 13 h and performed nearly 300 scientific and technical experiments.

Skylab reemphasized the intrinsic value of the human operator in space. A thermal problem caused by the loss of the micrometeoroid shield and the failure of the solar array wing to deploy and resulting loss of the electric power source would have rendered Skylab uninhabitable without direct human intervention [15, 43]. Guided by ground staff, the Skylab team successfully released the solar wing and rectified the problem. An intravehicular activity was required next to deploy a parasol, specially built at the MSC and brought by the crew, to provide thermal protection to the orbital workshop. For the first 4 days, the crew lived in the Apollo Command Module, waiting for the workshop to cool