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Gilles Clément

Fundamentals of Space Medicine

Second Edition

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by

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Foreword

In the summer of 1993, I was fortunate enough to be a student in the International Space University summer session program (SSP), which convened in my then hometown of Huntsville, AL. I was one of the two lucky selectees to represent the NASA Marshall Space Flight Center at SSP'93. ISU has since changed the name of the SSP to Space Studies Program. This happened several years back when we realized that when an SSP convened in the southern hemisphere, such as Chile in 2000, it did not occur during "summer." But that's another story.

The story of 1993 is that attending SSP changed my life – at many levels, all good. Because that summer, this French gentleman approached me during the SSP tour of the Jack Daniel's Distillery up in Lynchburg, TN. In case you're not familiar with the nuances of alcohol regulation in the southeastern United States, Lynchburg is in a "dry" county, so we were not able to sample the product! So the French gentleman and I had a very enjoyable, memorable, and sober conversation. He later turned up to deliver life sciences lectures in the SSP, which were all just great! Little did we know where things would go from there.

Fast-forward to 2004 and the SSP session in Adelaide, Australia. I think the name change happened at about that time. Over the years, I had also become quite entangled with the ISU, returning to the SSP in 1994 in Barcelona as a team project "expert," joining the ISU faculty in 1998, and teaching at SSP sessions nearly annually since then. Now, here I am in Strasbourg as the ISU Associate Dean and SSP Director! At every SSP session I attended, Gilles Clément was always there, doing an absolutely marvelous job of directing the Space Life Sciences Department and giving lectures that absolutely blew everyone away. His creativity and use of animation, video clips, and sound were inspirational to me. I've incorporated many of his "tricks" and showmanship into my somewhat less than entertaining lectures on satellite subsystems design and other such technical topics.

He and I developed a close professional relationship over the years. It was always a joy to arrive at an SSP and see Gilles, along with our many other colleagues and associates. The best memories of those times are of when we would all be together talking, having a few beers, or just hanging out. In 2004, due primarily to cost constraints, many of the usual suspects with whom Gilles and I usually hung out during SSPs were not able to come. So basically, it was just us. We were of course obliged to uphold the traditional night out for beers, banter, and catching up, so we located the Belgian Beer Café in Adelaide and made it our place of retreat. One thing led to another, and well, here we are. I've been his trusty sidekick and editor ever since.

Gilles Clément not only brings an enormous talent to the classroom. He has marshaled his inquisitive nature and remarkable cleverness to orchestrate what must be one of the most impressive research careers in space life sciences ever. He has and continues to perform research on astronauts and cosmonauts, something he's been doing for nearly 30 years now. He has flown experiments on *Salyut*, *Mir*, the space shuttle, and the International Space Station, testing over 100 humans flying in space. His ingenuity and insight have led to a plethora of discoveries and enormously enriched the body of knowledge regarding how microgravity and the space environment affect the human vestibular system. Gilles knows how to translate and transfer research work done in ground-based laboratories into reliable flyable space-based experiments with maximum information return on investment using elegant and simple experimental designs. I have been and continue to be profoundly impressed with how easy it is for him to develop an idea, turn that idea into a scientific hypothesis, and then develop an experimental method and the hardware to effectively and efficiently collect the data needed to resolve the question. Which raises more questions, leading to even more brilliant ideas and experiments. He knows how to do it better than anyone else I have ever worked with.

For me, editing this book was a joy. It gave me the opportunity to dust off my bioengineering degree and to refresh things I knew while learning a whole lot of new things that I didn't. I've enjoyed editing the other three books he has published since 2004, including *Artificial Gravity*, to which I could actually contribute content! It is a wonderful thing that Gilles has now composed four amazing books, sharing his experience and knowledge in a way that is accessible and enjoyable. I appreciate that he's taken the time to revise this one – I know that many students and professionals alike will benefit from this publication and hopefully be inspired by what they find between the covers. I know I am.

15 November 2010

Angie Bukley, Ph.D.
Aerospace Engineer
ISU Associate Dean & SSP Director
Strasbourg, France

Preface

I wrote the first edition of *Fundamentals of Space Medicine* in 2003, when the *Columbia* tragedy grounded the space shuttle for nearly 3 years. My friend Doug Hamilton, a flight surgeon at the NASA Johnson Space Center who knew personally some of the *Columbia* crewmembers, had written a touching preface, dedicating this book to the memory of space travelers who give their lives for the advancement of space life sciences in general and space medicine in particular.

Today, I am writing the second edition of *Fundamentals of Space Medicine* just as the space shuttle will soon complete its last two space missions. By the middle of 2011, the shuttle fleet will be grounded forever, and a page in the history of space exploration will be turned. For the foreseeable future, the only vehicles allowing access of humans to space will be the Russian *Soyuz* and the Chinese *Shenzhou*. Russian, European, and Japanese automatic cargo vehicles will also dock with the International Space Station (ISS) to bring resources for the crew, equipment, fuel, and to return trash.

Fortunately, new spacecraft are in development, boosted by the commercial space and space tourism opportunities. The *Orion* and other new space vehicles developed by commercial companies for the National Aeronautics & Space Administration (NASA) in the United States will hopefully soon provide human access to the ISS. On a different scale, the commercial version of *SpaceShipTwo* is scheduled to fly by next year and will carry loads of paying passengers on suborbital flights up to 100 km in altitude, the official frontier of space. Much needs to be learned on the adaptation of the human body to the first minutes of microgravity, which was never fully investigated on board *Soyuz* and the space shuttle. So the advent of suborbital flight might prove an interesting opportunity for space medicine as well.

The International Space Station is now in its tenth year of existence, with a permanent crew of 6 people and 13 world-class laboratories equipped for state-of-the-art research in life sciences, material sciences, Earth observations, and space science. During the past decade, many experiments and observations were conducted in orbit in the area of space biology, physiology, and medicine, which have complemented the results previously obtained on the *Mir* and *Skylab* missions. The equipment and procedures used in orbit have become more and more accurate and refined, bringing new insights into the mechanisms of body adaptation to the conditions of spaceflight. Ground-based simulations of these effects, as well as studies in analog environments on Earth, have also provided useful models and new research questions. The main results of these experiments are included in this new edition, together with the results of the latest bio-satellite missions and ground-based studies in analog environments on Earth.

Why this title, *Fundamentals of Space Medicine?* Space medicine and space physiology are often viewed as two aspects of space life sciences, with the former being more operational, and the latter being more investigational. Space medicine tries to solve medical problems encountered during space missions. These problems include some adaptive changes to the environment (microgravity, radiation, temperature, and pressure) as well as some non-pathologic changes that become maladaptive on return to Earth (e.g., bone loss). Space physiology tries to characterize bodily responses to space, especially microgravity. It provides the necessary knowledge, hence the "fundamentals," required for an efficient space medicine.

Space physiology and medicine is as old as the first flight of humans in a hot air balloon, when the symptoms of hypoxia were first discovered (at the expense of one pilot's life). The interest in this field of research kept growing along with the space program and the opportunities it provided for more and more humans to fly in space on board capsules, shuttles, space stations, and soon suborbital spaceplanes. The future of human spaceflight will inevitably lead to human missions to Mars. These missions will be of long duration (30+ months) in isolated and somewhat confined habitats, with the crew experiencing several transitions in levels of gravity (1–0 g, 0–0.38 g, 0.38–0 g, and 0–1 g), dangerous radiation, and the challenges of landing and living on their own on another planet.

In *The Fundamentals of Space Medicine* Second Edition, special emphasis has been placed on the challenges, tasks, and research questions that must be addressed before safely sending humans to explore Mars. The greatest test for space medicine will be the projected nearly 3-year round-trip to Mars, whereas our current knowledge on humans in space does now not exceed 14 months and for only one individual, and the cumulative time in space by all astronauts and cosmonauts as of today is comparable to the lifetime of one single individual. The Achilles' heel of the Mars mission may be some adverse reactions of the human body, such as bone loss, decreased motor and sensory capabilities, or simply psychological issues. A chain is as strong as its weakest link. Possible ways to prevent problems and countermeasures are discussed throughout the book.

This book reflects *what we do know* in space life sciences at the beginning of the twenty-first century. It also points to the missing data, i.e., *what we don't know* and *what we should know* before committing to increased access for humans in space, including space commercial participants, by contrast with the professional astronauts, and for longer duration exploratory missions.

The format of the book is intended to facilitate its use by professors, undergraduate or graduate students, space life scientists, and space enthusiasts. It reviews step by step the changes in the major body functions during spaceflight, from the cellular level to the behavioral and cognitive levels. To better appreciate these changes, each chapter starts with a brief review of the basic principles of these human physiological functions on Earth:

- Chapter 1 begins with an introduction to the environmental challenges that spaceflight poses to the human body, and continues with a short history of space life sciences research.
- Chapter 2 reviews the effects of microgravity and radiation at the cellular level on bacteria, animals, plants, and humans, including the issues of reproduction and development.
- The following chapters each review the effects of spaceflight on the major human body functions: Chapter 3: Neuro-sensory function (the brain in space); Chapter 4: Cardio-vascular function (the heart in space); Chapter 5: Musculo-skeletal function

(the muscle and bone in space); Chapter 6: Psychological issues (the mind in space).

- However, every system or process must ultimately be viewed in the context of the entire body. The consequences of the aforementioned changes at a function level on the health and well being of the astronauts are therefore described in the Chapter 7: Operational Space Medicine.
- Chapter 8 focuses on the technical aspects related to life support systems, including radiation shielding, and the challenges for a closed, environmental system for exploration missions.
- Chapter 9 concludes this review with some tips from the author on how to proceed with proposing and planning a space experiment that uses humans as test subjects, given the available resources and constraints of current space missions.

Each chapter corresponds to one core lecture of the Space Life Sciences Department of the International Space University Space Studies Program. These lectures were developed with the help of many people from all over the world in a collegial and collaborative environment. In particular, the sections related to the medical effects of spaceflight are a contribution of my old friend and "partner in crime" at ISU, Doug "Hami" Hamilton. Some of the updates that are included in this revision have been taken nearly verbatim from books that I have published since the first edition of this book came out.

As a neurophysiologist actively participating in space research since 1982, with experiments manifested on *Salyut*, *Mir*, the space shuttle, and the International Space Station, I know what it takes to collect data during relatively simple space experiments, and then try to make sense of the sparse, often contradictory, results in a scientific paper. This book provides a summary of the main results, observations, and trends described in the literature. I apologize to the authors of the scientific publications if all of their interpretations are not included. The detailed descriptions of this research and the findings can be found in the studies listed in the bibliography. A list of other books on space life sciences is also provided.

Some space-related physiological changes and their underlying mechanisms and interpretations are sometimes described in the text in greater detail than what is required for a plenary academic lecture. For the courses I teach at ISU I have prepared PowerPoint presentations corresponding to each of the chapters in this book. These presentations include key concepts in bullet-form illustrated by recent relevant photographs and video clips. PDF versions of these presentations as well as the video clips are included on the website Springer Extras.

The first edition of this book has been translated into Chinese (see front cover in Figure 1). Should there be sufficient demand, no doubt the publisher of this book would be interested in producing other translated versions.

Finally, thanks to Angie Bukley for editing this book and being there for me.

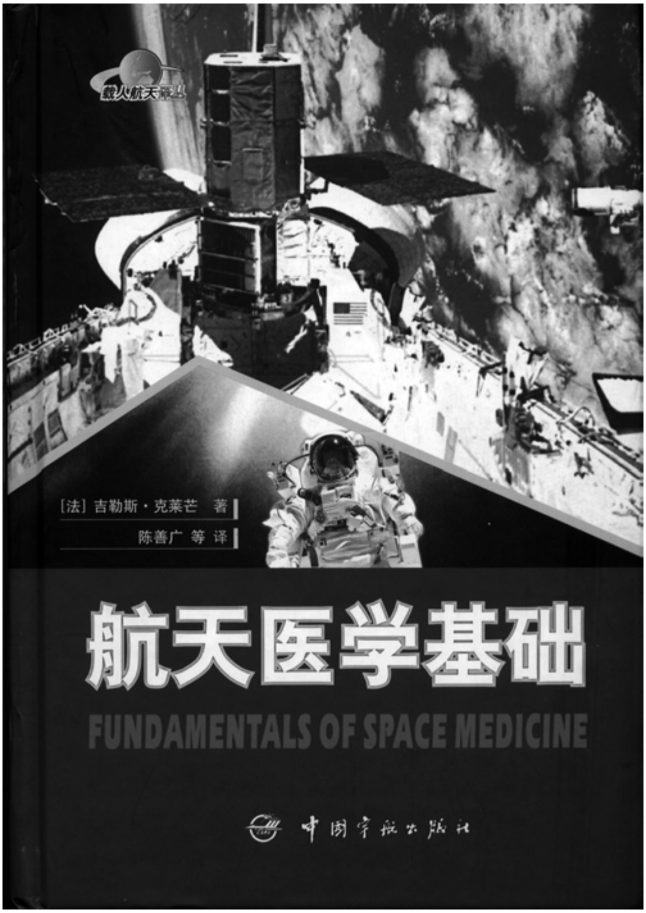

Figure 1 **The Front Cover of the Chinese Version of Fundamentals of Space Medicine (First Edition).**

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Chapter 1

Introduction to Space Life Sciences

This first chapter describes the hazards that the space environment poses to humans, and how spaceflight affects the human body (where we are). We will then review the historical context of human spaceflight (how we got there), and end with the challenges facing humans in space (where do we go from here) (Figure 1.1).

1.1. Space life sciences: what is it?

1.1.1. Objectives

Life sciences are specifically devoted to the workings of the living world, from bacteria and plants to humans, including their origins, history, characteristics, habits, you name it.

The study of life on Earth ranges from elucidating the evolution of the earliest self-replicating nucleic acids to describing a global ecology comprising over 3 million species, including humans. However, throughout its evolution, organisms on Earth have experienced only a 1-g environment. The influence of this omnipresent force is not well understood, except that there is clearly a biological response to gravity in the structure and functioning of living things. The plant world has evolved gravity sensors; roots grow “down” and shoots grow “up.” Animals have gravity sensors in the inner ear. Many fertilized eggs and developing embryos (amphibians, fish, birds, and mammals) also have clear responses to gravity. For example, the amphibian egg orients itself with respect to gravity within a few minutes after fertilization. During that short time the dorso-ventral and anterior-posterior axes of the future embryo are established. Do we conclude therefore that the gravitational input is a required stimulus for the establishment of these axes?

To better understand a system, the scientific method consists of studying the consequences of its exclusion. This approach has led to considerable advances in the knowledge of human physiology, thanks to the nineteenth century physiologist Claude Bernard, who set out the principles of experimental medicine. Clearly, the removal of gravity is a desirable, even necessary, step toward understanding its role in living organisms. In a sense, removal of gravity for studying the gravity-sensing mechanisms is like switching off the light for studying its role in vision. Transition into weightlessness abolishes the stimulus of gravity by a procedure physiologically equivalent to shutting off the light. What can be accomplished in such an elegant fashion aloft can never be done in Earth-based laboratories.

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Figure 1.1. The Goal of Space Medicine Is to Develop Methods to Keep Humans Healthy in Space for Extended Periods of Time, as Well as Improve Overall Health of People of All Ages on Earth. (Credit Philippe Tauzin).

Space physiology is of basic scientific interest and deals with fundamental questions concerning the role of gravity in life processes. Space medicine is another, albeit more applied, research component concerned with the health and welfare of the astronauts and space travelers. These two objectives complement one another and constitute the field of space life sciences. In short, space life sciences open a door to understanding ourselves, our evolution, and the workings of our world without the constraining barrier of gravity.

Space life sciences are dedicated to the following three objectives:

Enhance fundamental knowledge in cell biology and human physiology – Access to a space laboratory where gravity is not sensed facilitates research on the cellular and molecular mechanisms involved in sensing forces as low as 10^{-3} g and subsequently transducing this signal to a neural or hormonal signal. A major challenge to our understanding and mastery of these biological responses is to study selected species of higher plants and animals through several generations in absence of gravity. How do individual cells perceive gravity? What is the threshold of perception? How is the response to gravity mediated? Does gravity play a determinant role in the early development and long-term evolution of the living organism? These studies of the early development and subsequent life cycles of representative samples of plants and animals in the absence of gravity are of basic importance to the field of developmental biology.

Protect the health of astronauts – As was amply demonstrated by Pasteur, as well as countless successors, investigations in medicine and agriculture contribute to and benefit from basic research. Understanding the effect of gravity on humans and plants has enormous practical significance for human spaceflight. For example, the process of bone demineralization seen in humans and animals as a progressive phenomenon occurring during spaceflight is not only a serious medical problem. It also raises the question of abnormalities in the development of bones, shells, and the otoliths of the inner ear in species developing in the absence of gravity. The study of such abnormalities should provide insight into the process of biomineralization and the control of gene transcription.

Develop advanced technology and applications for space and ground-based research – In addition to the scientific need to study basic plant and animal interactions with gravity, there is a practical need to study their responses. These are essential to our ultimate ability to sustain humans for a year or more on the surface of extraterrestrial bodies or in spaceflight missions of long duration where re-supply is not possible, and food must be produced in situ. Experiments during long-duration space missions will determine which plants and animals are most efficient and best suited for our needs. For instance, can soybeans germinate, grow normally, produce optimum crops of new soybeans for food and new seed for ensuring future crops? All of this biological cycling, plus the development of equipment for water and atmospheric recycling, plus management of waste, will also bring important benefits for terrestrial applications. Also, the absence of gravity is used to eliminate micro convection in crystal growth, in electrophoresis, and in biochemical reactions. The resulting products can be used for both research and commercial application.

Space life sciences include the sciences of physiology, medicine, and biology, and are linked with the sciences of physics, chemistry, geology, engineering, and astronomy. Space life sciences research not only help us to gain new knowledge of our own human function and our capacity to live and work in space but also to explore fundamental questions about gravity's role in the formation, evolution, maintenance, and aging processes of life on Earth (Table 1.1).

Table 1.1. Major Applications of Space Life Sciences Research.

Biology

- Advance understanding of cell behavior
- Improve crop yields using less nutrients and smaller surface and volume

Biotechnology

- Provide information to design a new class of drugs to target specific proteins and cure specific diseases
- Culture tissue for use in cancer research, surgery, bone cartilage, and nerve injuries

Medicine

- Enhance medical understanding of disease processes such as osteoporosis
- Advance fundamental understanding of the nervous system and develop new methods to prevent and treat various neurological disorders
- Develop methods to keep humans healthy in low-gravity environments for extended time periods

Education

- Use science on orbit to encourage and strengthen science education on Earth

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1.1.2. The space environment

The space environment (radiation, microgravity, vacuum, magnetic fields) as well as the local planetary environments (Moon, Mars) have been extensively reviewed in Peter Eckart's book *Spaceflight Life Support and Biospherics* (1996). In this section, we will mainly focus on microgravity. The medical issues related to space radiation will be developed in Chapter 8.

1.1.2.1. Microgravity

The presence of Earth creates a gravitational field that acts to attract objects with a force inversely proportional to the square of the distance between the center of the object and the center of Earth. When we measure the acceleration of an object acted upon only by Earth's gravity at Earth's surface, we commonly refer to it as *1 g* or one Earth's gravity. This acceleration is approximately 9.8 m/s^2.

We can interpret the term *microgravity* in a number of ways, depending upon the context [Rogers et al. 1997]. The prefix micro- derives from the original Greek *mikros,* meaning "small." By this definition, a microgravity environment is one that imparts to an object a net acceleration that is small compared with that produced by Earth at its surface. We can achieve such an environment by using various methods, including Earth-based drop towers, parabolic aircraft flights, and Earth-orbiting laboratories. In practice, such accelerations will range from about 1% of Earth's gravitational acceleration (on board an aircraft in parabolic flight) to better than one part in a million (on board a space station). Earth-based drop towers create microgravity environments with intermediate values of residual acceleration.

Quantitative systems of measurement, such as the metric system, commonly use micro- to mean one part in a million. By this second definition, the acceleration imparted to an object in microgravity will be 10^{-6} of that measured at Earth's surface.

The use of the term *microgravity* in this book corresponds to the first definition: small gravity levels or low gravity.

Microgravity can be created in two ways. Because gravitational pull diminishes with distance, one way to create a microgravity environment is to travel away from Earth. To reach a point where Earth's gravitational pull is reduced to one-millionth of that at the surface, we would have to travel into space a distance of 6.37 million kilometers from Earth (almost 17 times farther away than the Moon). This approach is impractical, except for automated spacecraft.

However, the act of free fall can create a more practical microgravity environment. Although aircraft, drop tower facilities, and small rockets can establish a microgravity environment, all of these laboratories share a common problem. After a few seconds or minutes of low-g, Earth gets in the way and the free-fall stops. To establish microgravity conditions for long periods of time, one must use spacecraft in orbit. They are launched into a trajectory that arcs above Earth at the right speed to keep them falling while maintaining a constant altitude above the surface.

Newton [1687] envisioned a cannon at the top of a very tall mountain extending above Earth's atmosphere so that friction with the air would not be a factor, firing cannonballs parallel to the ground. Newton demonstrated how additional cannonballs would travel farther from the mountain each time if the cannon fired using more black

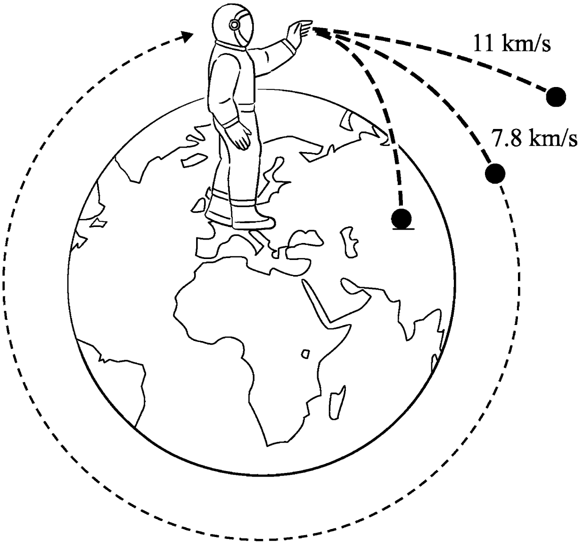

Figure 1.2. Artificial Satellites Are Made to Orbit Earth When Their Velocity Is Equal or Higher Than 7.8 km/s. When in Orbit, the Spacecraft and Its Inhabitants Are in a State of Continuous Free-Fall with No Apparent Perception of Gravity. (Credit Philippe Tauzin).

powder. With each shot, the path would lengthen, and soon the cannonballs would disappear over the horizon. Eventually, if one fired a cannon with enough energy, the cannonball would fall entirely around Earth and come back to its starting point. The cannonball would begin to orbit Earth. Provided no force other than gravity interfered with the cannonball motion, it would continue circling Earth in that orbit (Figure 1.2).

This is how the space shuttle stays in orbit. It launches into a trajectory that arcs above Earth so that the orbiter travels at the right speed to keep it falling while maintaining a constant altitude above the surface. For example, if the space shuttle climbs to a 320-km high orbit, it must travel at a speed of about 27,740 km/h to achieve a stable orbit. At that speed and altitude, due to the extremely low friction of the upper atmosphere, the space shuttle executes a falling path parallel to the curvature of Earth. In other words, the spacecraft generates a centrifugal acceleration that counterbalances Earth's gravitational acceleration at that vehicle's center of mass. The spacecraft is therefore in a state of free-fall around Earth, and its occupants are in a microgravity environment. Gravity *per se* is only reduced by about 10% at the altitude of low Earth orbit (LEO), but the more relevant fact is that gravitational acceleration is essentially canceled out by the centrifugal acceleration of the spacecraft.

1.1.2.2. Other factors of the space environment

Beside microgravity, during spaceflight living organisms are also affected by ionizing radiation, isolation, confinement, and changes in circadian rhythms (the 24-h day-night cycle). In plants, for example, spaceflight offers the unique opportunity to separate the gravitational input from other environmental stimuli known to influence

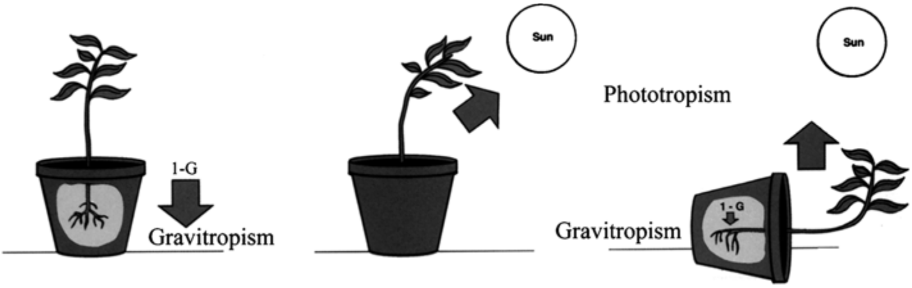

Figure 1.3. Gravitropism Is the Way Plants Grow in Response to the Pull of Gravity. When Placed Near a Window, Plants Exhibit Phototropism (Bending Toward the Light Source). This Behavior Can Be Easily Observed by Placing a Plant on Its Side; Within Minutes the Roots and Stem Begin to Reorient Themselves in Response to Both Gravity and Light. (Credit NASA).

plant growth, for example, phototropism (Figure 1.3), water tropism, and the circadian influences of the terrestrial environment. Spaceflight thus provides the opportunity to distinguish between the various tropic responses and to investigate the mechanisms of stimulus detection and response.

The absence of natural light in spacecraft may have significant effects on humans, too. A typical person spends his days outdoors, exposed to light provided by the Sun's rays (filtered through the ozone layer), including a small but important amount of mid- and near-ultraviolet light, and approximately equal portions of the various colors of visible light. Indoor lighting in most offices and in spacecraft is of a much lower intensity and, if emitted by fluorescent "daylight" or "cool-white" bulbs, is deficient in ultraviolet light (and the blues and reds) and excessive in the light colors (yellow-green) that are best perceived as brightness by the retina.

If the only effect of light on humans was to generate subjective brightness, then this artificial light spectrum might be adequate. It has become clear, however, that light has numerous additional physiological and behavioral effects. For example, light exerts direct effects on chemicals near the surface of the body, photo activating vitamin D precursors and destroying circulating photo-absorbent compounds (melanin). It also exerts indirect effects via the eye and brain on neuroendocrine functions, circadian rhythms, secretions from the pineal organ, and, most clearly, on mood. Many people exhibit major swings in mood seasonally, in particular toward depression in the fall and winter, when the hours of daylight are the shortest. When pathological, the *seasonal affective disorder syndrome* is a disease related to excessive secretion of the pineal hormone, melatonin, which also may be treatable with several hours per day of supplemental light. While not yet proved, it seems highly likely that prolonged exposure to inadequate lighting (that is, the wrong spectrum, or too low an intensity, or too few hours per day of light) may adversely affect mood and performance.

Low-power light emitting diodes (LED) are fast becoming a "green" lighting alternative for conventional lighting. LED are known to use less electricity, to be quieter, last longer, and produce a low amount of heat compared to conventional light sources. Recent studies demonstrated that LED with a spectrum of blue, orange and red provided the exact bandwidth for plants to grow and produce food on the ISS. As in our home, the compact florescent and other legacy lighting sources will be progressively replaced with LED on board the ISS.

The effects of spaceflight on biological specimens might also be related to other factors. Even the gentlest of launch vehicles produces enormous amounts of noise and vibration, plus elevated g forces, until orbital velocity is achieved, or during the re-entry into Earth's atmosphere. Once in orbit, machines and astronauts continue to produce vibrations that are difficult to control. The space environment also exposes animals and individuals to high-energy radiation unlike anything they experience on Earth. To control these and other external factors (for example, fluctuations in atmospheric pressure as astronauts enter and exit a spacecraft), the biologists studying the effects of microgravity *per se* ideally need onboard centrifuges that can expose control specimens to the level of gravity found on Earth's surface [Wassersug, 2001].

1.1.3. Justification for human spaceflight

1.1.3.1. Humans versus robots

The debate over space exploration is often framed as humans versus robots. Some scientists fear that sending humans to the Moon and Mars might preclude the pursuit of high quality science. On the other hand, some proponents of human exploration are concerned that doing as much science as possible using robots would diminish interest in sending humans. Nevertheless, humans will always be in command. The question is where would they most effectively stand?

Space exploration should be thought of as a partnership to which robots and humans each contribute important capabilities. Opposing robotics versus human crews is like comparing apples and oranges. The discussion must be framed in terms of relative strengths of humans and robots in exploring the Moon and Mars. For example, robots are particularly good at repetitive tasks. In general, robots excel in gathering large amounts of data and doing simple analyses. Hence, they can be designed for reconnaissance, which involves highly repetitive actions and simple analysis. Although they are difficult to reconfigure for new tasks, robots are also highly predictable and can be directed to test hypotheses suggested by the data they gather. However, robots are subject to mechanical failure, design and manufacturing errors, and errors by human operators. Also, before robots can explore and find evidence of life on Mars, for instance, their functional capabilities, particularly their mobility, need to be radically improved and enhanced. In addition, the delay in communication between Mars and Earth (in the order of 40 min round trip) poses a serious problem for teleoperation maneuvers.

People, on the other hand, are capable of integrating and analyzing diverse sensory inputs and of seeing connections generally beyond the ability of robots. Humans can respond to new situations and adapt their strategies accordingly. In addition, they are intelligent operators and efficient end-effectors. They may easily do better than automated systems in any number of situations, either by deriving a creative solution from a good first hand look at a problem or by delivering a more brainless kick in the right place to free a stuck antenna. Either may be mission saving. Finally, only humans are adept at field science, which demands all of these properties. Obviously, humans would have a clear role in doing geological fieldwork and in searching for life on Mars.

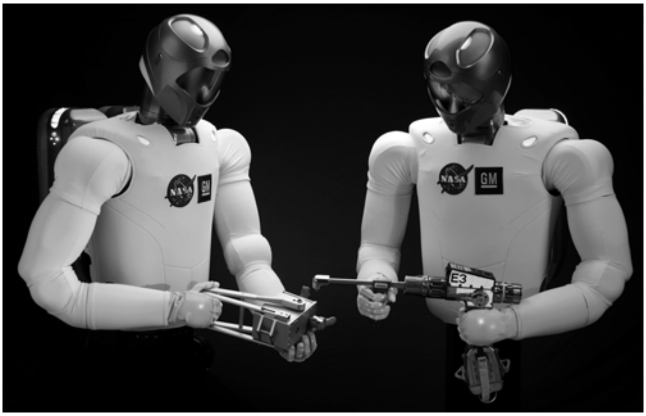

Figure 1.4. Robonaut 2 Is a Dexterous Humanoid Robot Developed Jointly by NASA and General Motors. These Social Robots Are Designed to Use the Same Tools as Humans, Allowing Them to Work Safely Side-by-Side Humans on Earth and in Space. (Credit NASA).

Humans are also less predictable than robots and subject to illness, homesickness, stress resulting from confinement, hunger, thirst, and other human characteristics. They need protective space suits and pressurized habitats. Hence, they require far greater and more complicated and expensive support than robots. The combined potential of humans and robots is a perfect example of the sum equaling more than the parts. It will allow us to go farther and achieve more than we can probably even imagine today. A future generation of robots, the so-called *social robots*, has promise both in space and on Earth, not as replacements for humans but as companions that can carry out key supporting roles. Dexterous robots with human-like hands and arms, able to use the same tools as astronauts, are currently undergoing extensive testing on board the ISS (Figure 1.4). In the future these social robots may assist or stand in for astronauts during space walks and planetary exploration or for tasks too difficult or dangerous for humans.

1.1.3.2. Space science

There is often criticism that human missions are disproportionately costly to their scientific yield as compared to automatic (unmanned) platforms such as those designed for Solar System exploration or Earth's observation. A direct comparison is not justified, however. Automatic probes have indeed returned spectacular results, but it is wrong to compare these directly with human flights. Historically, space life sciences are a rather recent discipline. In most space agencies, at least until recently, the term "space science" refers to space physical sciences, such as astrophysics or search for life on other planets. Perhaps reminiscent of this past, human spaceflight critics often discount the value of space life sciences on the "Discovery Ledger (Big Book)".[1]

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[1] In a February 2003 interview to the *Chicago Tribune,* a physics professor at the University of Maryland and a director at the American Physical Society, a professional organization of physicists, said: "The International Space Station is not exploration; it's going in circles closer to the Earth than Baltimore is to New York". He added: "It is the single greatest obstacle of continued exploration of the Solar System—it's blocking just about everything".

This point of view is often due to the following fundamental differences: physical sciences leads to more concrete discoveries in a relatively unexplored sphere (once a new star is discovered, it is easy to confirm its presence), whereas space life sciences is an inherently inexact science, which must take into account background physiological variability and requires repeated measurements. For instance, large clinical trials are needed to determine the efficacy of a new drug. It may be obvious that space life sciences suffer from the small number of subjects studied and the many confounding factors that are difficult to control. But with all of this, it is likely that the life sciences data obtained in LEO studies will be practically used for going further (such as establishing a Mars base) or for improving our knowledge of clinical and aging disorders on Earth, long before we can make use of the information on the magnetic field of Neptune [Barratt, 1995].

It is true that the cost of human-based space infrastructures, such as the ISS, is much higher than unmanned missions. However, the primary purpose for the ISS was a political one. The ISS is a major accomplishment for all countries involved even in its current incomplete state. It is the largest on-orbit structure ever built and the largest multi-national cooperative project in history. In building the ISS infrastructure and research equipment, aerospace companies are acquiring unique capabilities that make them recognized world players in areas such as space structures, automation, robotics, avionics, fluid handling, advanced life support systems and medical equipment. Both in view of the need to develop advanced technologies and by virtue of the research carried out on board, the ISS can have a significant impact on the competitiveness of aerospace industry. In the same way that one would not charge the cost of a road-system to a single car (or even the first dozen cars), the cost of the ISS cannot be endorsed by the scientific return of its first experiments.

The opportunities for in-depth studies in space life sciences have indeed been sparse. This is simply the nature of the current space program, with much to do and a few flight opportunities that must be shared. Experiments that might take weeks on Earth take years to plan and execute in space. Limitations of the spaceflight environment have also limited the number of control experiments and have often kept the number of specimens studied far from statistical ideal. Often space studies are paralleled by Earth-based simulation studies using centrifuges or clinostats, but results in actual microgravity are somewhat different.

Another argument often posed against space life sciences is that no Nobel prizes have been given in this field of research. Although a true statement, there are several instances, however, of Nobel Prizes formerly delivered in life sciences related fields that would presumably not have been presented based on the recent results obtained in space. For example, Robert Bàràny, a Viennese otolaryngologist, received the Nobel Prize of Medicine in 1906 for his discovery of a clinical test aimed at evaluating the functionality of the balance organs in the inner ear (see Chapter 3, Section 3.2.1). During this test, irrigation of the external auditory ear with water or air above or below body temperature generates rhythmic eye movements (nystagmus) and the subject experiences slight vertigo. Bàràny's theory was that the caloric irrigation of the ear canal generated eye movements (the so-called caloric nystagmus) because of the heat, gravity-driven convection within the canal fluid [Barany, 1906]. A space experiment carried out on board *Spacelab* in 1983 proved this theory to be wrong since caloric nystagmus was also observed in microgravity, where no heat current convection is generated. Later studies revealed that it is more likely the changes in pressure or temperature that are at the origin of the eye movement response [Scherer et al., 1986].

1.1.4. Where we are

Human spaceflight began in April 1961 with Yuri Gagarin's single orbit of the Earth on board *Vostok-1*. Exactly 50 years later, in April 2011, a total of 520 astronauts, cosmonauts, and taîkonauts (the name given to Chinese astronauts) will have flown in space,[2] an average of about 10 per year. The total number of days spent in space will be about 36,500 crew days, or 100 years. It is interesting, or rather sad, to note that female astronauts and cosmonauts comprise only 11% of these 520 flown individuals (56 to be exact). Females also contributed to about 11% of all human flights (129) and the total duration of all flights for female astronauts and cosmonauts is less than 8 years.

All together, these 520 humans will have spent about 36,500 days in space. So, the average amount of time spent in space by astronauts and cosmonauts is 36,500 days/520 = 70 days, or a little more than 2 months. If we include the re-flights, the number of flown humans goes up to 1,155 (806 for the shuttle only, nearly 70%!). However, most of them have spent less than 30 days in space, even by cumulating three or four flights. The mean duration of all human spaceflights to date is about 30 days, but the median time spent in orbit is close to 12 days (Figure 1.5). Flight duration longer than 6 months is limited to about 60 individuals, and only four individuals have experienced continuous spaceflight longer than 1 year (Figure 1.6). By counting the re-flights, 25 individuals (including one female) have cumulated the equivalent of 1 year or more in orbit.

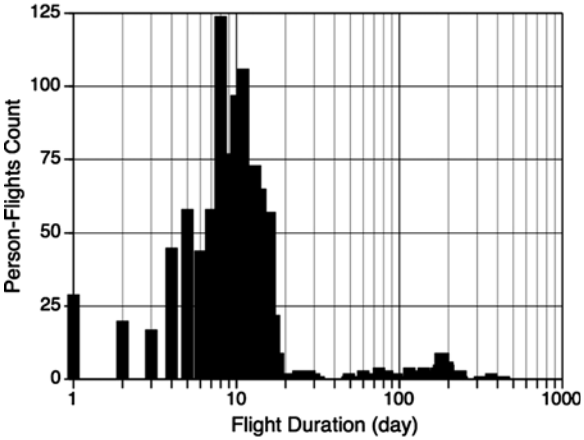

Figure 1.5. Number of Human Spaceflights as a Function of Flight Duration from 1961 to 2010. Note the Logarithmic Scale for Flight Duration. Most Human Flights Were of Short Duration (8–14 days) on Board Soyuz or the Space Shuttle.

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[2] Provided that *STS-133*, *Soyuz TMA-20*, and *STS-134* launch on time (these calculations were made on 13 October 2010).

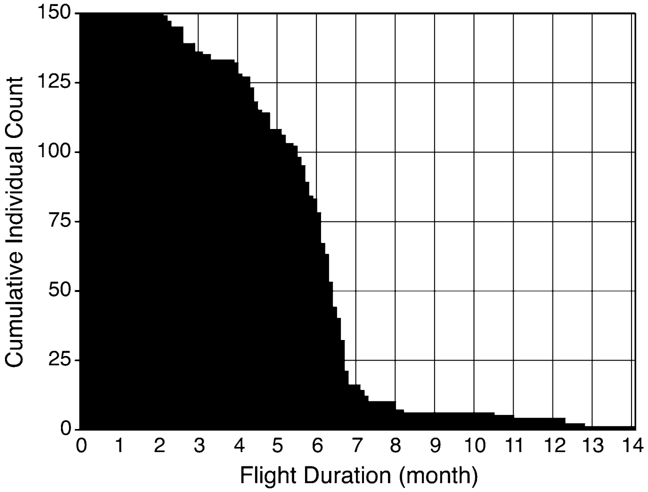

Figure 1.6. Cumulative Histogram Showing the Astronaut and Cosmonaut Count as a Function of (Single) Flight Duration.

Had all the astronauts and cosmonauts been the subjects of space life sciences investigations during their spaceflight, the total amount of collected data would be limited to about one human lifetime. The total amount of collected data on female subjects would be limited to 8 years – the concept of women flying in space is still at its infancy. Yet, since life sciences investigations were not conducted on all astronauts and cosmonauts, and since most of them have flown more than once, the limited number of individuals and observations makes the significance of this data even lower.

This simple arithmetic is to illustrate how little research time – on how few space flyers – is currently available to determine the effects of spaceflight on the human body. A comparison between space research and extreme environment research would undoubtedly show that much more has been accomplished on Mount Everest or during polar expeditions during the same period.[3]

The record of spaceflight duration is currently held by Dr. Valery Polyakov, a Russian physician, who spent 437 days during a single mission on board the space station *Mir* in 1994–1995. This was his second spaceflight, though. In 1989, he had already spent 242 days on board *Mir*, so his total time spent in space actually is 679 days, or about 22 months.

But this is not the longest duration in space for a single individual. Sergey Krikalyov has logged 803 days during six stays on board *Mir*, the space shuttle, and the ISS, and he currently holds the all-time cumulative total for days in space. Beside Polyakov and Krikalyov, eight other cosmonauts have spent more than 500 days in space,

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[3] About 2,700 individuals have successfully climbed to the top of Mount Everest since May 1953. As of 2009 about 4,100 ascents have been made. Over 216 people have died trying. About 440 individuals have completed expeditions to the North Pole or the South Pole since 1865 and 1908, respectively [Source: www.adventurestats.com].

accumulated over two to five spaceflights. This cumulative time in microgravity is about equal to the total exposure to microgravity to be experienced during a mission to Mars. The ISS allows extensive investigations on humans in space. However, the nominal duration of a stay in orbit for Expedition crews on ISS does not exceed 6 months. Therefore, no data is gained anymore during very long spaceflights. Although we know that humans can survive to long duration in space repeatedly, the data collected so far is extremely limited.

There is a general perception that because a small number of cosmonauts have survived in LEO for as long as 1 year or so, there are no major physiological problems likely to preclude longer-duration human planetary exploration missions. One must admit that, over the years, there has been access only to anecdotal data from the Russian space program. This anecdotal information is, while interesting, not sufficiently reliable for drawing conclusions for a number of reasons. There are differences in the scientific method, the experimental protocols, and the equipment. The results are also not published in peer-reviewed international scientific journals. Fortunately, the increased recent cooperative activities between Russia and its partners of the ISS now allow a standardization of experimental procedures and better data exchange.

1.2. How we got there

1.2.1. Major space life sciences events

1.2.1.1. The pioneers

The first powered flight in 1903 by the Wright Brothers at Kitty Hawk beach in North Carolina is traditionally considered as the milestone in manned flight and aerospace medicine. In mythology, Icarus was the first victim of a flying adventure, when he and his father Daedalus tried to escape their prison on the island of Crete by flying using waxed feathers. The legend says that Icarus, ignoring both advice and warning, flew too close to the Sun. The heat softened the wax and the feathers detached, precipitating a dreadful fall for Icarus.

However, there were no witnesses to the Icarus and Daedalus flight. This was not the case for the second human flight in history, though. In June 1783, two brothers, Jacques Etienne and Joseph Michel Montgolfier, sent a large, smoked-filled bag 35 ft into the air. This first balloon flight was recorded by the French Academy of Sciences. Three months later, a duck, a rooster, and a sheep became the first passengers in a balloon, since no one knew whether a human could survive the flight. All three animals survived the flight, although the duck was found with a broken leg, presumably due to a kick from the sheep after landing. Finally, on November 21, 1783, human flight was attempted before a vast crowd that included the king and queen of France and recognized scientists [Tillet et al., 1783]. Pilatre de Roziers[4] and the Marquis d'Arlandes[5] piloted what became the first known aerial voyage of humankind (Figure 1.7).

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[4] The word "pilot" is derived from his name.

[5] The Marquis d'Arlandes was born in my hometown, Anneyron, a small village in the south of France.

Figure 1.7. Drawing of the First Manned Balloon Flight Taking Off in Front of the Château de la Muette with passengers Pilatre de Roziers and the Marquis d'Arlandes. (Source Unknown).

After this event, ballooning became quite popular for over half a century in Europe. Ten days after the first manned hot air flight, a French physicist named J. A. C. Charles made the first human flight in a hydrogen-filled balloon. When he reached an altitude of 2,750 m, he began to experience physiologically some of the realities of this new environment. He complained of the penetrating cold at this altitude and a sharp pressure pain in one ear as he descended. This is the first description of symptoms experienced in aerospace medicine. In 1784 in England, after several animals were used in free flight tests, Mrs. Elisabeth Tible became the first woman to fly a balloon, and Jean-Pierre Blanchard became the first to cross the Channel from England to France. Feeling outdone, Pilatre de Roziers built a new balloon, using a combination of hot air envelope and a small hydrogen balloon, to fly from France to England. In January 1785, he left France, and after a few minutes in-flight the burner's flame ignited the small hydrogen balloon, creating an inferno. Ironically, the first to fly in a balloon became the first balloon casualty. The hazards of high altitude flight were demonstrated in following flights, where balloonists experienced and described for the first time the symptoms of hypoxia (altitude sickness, increase in heart rate, fatigue) [DeHart, 1985].

1.2.1.2. Animal spaceflight

In the 1950s, as human spaceflight began to be seriously considered, most scientists and engineers projected that if spaceflight became a reality it would build upon logical building blocks. First, a human would be sent into space as a passenger in a capsule (Projects Vostok and Mercury). Second, the passengers would acquire some control over the space vehicle (Projects Soyuz and Gemini). Third, a reusable space vehicle would be developed that would take humans into LEO and return them. Next, a permanent space station would be constructed in LEO through the utilization of the reusable space vehicle. Finally, lunar and interplanetary flights would be launched from the space station using relatively low-thrust and reusable (and thus lower cost) space vehicles.

Just like for balloon flights, animals were sent up in rockets before humans to test if a living being could withstand and survive a journey into space (Figure 1.8). The first successful spaceflight involving living creatures came on September 20, 1951, when the former Soviet Union launched a sounding rocket with a capsule including a monkey and 11 mice. A few attempts to fly animals had been made before (in fact, since 1948 in the nose cones of captured German V-2 rockets during U.S. launch tests), but something always went wrong. These attempts were made with one main purpose: to study the effects of exposure to solar radiation at high altitude, and to determine the effects, if any, of weightlessness [Lujan and White, 1994].

Orbital flight then began on October 4, 1957, when the former Soviet Union sent the *Sputnik-1* satellite into space. This was an unmanned satellite, but before the end of the year a second satellite, *Sputnik-2*, was launched carrying the first living creature into orbit, a dog named Laika. Laika had been equipped with a comprehensive array of telemetry sensors, which gave continuous physiological information to tracking stations. The cabin conditioning system maintained sea-level atmospheric pressure within

Figure 1.8. Rats and Cats Were the First Living Passengers on a Suborbital Flight in a French Rocket in the 60s. (Credit CNES).

the cabin, and Laika survived 6 days before depletion of the oxygen stores caused asphyxiation. Laika's flight demonstrated that spaceflight was tolerable to animals. Twelve other dogs, as well as mice, rats, and a variety of plants were then sent into space for longer and longer duration between 1958 and 1966. In 1996, a Soviet biosatellite *Cosmos* mission carried two dogs in orbit for 23 days. The dogs were observed via video transmission and biomedical telemetry. Their spacecraft landed safely.

In 1959, one rhesus and one squirrel monkey rode in the nose cone of a U.S. missile during a non-orbital flight, successfully withstanding 38 times the normal pull of gravity and a weightless period of about 9 min. Their survival of speeds over 18,000 km/h was the first step toward putting a human into space. Although one of the monkeys died from the effects of anesthesia given to allow the removal of electrodes implanted for the spaceflight, a subsequent autopsy revealed that the monkey had suffered no adverse effects from the flight. Between 1959 and 1961, three other monkeys made suborbital flights in Mercury capsules, and one monkey flew two orbits around Earth in a Mercury capsule in preparation for the next, human flight (Figure 1.9). These experiments paved the way for human expeditions.

A comprehensive list of all the animal species that have flown in space is published in the book *Fundamentals of Space Biology* by Clément and Slenzka [2006, Springer]. While these animals were in space, instruments monitored various physiological responses as the animals experienced the stresses of launch, re-entry, and the weightless environment. The results of these animal flights showed that:

(a) Pulse and respiration rates, during both the ballistic and the orbital flights, remained within normal limits throughout the weightless state. Cardiac function, as evaluated from the electrocardiograms and pressure records, was also unaffected by the flights.

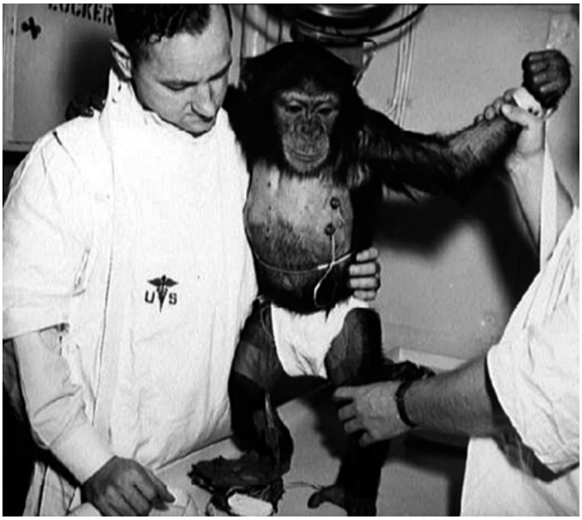

Figure 1.9. Chimpanzee Ham with Biosensors Attached Is Being Prepared for His Trip in the Mercury-Redstone 2 on January 31, 1961. (Credit NASA).

(b) Blood pressures, in both the systemic arterial tree and the low-pressure system, were not significantly changed from preflight values during 3 h of the weightless state.
(c) Performance of a series of tasks of graded motivation and difficulty was unaffected by the weightless state.
(d) Animals trained in the laboratory to perform during the simulated acceleration, noise, and vibration of launch and re-entry were able to maintain performance throughout an actual flight.

On the basis of these results, it was concluded that the physical and mental demands that the astronauts would encounter during spaceflight "would not be excessive," and the adequacy of the life support system was demonstrated [Henry, 1963].

1.2.1.3. Humans in space

Earlier, in late 1958, the new National Aeronautics & Space Administration (NASA) had announced Project Mercury, its first major undertaking. The objectives were threefold: to place a human spacecraft into orbital flight around Earth, observe human performance in such conditions, and recover the human and the spacecraft safely. At this early point in the U.S. space program, many questions remained. Could a human perform normally as a pilot-engineer-experimenter in the harsh conditions of weightless flight? If yes, who were the right people (with the right stuff) for this challenge?

In 1959, NASA received and screened 508 service records of a group of talented test pilots, from which 110 candidates were assembled. One month later, through a variety of interviews and a battery of written tests, the NASA selection committee brought down this group to 32 candidates. Each candidate endured even more stringent physical, psychological, and mental examinations, including total body X-rays, pressure suit tests, cognitive exercises, and a series of unnerving interviews. Of the 32 candidates, 18 were recommended for Project Mercury without medical reservations. At a press conference, NASA introduced the seven Mercury astronauts to the public.

The following year, the Soviet Union announced that 20 fighter pilots had been selected for its space program. Physiological studies and special psychophysiological methods "permitted the selection of people best fitted to discharge the missions accurately and who had the most stable nerves and emotional health," according to the Soviet report. In 1962, 5 female parachutists joined this first group of 20 male cosmonauts.

On April 12, 1961, Yuri Gagarin became the first human to orbit Earth. According to the press release, Gagarin felt "perfectly well" throughout the orbiting phase and also during the period of weightlessness. It was noted, however, that "measures" had been taken to protect the spacecraft from the hazards of space radiation.

Six weeks later, U.S. President Kennedy would announce as a national objective an accelerated space program to accomplish a landing on the Moon before the end of the decade. However, after the suborbital flights of Alan Shepard and Gus Grissom in May and July 1961, respectively, observations made during U.S. orbital spaceflights with monkeys raised some concerns. Variations in cardiac rhythm had been recorded in one chimpanzee during a three-orbit mission [Stringly, 1962]. It was found that the problem came from faulty instrumentation, and that the data were therefore invalid. Accordingly, it was recommended that John Glenn's orbital flight proceed as scheduled.

Figure 1.10. Russian Cosmonauts Yuri Gagarin and Valentina Tereshkova Were the First Male and Female Humans into Space. (Source Unknown).

In August of the same year after Grissom's suborbital flight in July, the USSR launched Cosmonaut Gherman S. Titov into orbit. The following day, Titov successfully landed after 17 orbits in 25 h and 18 min. This was the first human flight of more than one orbit, and the first test of human responses to prolonged weightlessness. Two years later, in 1963, Valentina Tereshkova became the first woman in space (Figure 1.10). She remained in space for nearly 3 days and orbited the Earth 48 times. Unlike earlier Soviet spaceflights, Tereshkova was permitted to operate the controls manually. After her spacecraft reentered Earth's atmosphere, Tereshkova parachuted to the ground, as was typical of cosmonauts at that time. Although her spaceflight was announced as successful, it was 19 years until another woman flew in space, Svetlana Savitskaya, aboard *Soyuz T-7* and *Salyut-7* in 1982. Apparently, something went so wrong during Tereshkova's flight that no further flights included women. Savitskaya must have turned out all right, since she flew twice, and during her second mission on board *Soyuz T-12* and *Salyut-7* in July 1984, was the first woman to ever perform a space walk. The third and last female Russian cosmonaut flew in 1997 on board the space shuttle and *Mir*.

Soviet Cosmonaut Aleksei Leonov made the first space walk during the *Voskhod-2* mission on March 18, 1965. He was followed by U.S. Astronaut Edward White, who stepped out of *Gemini-4* for 20 min. White propelled himself away from the spacecraft with a special gun that gushed out compressed oxygen to move him in any direction. However, because his propulsion gun ran out of fuel, he had to pull on his life support system umbilical line to maneuver around and reenter the spacecraft.

1.2.1.4. Space life sciences investigations

The Mercury flights had made it clear that the body undergoes some real changes during and after spaceflight, such as measurable weight loss. A more complex set of in-flight medical studies was carried out during the Gemini missions, which served as precursors to the lunar missions. Among those missions, *Gemini-7*'s (December 1965) primary objective was to conduct a 2-week mission and evaluate the effects of long-duration exposure to weightlessness on its crew. Many medical experiments were conducted in-flight, including on vision and sleep. Extensive testing, for example on balance, was also performed just after landing. Blood and urine samples were collected throughout the mission for analysis, and astronauts exercised twice daily using rubber bungee cords.

Of particular interest was the visual acuity experiment, which was driven by earlier observations of Mercury astronauts who thought their ability to identify small objects on Earth's surface was enhanced in weightlessness. This experiment used a visual acuity goggle combined with measured optical properties of ground objects and their natural lighting, as well as the atmosphere and spacecraft window. The results failed to show that visual acuity was improved while in space.

Also interesting is the *Gemini-11* flight (September 1966), where artificial gravity was (accidentally) first tested in space. The Gemini spacecraft was tethered to an Agena target vehicle by a long Dacron line, causing the two vehicles to spin slowly around each other. According to the Gemini commander, a TV camera fell "down" in the direction of the centrifugal force, but the crew did not perceive any changes [Clément and Bukley, 2007].

Significant orthostatic hypotension and weight loss were observed in the crewmembers of *Gemini-3*, *-4*, *-5*, and *−6* immediately after flight (see Chapter 4, Section 4.3.4). Also, red blood cell mass losses in the order of 20% were noted after the 8-day Gemini flight. Scientists were concerned that spaceflight might affect the balance of body fluids and electrolytes because fluid losses can contribute to both of these symptoms. This led to a series of ground-based studies to simulate some of the conditions of spaceflight. These studies utilized bed rest and water immersion as a means of simulating microgravity. In addition, *Biosatellite-3* was launched in 1969, 3 weeks before the first men were to land on the Moon, with a monkey passenger. The flight was planned for a full month, but the monkey was brought down, ill from loss of body fluids, after only 9 days. It died shortly after landing. Despite the concern that the same problem could occur to humans, the Apollo missions to the Moon proceeded as planned.

During the Apollo missions, a medical program was developed that would make provision for emergency treatment during the course of the mission in case a serious illness occurred. Indeed, during the orbital flights of Mercury and Gemini, it was always possible to abort the mission and recover the astronaut within a reasonable time should an in-flight medical emergency occur. This alternative was greatly reduced during Apollo. The events of *Apollo-13* showed that this medical program proved effective. Biomedical findings of the Apollo program revealed a decrease in postflight exercise capacity and red blood cell number, a loss of bone mineral, and the relatively high metabolic cost of extra-vehicular activity. In addition, symptoms of space motion sickness such as nausea and vomiting, earlier described by Soviet cosmonauts, were experienced. These observations raised another concern for future human spaceflights, and therefore constituted the starting point of detailed life sciences investigations in the *Skylab* program in the 1970's.

The U.S. *Skylab* (Figure 1.11) and the Soviet *Salyut* space stations allowed scientists to conduct investigations on board large orbiting facilities during missions lasting up to 3 months. They gave a basic picture of how the body reacts and adapts to the space environment. The number of subjects was, however, still limited.

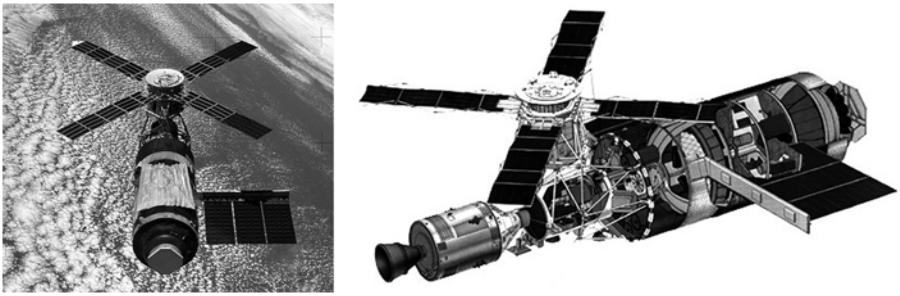

Figure 1.11. Actual Photograph (*Left*) and Drawing (*Right*) of the U.S. Skylab Space Station Showing the Orbital Module Laboratory with "Transparent" Walls and the Apollo Crew Return Vehicle. The Volume of the Laboratory Was About 350 m^3. The Nine Astronauts Visiting Skylab in 1973 and 1974 Logged About 2,000 h of Scientific and Medical Experiments During Three Missions Lasting 28, 59, and 84 days, Respectively. (Credit NASA).

Figure 1.12. Landing of the Space Shuttle at the Kennedy Space Center. (Credit NASA).

The space shuttle (or Space Transportation System, STS), which began flying in 1981, provided the opportunity to test more crewmembers. Also, as the first spacecraft that could be used again and again, the space shuttle has provided space life scientists with a more regular opportunity to conduct experiments, and to repeat and refine those experiments. However, with the space shuttle, other concerns appeared. It was remarkably different from the previous spacecraft because it returned to Earth by landing on a runway (Figure 1.12).

Critical issues existed concerning the ability of crews to perform the visual and manual tasks involved in piloting and landing the shuttle, and their capacity to achieve unaided egress after long exposure to weightlessness. It was later found that the astronaut-pilots were able to pilot and manually land the space shuttle, as long as the flight duration did not exceed 2 weeks. Such critical achievement was in part due to the development of special simulators built to train crews to fly and land the space shuttle, in what is now popularly termed a "virtual reality" setting. In fact, astronauts returning from shuttle missions reported that the simulations were so accurate they felt they had flown the mission many times.

1.2.1.5. Today's access to space

In 134 flights between 1981 and 2010, the space shuttle has repeatedly demonstrated unique capabilities as space transporter, repair ship, scientific platform, and research center. It first accomplished its role of "shuttle" by rendezvous and docking with *Mir* in 1995, a few months after the end of Valery Polyakov's 14-month mission. From February 1994 to June 1998, NASA space shuttles made 11 flights to the Russian space station *Mir*, and U.S. astronauts spent seven residencies, or "increments," on board *Mir*. space shuttles also conducted crew exchanges and delivered supplies and equipment. The space shuttle was then the first spacecraft to dock with the ISS, in May 1999. Since the permanent crew occupation of the ISS in November 2000, the space shuttle has ensured most of the crew transport, together with the *Soyuz*, between Earth and the ISS.

More than four times as large as *Mir*, the ISS consists of 16 pressurized modules with a combined volume of around 1,200 m^3 (Figure 1.13). These modules include laboratories, docking compartments, airlocks, nodes, and living quarters. As of July 2010, 14 of these components were already in orbit. The research laboratories include the Russian *Zvezda* and *Rassvet* modules, the U.S. *Destiny* module, the Japanese *Kibo* module, and the European *Columbus* module. The remaining two laboratories waiting to be launched are the Russian *Nauka* module and the European *Leonardo* module.

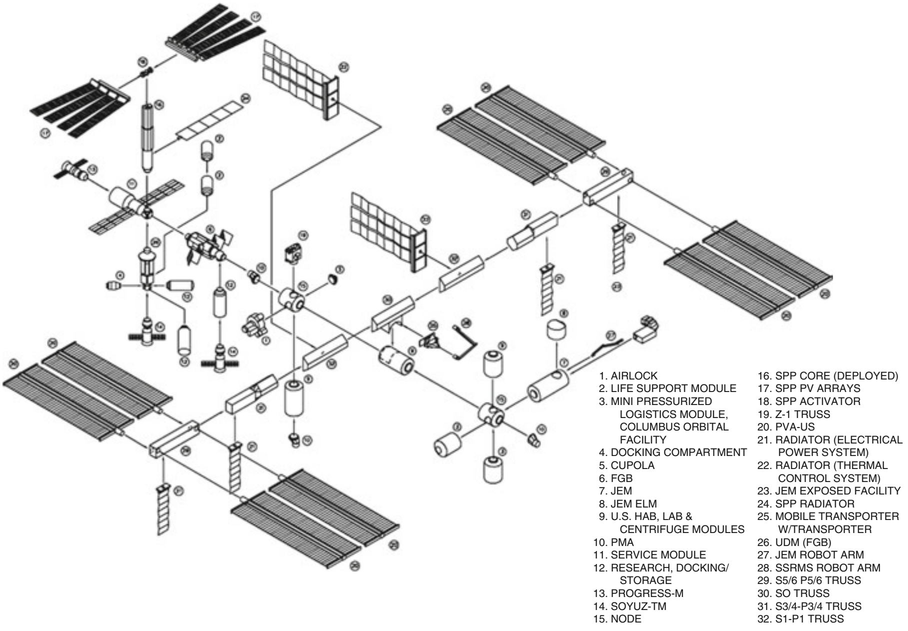

Figure 1.13. The International Space Station. (Credit NASA).

Each module was or will be launched either by the space shuttle, or by Proton or Soyuz rockets. ISS assembly will be completed by 2011, by which point the ISS will have a mass in excess of 400 metric tons.

The gravity environment on the station is described as "micro-gravity," as the weightlessness is imperfect. This is caused by four separate effects: (a) the drag resulting from the residual atmosphere; (b) vibratory acceleration caused by mechanical systems and the crew; (c) orbital corrections by the on-board gyroscopes or thrusters; and (d) the distance from the real center of mass of the ISS.

Normal air pressure on the ISS is 101.3 kPa (14.7psi), the same as at sea level on Earth. The time zone used on board the ISS is Coordinated Universal Time (UTC, also called GMT). In general, the crew works 10 h/day on a weekday, and 5 h on Saturdays, with the rest of the time their own for relaxation, games, or work catch-up. The ISS does not feature a shower. Instead, crewmembers wash using a water jet and wet wipes, with soap dispensed from a toothpaste tube-like container. Crews are also provided with rinseless shampoo and edible toothpaste to save water. There are two space toilets on the ISS, located in *Zvezda* and *Destiny*.

Most of the space food eaten by station crews is frozen, refrigerated, or canned. Menus are prepared by the astronauts, with the help of a dietitian, before their flight to the ISS. Each crewmember has individual food packages and cooks them using the onboard galley, which features two food warmers, a refrigerator, and a water dispenser that provides both heated and unheated water. Drinks are provided in dehydrated powder form, and are mixed with water before consumption. Drinks and soups are sipped from plastic bags with straws, while solid food is eaten with a knife and fork, which are attached to a tray with magnets to prevent them from floating away.

Each permanent station crew is given a sequential Expedition number. Expeditions have an average duration of 6 months. *Expeditions-1* through *−19* consisted of three-person crews (except for *Expeditions-7* to *−12*, which led to a reduction to two crewmembers following the space shuttle *Columbia* disaster). In May 2009, *Expedition-20* was the first ISS crew of six. The ISS is the most visited spacecraft in the history of spaceflight. As of September 2010, it had 294 visitors (195 individuals) from 15 different nationalities (Table 1.2). *Mir* had 137 visitors (104 individuals).

Emergency crew return vehicles will always be docked with the ISS while it is inhabited, to assure the return of all crewmembers. The *Soyuz* spacecraft, which has a crew capacity of three, is presently used. Following the retirement of the space shuttle, a number of other spacecraft are expected to fly to the station. Two, the *Orbital Sciences Cygnus* and *SpaceX Dragon* will fly under contracts with NASA, delivering cargo to the ISS until at least 2015. In addition, the *Orion* spacecraft, developed as a space shuttle replacement as part of NASA's Constellation program, was re-tasked by U.S. President Barack Obama on April 15, 2010, to provide lifeboat services to the ISS.

It is important to realize that the ISS is far more than a science platform alone. The ISS constitutes a highly visible signature in the sky for human endeavor, courage, spirit, and international peaceful collaboration, and it is the greatest technological challenge the human race has tackled so far. To a large part this was the early political motivation that led to its conception. In addition, and looking more towards the future, the ISS provides the gateway for human exploration of the Solar System. The ISS has also the potential for becoming an ideal tool to support educational activities.

Table 1.2. International Space Station Statistics as of September 2010. Sources: http://space.kursknet.ru/cosmos/english/other/siss.sht; http://en.wikipedia.org/wiki/List_of_International_Space_Station_visitors.

Total Residents and Visitors Since Start of Assembly	
Trips	294
Flyers	195
Women	30
ISS crewmembers	60
Tourists	7
Flights Since Start of Assembly (1999)	
American	34 Shuttle
Russian	4 Proton 23 Soyuz 37 Progress
European	1 ATV
Japanese	1 H-II TV
Space Walks (1999–2010)	
Number of astronauts	96
Number of EVA	292
Total duration (man-EVA hours)	1,829

In particular, educational programs encouraging and supporting the study of science, mathematics, technology, and engineering can be implemented on board the ISS, making use of its facilities and resources. Other education projects can be implemented that focus not only on science and technology but also on a larger variety of subjects, such as languages, composition, and art.

In April 2001, an American engineer and millionaire flew on a *Soyuz* and spent 8 days on board the ISS. His trip erupted in a controversy when NASA and the other ISS partners objected to a tourist visit in the middle of a critical series of assembly operations at the ISS. The ISS partners reluctantly gave their approval for a visit that was going to happen with or without their approval, in return for a promise by the Russian Space Agency to meet new standards for paying visitors in the future. Between April 2002 and October 2009 six other orbital space tourists flew to and from the ISS on *Soyuz* spacecraft through the space tourism company, Space Adventures, for a cost ranging from $25 to $30 million.

As a matter of fact, orbital “space tourists” “space participants,” or “commercial astronauts,” according to the new title awarded by the U.S. Federal Aviation Administration, had already flown on several occasions. A senator, a congressman, a teacher, and a prince from Saudi Arabia have flown on U.S. missions. A reporter, an engineer from a chocolate company, and guests from allied countries have flown on Soviet, now Russian, space missions. Before being a full ISS partner, Europe took the opportunity of a paying visitor on the *Soyuz* to allow its astronauts to have a regular access to *Mir* and the ISS for 1 week at a time, the so-called “Taxi” missions.

More affordable space tourism will be the result of new vehicles that make suborbital flights peaking at an altitude of 100–160 km (Figure 1.14). Passengers will experience 3–6 min of weightlessness, a view of a twinkle-free starfield, and a vista of

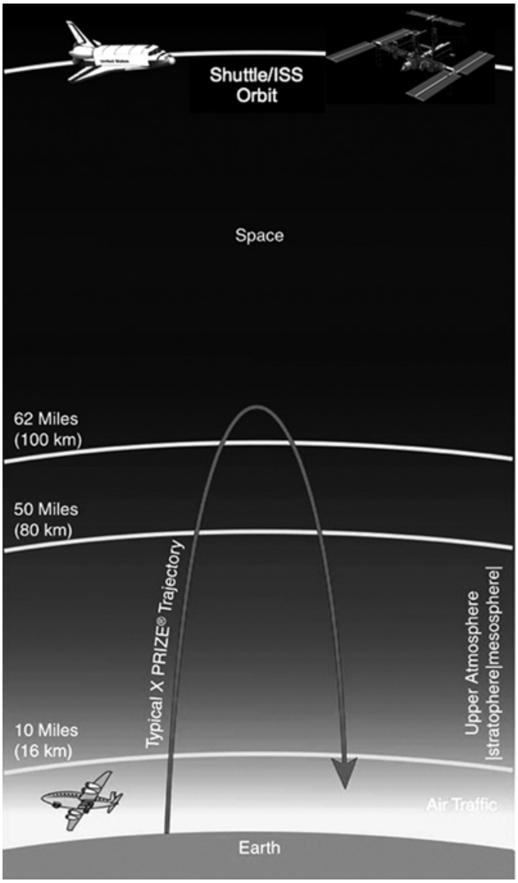

Figure 1.14. Suborbital Spaceflight Will Typically Go Above 100 km, Which Is Considered the Beginning of Space and Thus Entitles the Passengers of These Flights To Be Called "Astronauts." Although at a Much Lower Altitude Than the ISS, the Space Participants Will BeAble to Enjoy a Spectacular View of Earth and Microgravity for a Few Minutes. They Will Also Experience Considerable Accelerations During Launch and Re-entry, Presumably More So Than in the Space Shuttle. (Credit Ansari-X Prize).

the curved Earth below. On October 4, 2004, *SpaceShipOne,* designed by Burt Rutan of Scaled Composites, won the $10,000,000 Ansari-X Prize, which was awarded to the first private company that could fly a vehicle at an altitude of 100 km twice within 2 weeks. The 100-km altitude is beyond the Kármán Line, the arbitrarily defined boundary of space. Virgin Galactic, one of the leading space tourism groups, is planning to begin passenger service aboard the *VSS Enterprise*, a Scaled Composites *SpaceShipTwo* spacecraft. The initial seat price will be $200,000, but that price is expected to eventually fall to $20,000. To date, over 80,000 people have made down payments on bookings. No doubt about it, space tourism is a reality, and it's a good and necessary development for the future of human space exploration.

1.2.2. Surviving the Odyssey

Early predictions of the response of humans to spaceflight assumed that space adaptation would be analogous to human disease processes rather than to normal physiology. The predictions made by scientists about the ability of humans to endure spaceflight were indeed dire. Despite ground-based studies proving the contrary, there was true concern that the g forces of launch and re-entry (6–8 g for the earliest spacecraft) would render human passengers unconscious, severely impaired, or even dead. The mystique of this alien environment was so great that many feared a psychotic breakdown when humans would find themselves disconnected from and looking down on mother Earth.[6] Some physicians voiced concerns that bodily functions in weightlessness might suffer from a long list of calamities: swallowing, urination, and defecation would be impaired or impossible in the absence of gravity (although anyone who has ever swallowed while standing on their head hanging upside down could have proven otherwise); the bowels would not work without gravity; the heart might cavitate like a pump or beat so irregularly as to cause problems; sleep would be impaired; and muscles, including the heart, would become so weakened as to prohibit return to Earth [Churchill, 1999].

The first space missions showed, however, that with the proper protection, humans could survive a journey into space. Biomedical changes have been observed during spaceflight, due to the effects of microgravity, but also to other phenomenon, such as high launch and re-entry gravitational forces, radiation exposure, and psychological stress.

To illustrate of what we do know at this point, colleague and friend Susanne Churchill, in one of her lectures at the International Space University, used to describe the space journey of an hypothetical space traveler who experiences all of the known problems. We will use the same approach below.

So, let us take a journey with our hypothetical astronaut. She is in excellent health and fully trained for the rigors of her 3-month increment on board the ISS. Launch occurs as anticipated: a couple of hours before launch she had joined the others lying down in the seats of the space shuttle, strapped in, feet above head, as in the early Mercury, Gemini, or Apollo launches. But there, the similarity ends. For during shuttle lift-off she does not undergo the unpleasant gravity load, which went as high as 8 g on earlier flights. Instead, she experiences 3 g only twice. The first time comes and goes quickly near the 2-min mark, just before the two solid rocket boosters burn out and drop by parachute into the Atlantic Ocean. The final 3-g load comes 5 min later and lasts for a minute. Less than 10 min from lift-off, she finds herself floating in the weightlessness of space.

Without warning, however, she suddenly vomits and is overwhelmed with intense symptoms of motion sickness: nausea, a sense of dizziness, and disorientation. Her symptoms become worst when she moves about in the cabin or sees one of her fellow crewmembers floating upside-down. She is unable to keep food down and rejects even

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[6] This was one reason why the earliest spacecraft were totally automatic, with no controls for a disoriented or “crazed” pilot to use independently.

water to drink, so she quickly dehydrates. She is concerned that she could not help the rest of her crew with the rendezvous procedures of the shuttle with the ISS, because looking out of the windows triggers more symptoms. She takes some pills and is getting ready for sleep. However, when looking in the mirror above the washbasin, she realizes that her eyes seem smaller, her face is round and puffy (Figure 1.15), and her neck veins are bulging. The good news is that her wrinkles have disappeared and she looks younger. When undressing, she notices that her legs look like sticks. She tries to sleep but has a persistent backache, a definite feeling of sinus congestion, and keeps waking to discover that her arms are floating above her head. So disconcerting!

When she wakes up and dresses, she finds her clothes too short. Because of the absence of perceived gravity, her vertebrate disks are less compressed, making her height increase by 5–6 cm (Figure 1.16) and causing continuing back pain. Also, as a result of the fluid shift (which is also responsible for her puffy face and "chicken" legs) her waistline has shrunk about 4 cm, and she must tighten the bands of her pants. Her shoes have also become too loose.

Within a couple of days, the motion sickness symptoms begin to subside, though her face and legs remain changed. Her posture, too, is different, but not for the better. Joints go to their midpoint in zero gravity, so that the hips and knees are bent into a slight crouch. Her arms tend to float in front of her unless she consciously holds them down. When she sits at a workbench, she has to strap herself in place. Even so, her seated posture is to lean back. Nevertheless, she learns to move around in weightlessness by gently pushing and pulling her body with her fingertips.

Rendezvous and transfer to the ISS occur without incident, and she starts to settle for a 3-month stay on board with her two fellow crewmates. Personal hygiene is limited to "sponge" bathing; food becomes bland tasting, and she must add spices for interest.

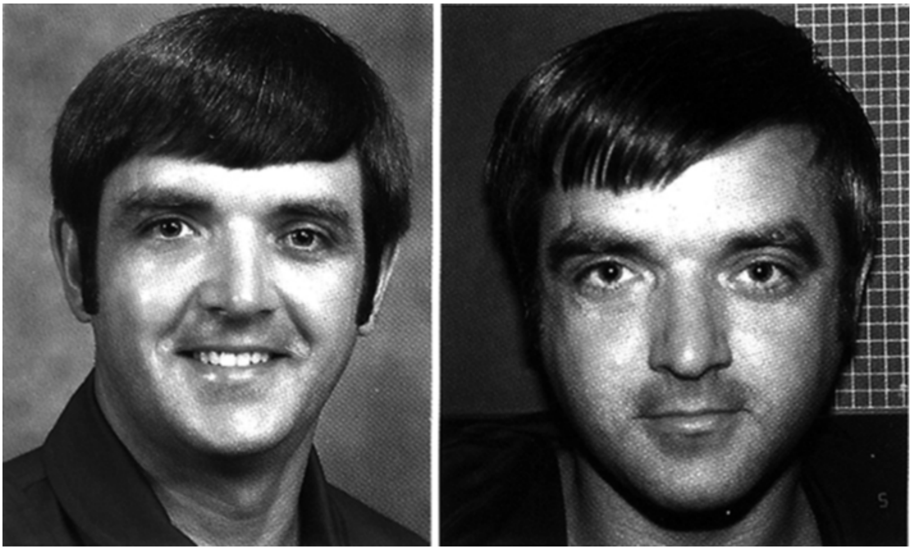


Figure 1.15. An Example of "Puffy Face." The Normal Face of an Astronaut on Earth (*Left*) Is Contrasted with His Swollen-Looking Face in Space (*Right*). (Credit NASA).

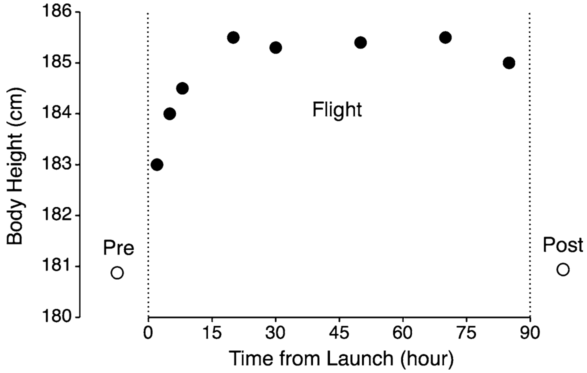


Figure 1.16. Diagram Showing the Increase in the Height of an Astronaut During the First Hours of a Space-Flight. (Adapted from Thornton and Moore [1987]).

There are experiments to monitor and several hours of exercise daily on the treadmill or cycle ergometer. After a few weeks, however, the routine becomes boring and it gets harder and harder to keep up with the exercise. The more she looks out of the window, the more she longs for the sounds of rain and wind, and the smell of flowers. The objects outside the station look “unreal in clarity.” However, when she closes her eyes, she experiences light flashes, especially when the ISS flies over the South Atlantic Anomaly. The crew starts to argue about the smallest things. One planned space walk has to be canceled because of a persistent irregular heartbeat in one crewmember. Since that incident, this crewmember seems to be withdrawing from the others. The weekly videoconferences with family and friends are eagerly anticipated, but she wonders why there has been no communication from her youngest child for several weeks. Has something happened? Anxiety arises, and she has a persistent pain in her lower abdomen, which, if it continues, might prompt an emergency evacuation to Earth.

But at last the time to return approaches. An interesting mixture of excitement and anxiety pervades the crew. Visions of favorite foods and what to do first are the main topics of conversation. Yet, the group has become so firmly a part of each other that the thoughts of reintegrating into Earth’s society are intimidating. But at last the crew is on its way home. When donning her re-entry space suit, she realizes it is too tight because she has grown a few centimeters. During the re-entry into Earth’s atmosphere our traveler experiences disorientation again when she tilts or rolls her head. After landing, she reports an unbelievable sense of “heaviness” and finds herself unable to stand up unassisted from her seat, much less walking down the stairs. Her heart is beating fast; she sweats and almost faints.

Even after several days of rehabilitation, balance is poor and walking uncoordinated. Muscle weakness is very evident; she quickly feels short of breath and is constantly thirsty. Weight loss that occurred in space is rapidly disappearing, but her physician tells her that she had lost much of bone density in her hips and that her immune system seems to be impaired. Now she is concerned because she remembers that the various bacterial colonies they were studying on board the ISS laboratories showed explosive growth rates! Several months later, though, all her body functions seem to have re-adapted to Earth’s gravity.

This story is not meant to discourage anyone from wanting to be an astronaut. In reality, not all people experience all of the adverse effects of spaceflight. It is rather meant to show how little we really know about the human body's response to spaceflight and how very dangerous this new environment can be. The interpretations for the observed physiological and psychological changes during spaceflight will be detailed in Chapters 3–6 of this book.

1.2.3. Life support systems

Spaceflight includes conditions such as vacuum, extreme temperatures, noise (mostly due to the life support systems), and radiation. Protecting humans from these harmful conditions requires the use of life support equipment and technologies such as space suits, pressurized and isolated living quarters, and radiation shielding.

In addition, certain basic physiological needs must be met for human beings to stay alive. On Earth, these needs are met by other life forms in conjunction with chemical processes that effectively use human waste products in conjunction with energy from the Sun to produce fresh supplies of food, oxygen, and clean water. In the artificial environment of a spacecraft, these materials must be provided, and human wastes removed, without relying on the natural resources of Earth's biosphere.

To date, space missions have used a simple "open" system, bringing along all necessary food, water, and air for the crew and venting waste products into space or collecting and storing them for return to Earth. When the point is reached where it is no longer cost effective or logistically possible to re-supply the spacecraft or habitat with water, atmosphere, and food, ways must be found to recycle all these components. This recycling of material is referred to as a "closed" system and can be achieved using physical-chemical systems, or better, using biological systems (Figure 1.17).

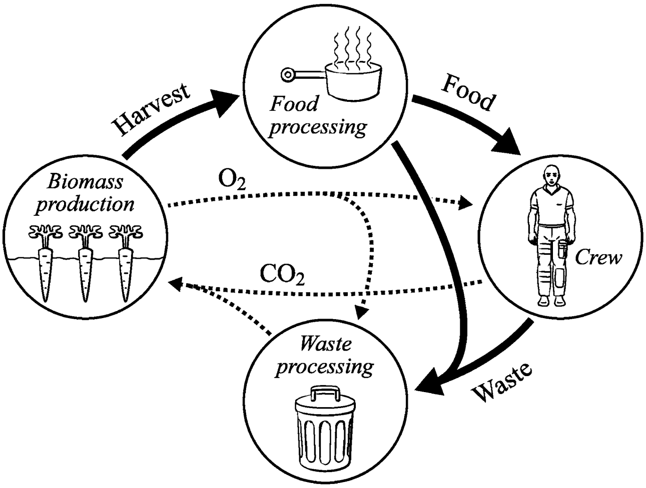


Figure 1.17. A Closed Ecological Life Support System Employs Biological Components and Uses Higher Plants. Higher Plants Are Easily Digestible and Are Customary Sources of Human Food. Besides Producing Food They Also Remove Carbon Dioxide from the Atmosphere, Produce Oxygen, and Purify Water Through the Process of Respiration. (Credit Philippe Tauzin).

Think of the human body as a sealed box with one pipe in and one pipe out. In go oxygen (O_2), water, and food; outcome solid and liquid wastes, bacteria, and carbon dioxide (CO_2). The outlet pipe is fed into a second sealed box, the closed (or controlled) ecological life support system (CELSS). The CELSS must be as “magical” as the first, for it must transform these by-products of the body into fresh supplies and pipe them back [Collins, 1990].

Trying to recreate the cycles of nature in a relatively small volume is a great technical challenge. Plants “breathe” CO_2 and “exhale” O_2, so in a broad sense human wastes are used by plants and vice versa. But in nature the nutrients, air, water, and energy are freely available. In a CELSS system all of these elements must be imported and carefully managed in a closed cycle. There are critical questions being addressed for CELSS during human missions. For example: How far can we reduce reliance on expendables? How well do biological and physical-chemical life support technologies work together over long periods of time? Is a “steady state” condition ever achieved with biological systems? How do various contaminants accumulate, and what are the long-term cleanliness issues? Eventually, in the case of interplanetary missions, is it possible to duplicate the functions of Earth in terms of human life support, without the benefit of Earth’s large buffers – oceans, atmosphere, land mass? How small can the requisite buffers be and yet maintain extremely high reliability over long periods of time in a hostile environment? Eckart [1996] has addressed most of these questions. We will summarize them in Chapter 8.

1.3. Challenges facing humans in space

1.3.1. Astronauts’ health maintenance

As it will be detailed in the following chapters, exposure to microgravity and the space environment has important medical and health implications, including bone loss (matrix and minerals), increased cancer risk from space radiation, spatial disorientation, orthostatic hypotension, and many others. One of the primary objectives of space life sciences is to ensure the health of crewmembers working on board the spacecraft and in the hostile environment outside their vehicles. Responsibilities of the operational medical program include preflight activities such as screening and selecting new astronaut candidates, health stabilization, in-flight activities such as the administration of countermeasures and medical care, and postflight procedures such as rescue after an emergency landing or rehabilitation for a prompt return of crewmembers to flight status [Nicogossian and Parker, 1982; Barratt and Pool, 2008].

1.3.1.1. Preflight

The minimal medical criteria for the selection of astronauts are different for those astronauts who actually pilot the vehicle (pilots), those who support onboard operations and perform extra-vehicular activities (mission specialists), and those passengers who just “participate” either as politicians, journalists, or tourists (see Chapter 7, Section 7.2.1).

Based on the knowledge of specific health risk factors associated with spaceflight, appropriate and proven tests are utilized in selecting the astronauts. Annual medical evaluations are then performed to identify and correct medical risks to maintain health, provide certification for flight duties, and ensure career longevity. These tests may include further clinical evaluation, e.g., using state-of-the-art imagery techniques, or fitness assessments in order to prescribe individualized exercise programs and provide one-on-one preflight and postflight conditioning activities. Both selection and periodic medical evaluations rely on the accepted ground-based standards of preventive medicine, health maintenance, and medical practice. These standards are revised on a periodic basis to ensure that they are fair and appropriate to meet the needs of human spaceflight.

During preflight training, the primary emphasis of medical support is on prevention. For example, the purpose of the Crew Health Stabilization program is to prevent flight crews from exposure to contagious illness just before launch. A preflight quarantine limits access to flight crew during 7 days just prior to launch. Even before this period, the health of an active duty crewmember family is of critical importance, and factors such as infectious disease and stress affecting a crewmember family may have serious adverse effects on the crewmember health and performance, as well as the health and performance of other crewmembers. Medical and dental care is provided to the crewmember's immediate family by an onsite flight medical clinic, as long as the crewmember is eligible for assignment to a spaceflight mission.

Crewmembers are also trained in the use of special countermeasures to offset spaceflight physical deconditioning and in medical monitoring and clinical practice procedures. Medical training for the crew, medical supervision of mission planning, schedules, payloads, exercise training, conditioning, and other health maintenance activities are all part of the preflight period.

1.3.1.2. In-flight

The primary emphasis of in-flight medical support is on health maintenance. Health monitoring and medical intervention, countermeasures to bodily function deconditioning, and environmental monitoring insure a comprehensive program tailored to crew and mission needs and for the periodic assessment of crew medical status, including the identification of potential and unexpected health risks.

Among these potential health risks are the levels of acceleration, vibration, and noise during launch, the exposure to toxic substances and pressure changes, and the risk due to radiation. With the possible exception of the immune system, bodily changes that occur after entering microgravity represent normal homeostatic responses to a new environment. The body's control systems recognize the lack of gravity and begin to adapt to this unique situation, not realizing that the ultimate plan is to return to 1 g after a transient visit to microgravity. In-flight, typical adaptive and pathophysiological changes occur in the heart and blood vessels (dysrhythmias), muscles (atrophy), bones (density loss, fractures, renal stones), nervous system (disorientation and nausea), and in the immune system (infection). Extra-vehicular activities (EVA), also called space walks, may also be responsible for strain on muscles and bones and decompression-related disorders.

Psycho-sociological issues become increasingly more important as space missions become longer, and spaceflight teams become larger and more heterogeneous. The isolated, confined, and hazardous environment of space create stress beyond that normally encountered on Earth, even when training for a space mission. Extended duration missions place an even greater stress on individual, interpersonal, and group relations for astronaut crews, between astronaut crews and ground control, and on astronaut families. Current countermeasures focus primarily on the individual, mission crew, and to some extent the families of mission crews, by providing psychological training and support through in-flight communications. Finally, for spaceflight missions, emphasis is not only on health maintenance, disease prevention, and environmental issues, but also on the provision of medical care to manage possible illnesses and injuries.

1.3.1.3. Postflight

The primary emphasis of postflight medical support is medical care. During return to Earth, piloting tasks are challenged by the presence of g forces in deconditioned individuals (Figure 1.18). After nominal landing, astronauts often exhibit difficulties in standing, a phenomenon known as postflight orthostatic intolerance (see Chapter 4, Section 4.1) and walking. These difficulties could prove dramatic in the case of a non-nominal landing where the crew may be required to suddenly egress the vehicle with no help from ground support.

Astronauts must have career longevity, normal life expectancy, with rehabilitation and recovery capabilities available upon their return from spaceflight. After landing, health monitoring and physical rehabilitation are performed to accelerate the return of crewmembers to normal Earth-based duties. An important factor to take into account is the return to flight status for pilot astronauts.

There is a large catalog of reported postflight symptoms captured in the mission medical debriefs that are collected after a space mission through interviews between the astronauts and crew flight surgeon. After every space shuttle mission, a NASA

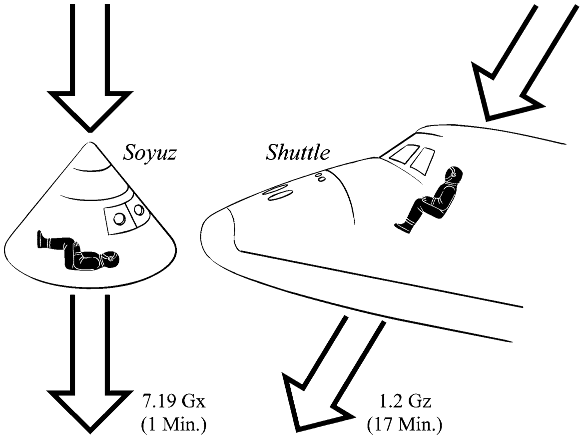


Figure 1.18. Direction of g Forces Experienced During Landing in a Soyuz Capsule (*Left*) and the Space Shuttle (*Right*). Lower g Forces Are Tolerated When Directed Along the Body Longitudinal Axis (Gz), in a Direction Parallel to the Big Blood Vessels. (Credit Philippe Tauzin).

flight surgeon holds a medical debrief with each crewmember on the day of landing and then 3 days later. Standardized debrief forms are used during these meetings, at which time the physician and crewmember discuss pre-, in-, and postflight medical issues. The crewmembers are interviewed about their experiences, using both open-ended and specific questions. Information from these debriefs is available in a database known as the Longitudinal Study of Astronaut Health (LSAH). NASA flight surgeons of the Flight Medicine Clinic at NASA Johnson Space Center provide the interface with the LSAH, which is a long-term program investigating whether the unique occupational exposures of astronauts are associated with increased health risks. Such studies are particularly relevant regarding the issue of radiation exposure.

1.3.2. Environmental health during space missions

During space missions, medical care does not only focus on health maintenance and disease prevention, but also on environmental issues. Spacecraft are closed compartments, and therefore standards for air, water, microbiology, toxicology, radiation, noise, and habitability must be established. In-flight environmental monitoring systems are available to prevent crew exposure to toxicological and microbial contamination of internal air, water, and surfaces; to radiation sources from within and external to the spacecraft; and to vibration and noise. These systems must have near real-time and archival sampling and provide a mechanism to alert crewmembers when measured values are outside acceptable limits.

Habitability of a spacecraft is vitally important to the crew's health, well being, and productivity, especially as mission duration increases. Habitability issues regarding the human presence in space includes human factor design considerations (colors, equipment layout, and hardware design), adequate and ergonomically correct work and living volume, with similarly adequate stowage volume. Areas must be designed that allow for restful sleep and personal space, with adequate lighting and exterior views. Schedules must produce interesting work, with sufficient rest and recreation periods to avoid chronic fatigue. Ideally, each crewmember should have private time and physical space for fitness and recreation, in order to keep his/her motivation.

Time and resources are set aside for personal hygiene and sanitation (see Chapter 8, Section 8.3.4). In addition, a healthy, palatable variety of food and beverage must be provided (Table 1.3). The daily food supply totals a high 3,000 cal, plus snacks. The meals also attempt to compensate for the body's tendency to lose essential minerals in microgravity, such as potassium, calcium, and nitrogen.

At the same time, the meals must be attractive, not like the early missions when astronauts had to suck their meals out of "tooth-paste" tubes or plastic bags without being able to see or smell the food. Nowadays, attention is given to individual crewmember preference with regard to palatability and nutritional adequacy of food items during missions.

Medical and psychological personnel have also an opportunity to review all design considerations early in the design process to ensure that spacecraft design and support systems meet medical and psychological requirements.

Table 1.3. The Space Shuttle Menu Currently Features More Than 70 Food Items and 20 Beverages. Shuttle Crewmembers Have a Varied Menu Every Day for 6 Days. Each Day, Three Meals Are Allowed, with a Repeat of Menus After 6 Days. The Pantry Also Provides Plenty of Foods for Snacks and in Between Meal Beverages and for Individual Menu Change.

Thermostabilized

- Heat processed foods ("off-the-shelf" items) in aluminum or bimetallic tins and retort pouches

Irradiated

- Foods preserved by exposure to ionizing radiation
- Packed in flexible foil laminated pouches

Intermediate Moisture

- Dried foods with low moisture content such as dried apricots
- Packed in flexible pouches

Freeze Dried

- Foods prepared to the ready-to-eat stage, frozen and then dried in a freeze dryer that removes the water by sublimation
- Freeze-dried foods such as fruits may be eaten as is while others require the addition of hot or cold water before consumption

Re-hydratable

- Dried foods and cereals re-hydrated with water produced by the shuttle orbiter's fuel cell system
- Packed in semi-rigid plastic container with septum for water injection

Natural Form

- Foods such as nuts, crunch bars, and cookies
- Packed in flexible plastic pouches

Beverages

- Dry beverage powder mixes
- Packed in re-hydratable containers

1.3.3. Human Mars mission

The eventual decision to go to Mars will be strongly influenced by non-scientific reasons. Science, though a factor, will not be the driver. Thus, the real issue here is, if humans are to go to any planetary body, what science and related activities can be performed to take maximum advantage of the presence of humans on these missions?

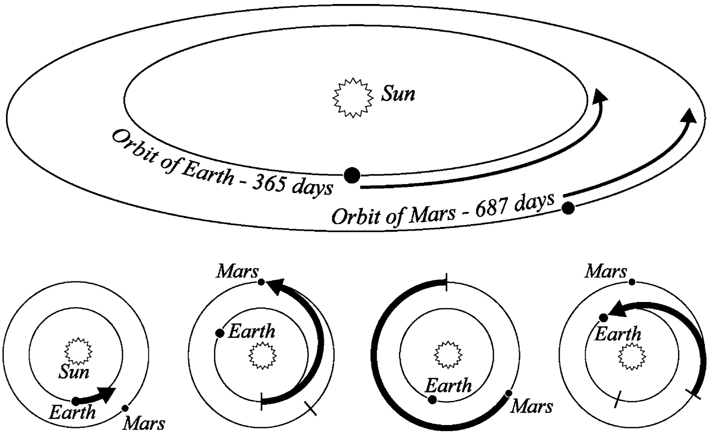
For many, the major science objective of sending humans to Mars is to search for evidence of past or current life on another planet, investigate the Martian climate, study Martian geology and geophysics, and prepare for future missions and sustained habitation. A human Mars mission can also be regarded as an important cultural task for humankind with the objective to globalize the view of our home planet Earth, thereby contributing to the solution of local conflicts. In any case, a human Mars mission would meet the natural human need to explore and expand to new regions.

Using the current rocket technology, traveling between Earth and Mars will require lots of fuel and good timing. The most fuel-efficient trajectory occurs when Earth is at a 6 o'clock position at launch and Mars is at about 4 o'clock – a juxtaposition that occurs just once every 26 months. The first leg will take about 6 months. Astronauts must wait on Mars for their launch toward home until Earth is in alignment. After their surface stay of approximately 500 days, the astronauts will ascend to orbit, rendezvous with the transit habitat, and return to Earth. Total mission duration will be about 30 months (Figure 1.19).

In 2004, NASA embarked on the new Vision for Space Exploration. This was an ambitious plan to send human missions to the Moon, Mars, and beyond as part of the Constellation program. Early in 2010, following the recommendations provided by the Augustine Commission [Augustine et al., 2009], U.S. President Barrack Obama announced the cancelation of this program. Instead, he called for a shift in focus, directing NASA's attention towards sending humans directly to Mars using international cooperation, as well as innovative and cost-effective new technologies.

The design decisions and plans outlined within the NASA Design Reference Architecture 5.0 [NASA DRA 2009] are likely to represent a relevant baseline for any future Mars mission. This reference mission is assumed to begin with cargo launches in the 2039 launch window and the crew launching in the 2041 window. Precursor missions to Martian orbit, as pledged by U.S. President Obama in an April 2010 speech at the NASA Kennedy Space Center, should occur by 2035.

The reference mission consists of two cargo spacecraft. The first will place the ascent stage and cargo on the surface of Mars. The second will place the surface habitat in Martian orbit. The ascent stage will land with an In Situ Resource Utilization (ISRU) unit that will produce oxygen from the Martian atmosphere along with methane brought from Earth to fuel the ascent stage. A crew of six will be launched 2 years later.



Depart Earth Out to Mars Stay on Mars Back to Earth

Figure 1.19. ***Top*: Schematic of the Orbits of Earth and Mars Showing Their Position for a More Fuel-Efficient Trajectory During Launch. *Bottom*: The Respective Positions of Earth and Mars Determine the Duration of Travel and Stay on the Martian Surface.**

The crew will be mixed gender and international with their roles being pilot, physician, geologist, biologist, and mechanical and electrical engineers. Upon arrival they will rendezvous in orbit with the habitat and use it to land on Mars. The transit module will remain in orbit for the duration of the surface mission.

Upon landing, the astronauts will take several weeks to adapt, during which they can somewhat recover from their microgravity transit and conduct only essential activities. After this period, they can engage in scientific research. A variety of robotic, pressurized, and unpressurized rovers, as well as scientific equipment and drills delivered by the landers, will be waiting for the crew. It is assumed that the landing will take place in an area believed to be relatively safe, but which will presumably not be of substantial scientific interest. From there the astronauts will use rovers to travel distances of up to hundreds of kilometers, to rougher, more interesting sites. The robotic rovers are intended for use in areas deemed to be particularly likely to contain life or evidence of past life. These areas must be protected from contamination at all costs to maintain the integrity of astrobiological investigations. The rovers will be teleoperated to investigate these sensitive areas without compromising planetary protection protocols.

Developing the technical capability to reach Mars is only one aspect of the necessary preparations; it is equally important to consider the human factors that would affect such a mission. How will the human body and mind react to extreme circumstances such as microgravity, radiation, and isolation? How does an astronaut perform his or her work if direct communication to Earth is not possible? How can a life support system keep the astronauts alive and healthy during a multi-year mission without possibility of re-supply? More studies and experiments must be performed to gain knowledge on these and numerous other topics to adequately prepare for a human mission to Mars [Smet et al., 2010].

Luckily, the Mars gravity of 0.38 g might act as a countermeasure to the physiological deconditioning that will take place in microgravity during the trip from Earth to Mars. However, landing maneuvers on Mars and Earth are characterized by maximum g-loads of up to 6 g due to atmospheric drag. If the interplanetary cruise is carried out at zero gravity level (i.e., if no artificial gravity is provided within the spacecraft), such high g levels in deconditioned astronauts appear critical for the health of the crew.

Any trip beyond low Earth orbit will involve radiation threats not faced by residents of the ISS, which sits inside the planet's magnetic field. A 30-month trip to Mars, including 6–9 months of travel time each way, would expose an astronaut to nearly the lifetime limit of radiation allowed under NASA guidelines. There are two primary forms of hazardous space radiation particles: high-energy particles emitted by the Sun during intense flares and more energetic cosmic rays from undetermined galactic sources. Solar and galactic radiation can cause severe cellular damage or even cancer (see Chapter 8, Section 8.3.5). The Martian atmosphere, about 1% as dense as Earth's, manages to stop just about all of the solar particles, but it lets most of the cosmic rays through. However, the crew needs to be protected against the occasional solar flare with a "storm shelter," e.g., with food racks and water tanks packed around the walls to absorb the radiation.

Cosmic rays are a different story. They are constantly present, coming from all directions. The radiation consists of heavy, slow-moving atomic nuclei that can do far more damage to more cells than the alpha and beta particles of solar flares. This radiation requires several meters of shielding for complete blockage, and since the nuclei come from all directions at all times, unlike the brief solar flares that last only a few hours or days, a storm shelter would be insufficient to protect the crew. The planet itself offers natural protection against cosmic rays by blocking half the sky. In addition, the habitats of the Mars base can be covered with thick layers of soil to provide full-time radiation protection, so nearly all the crew's radiation exposure would occur during the period of interplanetary travel. Even if such shielding methods prove difficult to engineers, some scientists believe that the cosmic ray doses can simply be endured. Exposure to a thin, continuous stream of radiation does far less damage than an equal magnitude of radiation delivered in 1 day. There is still the possibility of cancer, but this probability is rather low.

The combined solar and cosmic ray particle exposure is measured in Sieverts (1 Sv = 100 rem). An astronaut on a 6- to 9-month journey to Mars would be exposed to about 0.3 Sv, or 0.6 Sv on a round-trip. Another 15–18 months on the surface would bring another 0.4 Sv, for a total exposure of 1 Sv. Limits set by NASA vary with age and gender but range from 1 to 3 Sv. This dose would lead to a 3% increase in the probability of contracting a fatal cancer later in life, compared to an already existing 20% cancer risk for non-smokers on Earth, and would probably be acceptable to the volunteers for this mission. However, since the biological effects of cosmic radiation are poorly understood, the resulting cancer risk may conceivably be off by as much as a factor of 10, and thus jump to 30%, or drop to 0.3%.

Not much research can be done safely on Earth to investigate these radiation effects, as cosmic rays are difficult to generate, and no one would consent to being exposed to a theoretically fatal dosage. The ISS could provide a good testing ground because large numbers of astronauts will be exposed to modest amounts of radiation in their 6-month tours of duty, but a full investigation might require waiting decades until these astronauts retire and die either of natural causes or of cancer. Obviously Mars mission advocates have no intention of waiting that long. It actually makes the most sense to accept the radiation risk on the Mars mission. After all, this is a journey into the unknown, and the risk of radiation is mild compared to the dangers that explorers on Earth have faced, and overcome, in the past [Reifsnyder, 2001].

1.3.4. Countermeasures

We will see in the following chapters that the changes in human physiology during spaceflight are appropriate adaptations to the space environment. They are not life threatening for at least 14 months, which is the longest continuous period that humans have spent in space. That's the good news. The bad news is that adaptation to space creates problems upon returning to Earth. Difficulty in standing, dizziness, and muscle weakness pose problems after landing. Therefore, appropriate countermeasures must be developed that balance health risk against mission constraints, and particularly the limited resources regarding medical care possibilities.

Countermeasures refer to the application of procedures or therapeutic (physical, chemical, biological, or psychological) means to maintain health, reduce risk, and improve the safety of human spaceflight. The countermeasures typically aim at:

(a) Eliminating or preventing adverse and harmful effects on crew health. Examples include the provision of a substitute gravitational effect in orbit (artificial gravity), thus preventing microgravity from degrading the health of the astronauts.

(b) Mitigating the effect of adverse or harmful agents or enhancing the astronaut's ability to ward off the effects of these agents. Examples include preflight and in-flight exercise to counteract the effects of microgravity, in-flight administration of medications to prevent space motion sickness, and spacecraft design changes to minimize radiation exposure.

(c) Minimizing the effect of adverse or harmful agents on the crew once mal-adaptation, disease, or injury has been identified. Examples include fluid loading to minimize postflight orthostatic intolerance (Figure 1.20), or a postflight rehabilitation program to reverse space mission-induced musculo-skeletal or cardio-vascular deconditioning.

Preflight countermeasures include activities to support appropriate crew selection and psychological training, fitness and exercise, physiological adaptive training, a health stabilization program, and circadian shifting.

In-flight countermeasures include those activities necessary to maintain physiologic balance and health, mental and behavioral health, nutritional health, and physical fitness and mission performance. Typical physical exercise includes cycling, running on a treadmill, or rowing.

Postflight countermeasures include those activities necessary to assist the crewmembers in a return to preflight physical, physiological, and behavioral health baselines. Examples of countermeasures include, but are not limited to, circadian rhythm shifting, hormone replacement, and physical exercise.

Figure 1.20. A Shuttle Crewmember Prepares Containers of Drinking Water and Salt Tablets To Be Consumed by His Crewmates Prior to Re-entry. Fluid Loading Is a Standard Procedure on All Shuttle Flights, as an Effective Countermeasure to Orthostatic Intolerance upon Return to Earth's Gravity. (Credit NASA).

Figure 1.21. French Cosmonaut Jean-Pierre Hai-gneré Is Hand Carried by Bround Personnel After Returning from a 6-Month Stay on Board the Russian Space Station Mir. (Credit CNES).

For long-duration missions, the *Mir* and ISS experience indicates that current in-flight countermeasures are not optimal, to say the least. Evidence for this is provided by the images of the cosmonauts unable to stand immediately after returning to Earth after a long-duration stay on board *Mir*. They are helped from the spacecraft and "ceremoniously hauled around like nabobs in sedan chairs" (Figure 1.21). The situation with the ISS has not changed much. Astronauts on board the ISS exercise on a cycle-ergometer, a treadmill, or a resistive exercise device for up to 2 h/day. Yet, considerable muscle and bone loss is observed after landing (see Chapter 5, Section 5.1). Consequently, it is largely admitted that using the current countermeasure methods, humans would not be operational after landing on Mars.

1.3.5. Artificial gravity

One possible countermeasure to the effects of weightlessness is the use of artificially produced gravity on board the spacecraft. Artificial gravity could be accomplished either through rotation of the entire vehicle or by the inclusion of an onboard centrifuge. For a more complete description of the rationale for artificial gravity, the possible spacecraft design options, and its potential effect on a space crew, the reader is referred to the book *Artificial Gravity* by Clément and Bukley [2007, Springer].

The rationale for using centrifugation is that during rotation about an eccentric axis the resulting centrifugal force provides an apparent gravity vector. The centrifugal force produced by rotation is dependent upon two parameters of the rotating structure,

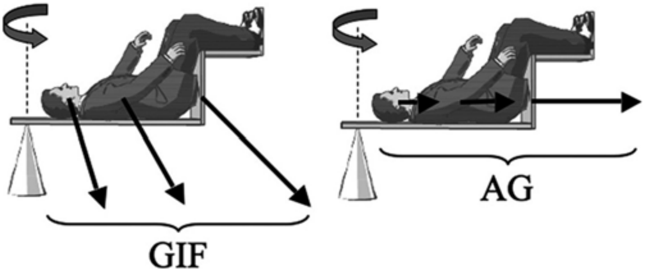


Figure 1.22. These Drawings Illustrate the Difference Between the Physical Effects of Centrifugation on Earth (*Left*) and in Space (*Right*). On Earth, the Gravito-Inertial Force (GIF) Is Tilted Relative to the Plane of Rotation. In Space, Artificial Gravity (AG) Is Aligned with the Plane of Rotation. Also Shown Is the Gravity Gradient in Both Conditions. For Example, in the Right Figure, the AG Level Is 1 g at the Feet and 0.38 g at the Head for a Rotation Rate of 20.8 rpm. (Adapted from Clément and Bukley [2007]).

the square of its angular rate (ω^2) and its radius r. On Earth the centrifugal force combines with the gravitational force, and the resulting vector, the so-called gravito-inertial force, is both larger in magnitude than the centrifugal force itself and tilted with respect to gravity. In microgravity, the subject will only be exposed to a centrifugal force, referred to as artificial gravity (Figure 1.22).

Because the centrifugal force depends on both rotational rate and radius, a specific increase in the artificial gravity level can be achieved either by increasing the radius or by increasing angular rate. This translates to a trade-off between cost and complexity, which depends mostly on the radius of the structure versus the physiological and psychological concerns, both of which depend mostly on its angular rate [Diamandis, 1997].

One significant drawback of a rotating environment is the Coriolis force that is generated every time a linear motion is attempted in any plane not parallel to the axis of rotation. The Coriolis force has a magnitude of $2\omega V$; where ω is the rotation rate for the rotating environment and V is the linear velocity of the moving object. When attempting any linear movement out of the plane of rotation, the Coriolis force combines with the centrifugal force to produce a different apparent gravity vector in magnitude alone or in both magnitude and direction. To a human in a rotating environment, this vector may be manifest in two ways. First, it adds to the apparent weight of a body moving in the direction of rotation and subtracts from the apparent weight when moving against the direction of motion. Second, when a body moves toward the center of rotation, the Coriolis force is exerted in the direction of rotation at right angles to the body's motion; when moving away from the center of rotation the force is opposite to the direction of rotation. By contrast, a motion parallel to the axis of rotation will generate no Coriolis force [Stone, 1973].

The Coriolis forces affect not only whole-body movements but also the vestibular system (see Chapter 3, Section 3.2.1). Rotation of the head out of the plane of rotation generates cross-coupled angular accelerations that induce stimulation of all three semicircular canals. Such head movements in a stationary environment do not normally stimulate some of the canals, and this results in illusory sensations of bodily or environmental motion. Nausea and vomiting may result after a few head movements, particularly if the angular velocity of the centrifuge is high. Based on ground-based studies performed in the 1970s using slow rotating rooms, it was postulated that the lightest acceptable system for providing "comfortable" artificial gravity using a rotating spacecraft would be one having a radius of rotation not lower than 12 m, rotating at 6 rpm, and providing a gravity level ranging from 0.3 to 1 g [Thompson, 1965; Hall, 2009]. More recent studies showed that the subjects in a rotating environment could tolerate a rotation rate up to 10 rpm, provided that the exposure is progressive [Lackner and DiZio, 2000], or even up to 23 rpm after habituation of the motion sickness symptoms [Young et al., 2001].

The "prescription" of how much acceleration/gravity over what period of time and in what direction is required for maintaining normal health is currently unknown and logistically very difficult to determine. A rotating spacecraft that provides a constant 1-g acceleration would be ideal. However, a maneuvering station presents serious design, financial, and operational challenges. Also, head movements and resultant Coriolis and cross-coupled accelerations on a rotating spacecraft may limit the usefulness of centrifugation for other than brief periods of intermittent stimulation. From a practical perspective, it is very likely that humans do not need gravity (or fraction of it) 24 h a day to remain healthy. If intermittent gravity is sufficient, we won't need a permanently rotating spacecraft to produce a constant gravity force. An onboard device such as a human rated short-radius centrifuge, presents a realistic near-term opportunity for providing this artificial gravity.

Several designs for an onboard short-radius centrifuge have been proposed. I was the Principal Investigator of an experiment using a human-rated centrifuge generating 0.5 or 1 g along the longitudinal body axis, which flew aboard the *Neurolab* mission of the space shuttle (STS-90) in 1998 (Figure 1.23). This experiment was (and remains) the first in-flight evaluation of artificial gravity on astronauts. The results of this experiment, described in more detail in Chapter 3, suggested that centrifugal force of 0.5 g was well tolerated by the crew, and that cardio-vascular deconditioning was reduced in those astronauts who rode the centrifuge 20 min every other day during a 16-day space mission [Clément and Reschke, 2008].

An interesting new approach is a human-powered centrifuge that couples exercise with artificial gravity [Greenleaf et al., 1977]. Exercise as a countermeasure was introduced in the days of the Gemini program. It has taken on various ingenious forms of elastic, pneumatic, mechanical, hydraulic, and electrical devices. These devices apply a force (not an acceleration), and they only partially protect crewmembers. For example, crewmembers wear a harness attached to an exercise bike or treadmill and are held "down" during exercise. Elastic devices can effectively create force, but not sustained acceleration. Doing such activities during centrifugation would be much more effective.

Various designs have been proposed, such as the "Twin Bike" of the University of Udine, the "Space Cycle" of the University of California at Irvine (Figure 1.24), and NASA Ames Research Center's human-powered centrifuge [Clément and Bukley, 2007]. It is believed that exercising under these increased inertial forces will decrease the amount of time required to exercise for maintaining health and fitness in space. If the results prove positive and the amount of exercise is reduced by centrifugation,

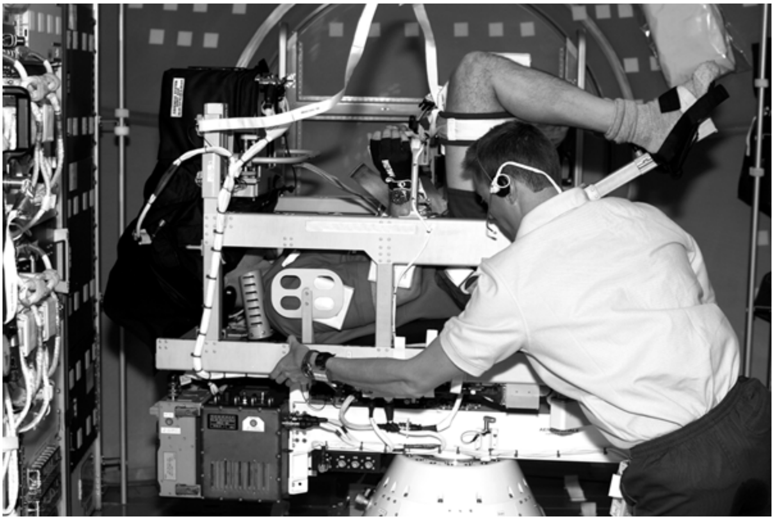


Figure 1.23. This 0.65-m Radius Human-Rated Centrifuge Developed by ESA Flew on Board the Neurolab Mission (STS-90). This Experiment Investigated the Adaptation of the Vestibular System in Astronauts by Detecting Changes in Perceived Motion and Orientation in Microgravity. (Credit NASA).

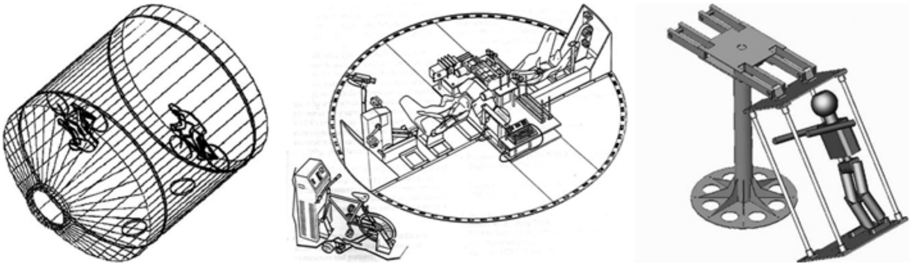


Figure 1.24. From Left to Right Are Depicted the Twin Bike, the NASA Human-Powered Centrifuge, and the Gondola of the Space Cycle (the Cycle Itself Is Not Shown). All These Devices Combine Physical Exercises and Sustained Inertial Forces Generated by Centrifugation. For More Details on These Devices, Readers Are Referred to the Book *Artificial Gravity* by Clément and Bukley [2007].

then such devices could be a good candidate countermeasure for the ISS, the spacecraft en route to Mars, or the Martian habitat.

1.3.6. A new science is born

Space life sciences is a young science, having come into existence with the first studies carried out on animals during the first suborbital flight less than 60 years ago. Since then, people have visited the Moon and have lived in space for about the period planned for a mission to Mars. Still, our understanding of how spaceflight affects living organisms remains rudimentary.

The ISS, now fully operational with a permanent crew of six, should prove an ideal platform for studying fundamental biological processes in microgravity. This will undoubtedly lead to the growth and development of a new science: gravitational physiology.

Gravity affects some materials and fluid dynamics. It is required for convective mixing and other weight-driven processes, such as draining of water through soil, and assuring that what goes up comes down. One might predict that plants would grow taller without gravity, yet the lack of gravity might facilitate increased levels of growth-inhibitory or aging environmental factors around the plants, thereby causing them to dwarf. Gravity also has a role to play in development of load-bearing structures. The scaling effect of gravity is well known: the percentage of body mass contributing to structural support is proportional to the size of a land animal (e.g., 20 g mouse=~5%, 70 kg human=~14%, and 7,000 kg elephant=~27%). This scaling effect in land animals would likely change in space and could result in a static scale comparable to marine mammals on Earth (~15% of mass as supporting tissues over a wide range of weights). Legs are bothersome in space and not only get in the way but also are involved in the fluid shifts that occur early in-flight. Whether legs would disappear over time without gravity (perhaps similar to the extra-terrestrial ET) or become more like grasping talons is unknown. Form follows function, and as function changes, so will form. How much change and what form organisms will assume over time in space is unknown [Morey-Holton, 1999].

Data to date suggest that certain biological structures have evolved to sense and oppose biomechanical loads, and those structures occur at the cellular level as well as at the organism level. There is evidence that the musculo-skeletal system of vertebrates change following acute exposure to space (see Chapter 5, Section 5.1). What will happen over multiple generations is speculative. The "functional hypothesis" theory suggests that what is not used is lost. If this theory holds over multiple generations in space, then gravity-dependent structures may ultimately disappear or assume a very different appearance in space. The next chapter reveals that we only have short snapshots of how small living organisms actually change in the space environment.

Another example is plants. Plants are the first organisms to be raised to the point of producing seeds in space, from seeds that were themselves raised in microgravity (see Chapter 2, Section 2.4). We now know that plants can grow in space, but the *Mir* and ISS studies have indicated that air and water require special management in microgravity. Further studies in this area are of paramount importance if one wants to move from the current physical-chemical to ecological closed life support systems.

Carrying out research in space often comes at a considerable cost (sometimes human, as demonstrated by the *Columbia* tragic event). The most striking difficulties are the small subject pool available, the lack of adequate controls, and the fact that science is, by necessity, secondary to mission safety when conducting experiments in such a hostile environment. Nevertheless, the success of the manned space program is dependent on the concomitant success of life sciences research in microgravity to solve the considerable dangers still faced by crewmembers on long-duration missions.

In this respect, the human Mars mission represents another fascinating challenge for space medicine. Such a mission, when it is undertaken, will probably be the longest period of exposure of any person to a reduced gravitational environment, and probably the longest period away from Earth, too. A recent report also suggested that radiation on Mars might be at much higher levels than previously believed. So high in fact, that it would make living there almost impossible. All together, these conditions make a human Mars mission a challenge from both the physiological and psychological points of view.

The historical record offers a rich set of examples of exploration – Christopher Columbus in his discovery of the New World, Vasco de Gama sailing directly from Portugal to India, and Lewis & Clark in the first overland expedition undertaken by the United States to the Pacific Coast, for example. These expeditions to unknown territories and back rank as some of the greatest voyages of discovery in human history. Because of the scientific and geographical discoveries that were made at the time, they stand in significance along the planned human exploration of Mars. They are many parallels between these jumps into *terra incognita* – unexplored land. All these historical expeditions took the necessary equipment, collective skill set, and vision to go into an unknown world in search of many things. The expeditions redefined, literally, a quest for scientific understanding about Earth and set the foundation for colonization. The small number of vessels and time frame are quite similar for the Mars mission and for the Vasco de Gama and Lewis & Clark's expeditions. However, the crew size was much larger and many lives were lost in the historical expeditions (Figure 1.25).

The public is presumably not ready for paying such a price in human lives for the Mars mission. Hence, more advances in research and technology are needed before the human exploration of Mars can be achieved with minimal risk. There is no doubt, however, that like the historical expeditions, the exploration of Mars will be extremely influential in terms of our knowledge of the world and satisfy the desire of humanity to explore and expand.

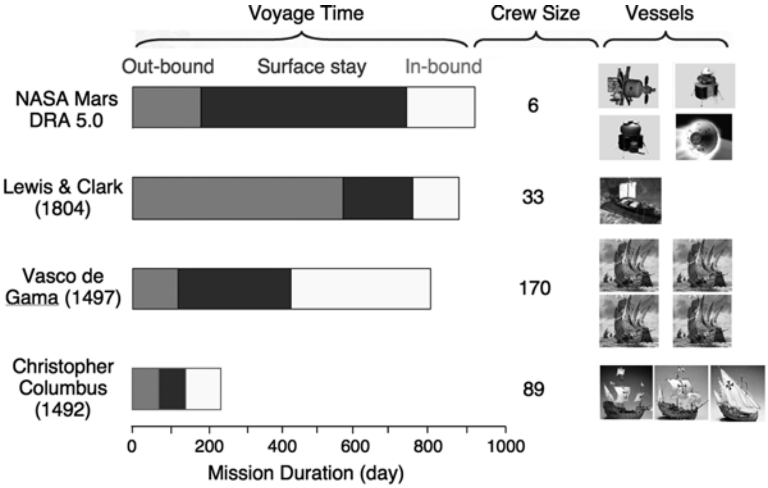


Figure 1.25. Historical Perspective for Human Exploration Missions. Comparison Between the NASA Mars Mission, Lewis and Clark's Expedition Across the Louisiana Territory, Vasco de Gama's First Direct Sailing from Europe to India, and Christopher Columbus's Discovery of America in Terms of Mission Duration, Number of Crew, and Vessels.

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Chapter 2

Space Biology

Gravity provides a directional stimulus that plays an important role in basic life processes in the cell, such as biosynthesis, membrane exchange, and cell growth and development. It is likely that the growth and development of plants are determined by hormones, whose transport is also influenced by gravity. Will these functions develop normally when deprived of the gravitational stimulus? This chapter will review the fundamental questions raised in the space environment in the areas of gravitational biology, developmental biology, plant biology, and radiobiology. For more details, the readers are referred to the book *Fundamentals of Space Biology* by Clément and Slenzka [2006, Springer] (Figure 2.1).

2.1. What is life?

It is generally admitted that, for scientific purposes, an object must meet six criteria to be considered alive: (1) movement (even plants move: stems shoot upward, flowers open and close, and leaves follow the movement of the Sun); (2) organization (animals and plants have organs, whose structure is nearly identical within the same species); (3) homeostasis (the ability to maintain constant conditions within the body); (4) energy (all living things absorb and use energy); (5) reproduction; and (6) growth (during the growth process, cells not only increase in number but they also develop into different types of cells that are needed to form the organs and tissues of the new individual) [DuTemple, 2000].

2.1.1. Life on Earth

Planet Earth is thought to be 4.6 billion years old. The first life form appeared about 4 billion years ago by the spontaneous aggregation of molecules that rapidly evolved into microscopic, relatively simple cells. Over the following millennia, these primitive cells evolved into at least 10 million different species, which represent Earth's existing biological diversity. All organisms, including animals, plants, fungi, and an untold collection of microbial species, have their common ancestral roots within these earliest life forms (Figure 2.2).

Chemical and fossil evidence indicates that life on Earth as we know it today evolved by natural selection from a few simple cells, called prokaryotes because they lacked nuclei. The earliest prokaryotes probably already had mechanisms that allowed them to replicate their genetic information, encoded in nucleic acids, and to express this information by translation into various proteins. Typical prokaryotic cells are bacteria (Figure 2.3). They are small, with relatively simple internal structures containing deoxyribonucleic acid (DNA), proteins, and small molecules. They replicate quickly

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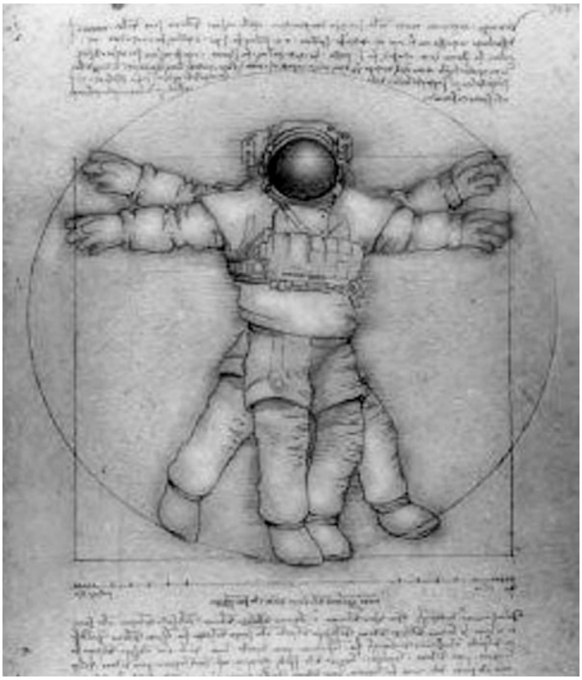

Figure 2.1. One Application of Space Research Is to Improve the Health of Astronauts in Space and That of People of All Ages on Earth. The Drawing by Leonardo Da Vinci, "Proportional Study of Man in the Manner of Vitruvius," Served as the Inspiration for Several Life Sciences Space Mission Patches, Including Skylab and Spacelab. (Source Unknown).

by simply dividing in two. A single cell can divide every 20 min and thereby give rise to 5 billion cells in less than 11 h. Their ability to divide quickly (growth rate) enables these cells to adapt rapidly to changes in their environment. Bacteria can utilize virtually any type of organic molecule as food, including sugars, amino acids, fats, hydrocarbons, and they get their energy in the form of adenosine triphosphate (ATP) from chemical processes in the absence or presence of oxygen.

About 1.5 billion years ago there appeared larger and more complex cells such as those found in "higher" organisms: the unicellular protists, fungi, plants, and the animals we know today. The important organelles of energy metabolism, plastids and mitochondria, originated 1.5–2 billion years ago through the symbiosis of prokaryotes. In this process, bacteria having one set of specialized functions were engulfed by host cells with complementary requirements and functions. These eukaryotic cells, or protozoa, have a nucleus, which contains the cell's DNA, and cytoplasm, where most of the cell's metabolic reactions occur. They get their ATP from aerobic oxidation of food molecules (respiration) or from sunlight (photosynthesis). Consequently, more than 2 billion years ago, the biota had used the process of photosynthesis to create an oxidizing atmosphere from one previously poor in oxygen. Carbon dioxide was also removed from the atmosphere in the form of carbonate precipitates.

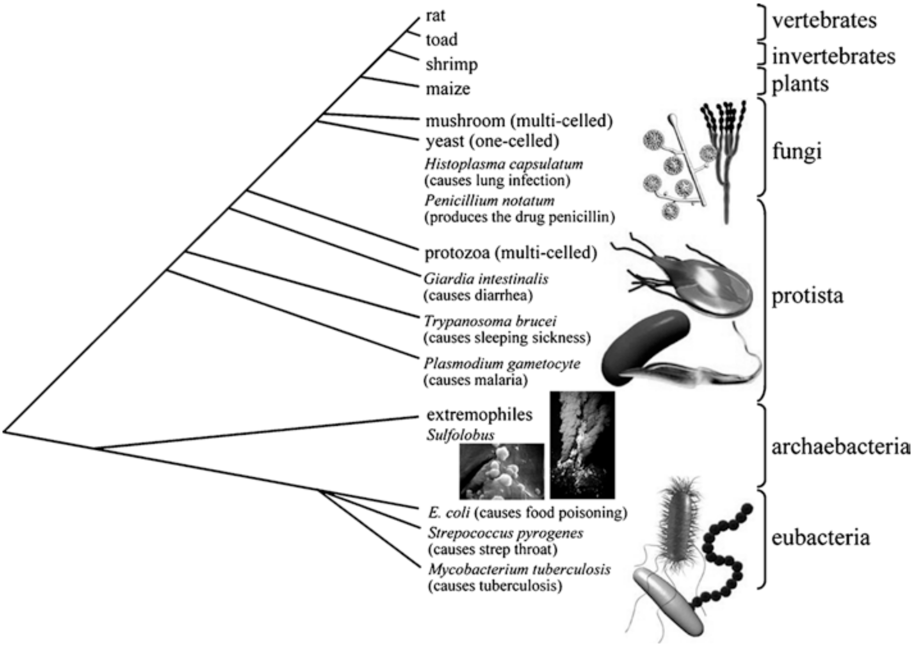

Figure 2.2. Evolution of Organisms Deduced from Their Gene Sequences. (Source Unknown).

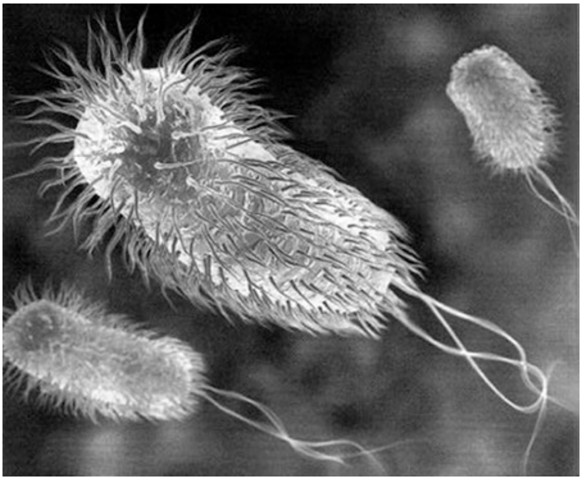

Figure 2.3. Escherichia coli Is the Most Well Known Bacteria. It Is Characterized by Rudimentary Chromosomes, Rapid Generation Time, and a Well-Defined Life Cycle. Like Other Bacteria, E. coli Is Able to Generate New Mutations When Challenged by Its Environment. (Source Unknown).

A myriad of bacteria, mollusks, corals, and other organisms contributed to vast limestone deposits and continue to do so today. With these and other processes, Earth's biosphere has transformed a once sterile planet, intermediate in character between Venus and Mars, into the living planet we now enjoy.

Bacteria have been detected or isolated from many hostile environments on Earth, including the dry, extremely cold surfaces and interstices of rocks in the dry valleys of the Antarctic, hot environments associated with submarine and terrestrial volcanoes and geothermal systems, and deep subsurface sediments and aquifers. Investigations in extreme terrestrial environments are in their infancy, and we still know little about either most of the organisms inhabiting these environments, also called extremophiles, or in many cases the geochemistry and geophysics of the environments themselves.

Nevertheless, in the last decade or so, a variety of novel organisms have been isolated. They include hyperthermophiles, which are capable of growing at 110°C, barophiles, capable of growing at the pressures found in the deepest ocean trenches, and anaerobes, which are capable of using iron, manganese, or even uranium as electron acceptors. Similarly, a variety of strategies have been identified by which microorganisms can survive environmental conditions that do not allow growth, including low temperature and low nutrient conditions (Table 2.1).

Table 2.1. Microorganisms with Particular Physiological and Nutritional Characteristics.

Physiological Characteristic	Description
Temperature	
• Psychrophile	• Optimal temperature for growth is 15°C or lower (range: 0–20°C)
• Psychrotroph	• Capable of growing at 5°C or below
• Mesophile	• Optimal temperature for growth is 37°C (range: 8–50°C)
• Thermophile	• Grows at 50°C or above
• Hyperthermophile	• Grows at 90°C or above (range: 80–113°C)
Oxygen	
• Aerobe	• Can tolerate 21%t oxygen present in an air atmosphere and has a strictly respiratory-type metabolism
• Anaerobe	• Grows in the absence of oxygen
• Facultative Anaerobe	• Can grow aerobically or anaerobically – characteristic of a large number of genera of bacteria including coliforms such as Escherichia coli
• Microaerophile	• Capable of oxygen-dependent growth but only at low levels
pH	
• Acidophile	• Grows at pH values less than 2
• Alkalophile	• Grows at pH values greater than 10
• Neutrophile	• Grows best at pH values near 7

(Continued)

Table 2.1. (Continued)

Physiological Characteristic	Description
Salinity	
• Halophile	• Requires salt for growth: classified as extreme (all are archaea) or moderate halophiles (15–20% NaCl)
Hydrostatic Pressure	
• Barophile (100 atm/ 1,000-m depth) (0.987 atm = 1 bar = 0.1 MPa)	• Obligate barophiles, no growth at 1 atm of pressure; barotolerant bacteria, growth at 1 atm but also at higher pressures. Deep-sea bacteria are called barophilic if they grow optimally under pressure and particularly if they grow optimally at or near their in-situ pressure
Nutrition	
• Autotroph	• Uses carbon dioxide as its sole source of carbon
• Heterotroph	• Unable to use carbon dioxide as its sole source of carbon and requires one or more organic compounds
• Chemoorganoheterotroph	• Derives energy from chemical compounds and uses organic compound
• Chemolithoautotroph	• Relies on chemical compounds for energy and uses inorganic compounds as a source of electrons
• Mixotroph	• Capable of growing both chemo-organo-hetero-trophically and chemolithoautotrophically; examples include sulfur-oxidizing bacteria
• Oligotroph	• Can develop on media containing minimal organic material (1–15 μg carbon/L)
• Copiotroph	• Requires nutrients at levels 100 times those of oligotrophs

An interesting, although alarming, discovery was made during the Apollo program. The *Apollo-12* Lunar Module landed on the Moon about 200 m away from an unmanned probe, *Surveyor-3*, which had landed there 2.5 years earlier. The astronauts of *Apollo-12* inspected the *Surveyor* spacecraft for damage and recovered an external camera for detailed analysis back on Earth. A specimen of bacteria (*Streptococcus mitis*) was found alive on the camera. Because of the precautions the astronauts had taken, it is almost certain that the germs were there before the probe was launched. This clearly demonstrates the threat of the contamination of other planets by an Earth's biotope.

These bacteria had survived for 31 months in the vacuum of the lunar atmosphere while exposed to considerable solar and cosmic radiation. They suffered huge monthly temperature swings and the complete lack of water, as if they had hibernated. In fact, freezing and drying, in the presence of the right protectants, are actually two ways normal bacteria can enter a state of suspended animation. And interestingly, if the right protectants are not supplied originally, the bacteria that die first supply them for the benefit of the surviving ones!

Likewise, spores of the Bacillus bacteria were found during the summer of 2000 in salt crystals buried 600 m below ground at a cavern in New Mexico. When they were extracted from the crystals in a laboratory and placed in a nutrient solution, the microorganisms revived and began to grow. These bacteria had survived in a state of suspended animation for 250 million years. Until now, the world's oldest living survivors were thought to be 25–40 million-year-old bacteria spores discovered in a bee preserved in amber. Traditionally, endospore and cyst development were considered the principal mechanisms for long-term survival by microorganisms, but it is now clear that many microorganisms have mechanisms for long-term survival that do not involve spore or cyst formation.

2.1.2. Life on Mars

Without exception, life in Earth's biosphere is carbon-based and is organized within a phase boundary or membrane that envelops reacting biomolecules. Every documented terrestrial cellular life form is a self-replicating entity that has genetic information in the form of nucleic acid polymers (DNA) coding for proteins. Biologically active systems require at a minimum liquid water, carbon, nitrogen, phosphate, sulfur, various metals, and a source of energy either in the form of solar radiation or from chemosynthetic processes.

The conditions that nurtured early self-replicating systems and their transition into microbial cells are speculative. In contrast, it is much easier to model the early stages of evolution. Origins-of-life experiments have outlined the synthesis of the basic building blocks of life, including amino acids, nucleotides, and simple polypeptides and polynucleotides. Yet creation of self-sustaining, self-replicating biological entities capable of evolution has not yet been achieved in the laboratory. Even if successful, this achievement would not necessarily mimic how life started on Earth or in other parts of the universe.

For life to originate, the presence of liquid water and a source of usable free energy are necessities. The synthesis and polymerization of basic organic building blocks of life on Earth eventually led to self-replicating nucleic acids coding for proteins, but the earliest replicating systems were not necessarily composed of amino acids and nucleotides. If extraterrestrial biological systems exist, their modes of information storage, retrieval, and processing and their enzymatic activity may not be identical to those of biological entities on Earth. Understanding this prebiotic evolution is one of the major goals of the astrobiology program, which is the study of biology of the early Earth and elsewhere in the universe.

In the search for extraterrestrial life, microbes are far more likely than multicellular organisms to retain viability on small Solar System bodies because they can adapt to a much wider range of environmental conditions. As mentioned already, single-cell organisms such as bacteria have infiltrated virtually every corner of Earth's biosphere and still constitute the bulk of Earth's biomass. They grow in temperate marine and terrestrial settings, within other microbial or multi-cellular organisms, in deep subsurface niches, and in extreme environments that would be lethal for other life forms. They often influence geochemical reactions within the biosphere and frequently play key roles in food chains and complex ecosystems.

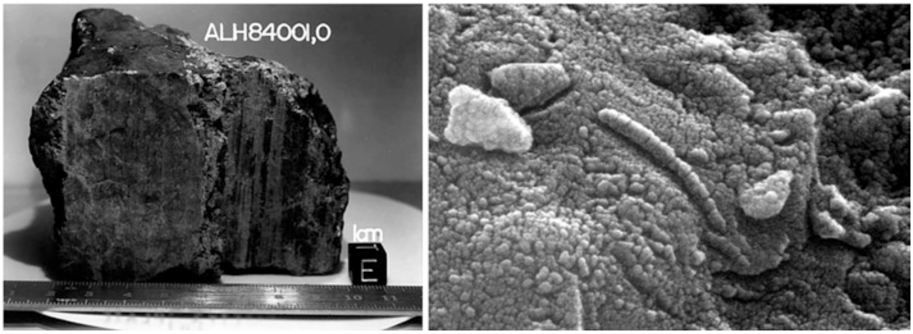

Figure 2.4. ***Left*: ALH84001 Is by Far the Oldest Martian Meteorite, with a Crystallization Age of 4.5 Billion Years. *Right*: The Small Amount of Carbonate in ALH84001 Is the Center of Attention Concerning the Possibility of Life on Mars.** (Credit NASA).

Figure 2.4 (left panel) shows a 4.5 billion-year-old rock that is a portion of a meteorite (ALH84001) that was dislodged from Mars and fell to Earth in Antarctica about 16 million years ago. It is believed to contain fossil evidence that primitive life may have existed on Mars more than 3.6 billion years ago. The small grains on the right panel in Figure 2.4 appear to have formed in fractures inside this rock in the presence of liquid water or other fluid. There is considerable debate about the origin of these carbonates. These grains are the sites of the three types of evidence that McKay and his colleagues [McKay et al., 1996] suggest represent fossil life on Mars.

2.2. Gravitational biology

Throughout its entire evolution, life on Earth has experienced only a 1-g environment. The influence of this omnipresent force is not well understood, except that there is clearly a biological response to gravity in the structure and functioning of living organisms. Gravitational biology aims to understand the molecular mechanisms whereby a cell detects gravity and converts this signal to a neuronal, ionic, hormonal, or functional response.

2.2.1. Questions

How are cells, as single unicellular organisms or as the basic units of multi-cellular organisms, sensitive to gravity (gravitropism)? How do plant cells detect the gravity vector and transform this force into hormonal and non-hormonal signals?

Changes in the physical environment surrounding cells, in vivo or in vitro, can lead indirectly to changes within the cell. Little is known about if or how individual cells sense mechanical signals, such as gravity, or how they transduce those signals into a biochemical response. A cellular mechano-sensing system might initiate changes in numerous signaling pathways. Spaceflight offers a unique opportunity for revealing the presence of such a system.

It is known that plants have gravity-sensing organs in their roots, which involve the sedimentation of particles, the so-called statoliths or amyloplasts. On Earth, in a root that is placed vertically, the statoliths are sedimented at the bottom end of the cell. When the root is placed horizontally for 3 h, the statoliths are then sedimented onto the lateral walls of the cell (Figure 2.5). Removal of the root abolishes the capacity to detect gravity (Figure 2.6).

Now, is it the movement of the statoliths through the cytoplasm, or the pressure they exert on other (lower) cellular components, that is involved in graviception? Unicellular organisms, like ciliates (paramecium) and flagellates (algae) have membrane ion channels that are activated by a mechanical load, like the weight of the cytoplasm [Häder et al., 2005]. In principle, any mass is subject to the force of gravity and consequently can be regarded as a gravity receptor, as indeed the statolith is. The body, or protoplasm, of all living cells is composed of a large variety of particles and aggregates of particles, suspended in a heterogeneous matrix. The normal force of gravity makes these particles tend to float or sink with respect to the other cell components, depending on their relative densities (Figure 2.7). The density of certain organelles can be significantly higher than one, which is the approximate density of cytoplasm. Consequently, at 1 g the organelles will apply a certain pressure on the filaments of the cytoskeleton. Such pressure disappears at 0 g with possible effects on the interactions between the players of the signal transduction chains that are embedded in the cytoskeleton.

Identification of direct gravitational effects at the cellular level is crucial. Direct effects are those caused by the interaction of the force of gravity with cellular

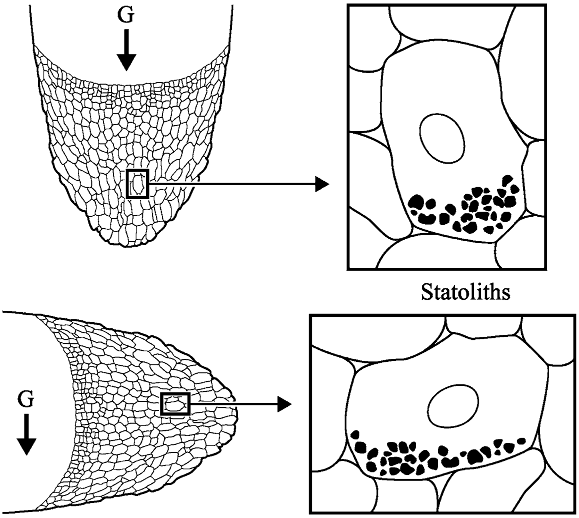

Figure 2.5. This Schematic of the Microscopic View of the Top of a Zea Maize Root Cap Shows the Statoliths (*Black Particles*) Sedimented at the Bottom of the Cells. The Statoliths Migrate onto the Lateral Walls of the Cells in the Direction of the Gravitational Force on Earth. (Adapted from Wilkins [1989]. Credit Philippe Tauzin).

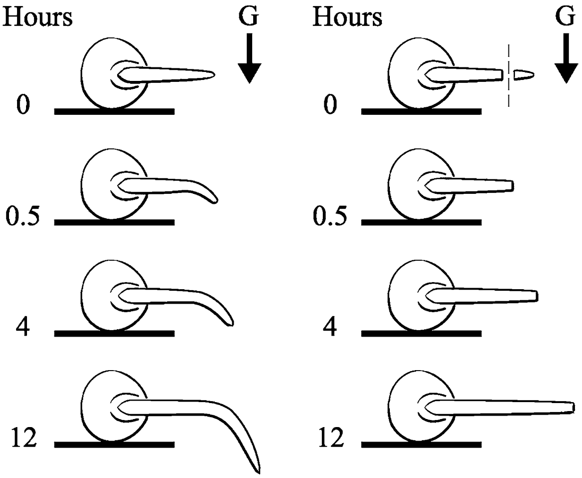

Figure 2.6. Time Sequence Showing the Gravitropic Response on Earth of the Seedling Root of Zea Maize Placed Horizontally at Time Zero (*Top*) and Photographed After 0.5, 4, and 12 h. After Removal of the Root Cap (*right*), the Seed Grows Straight for At Least 12 h. (Adapted from Wilkins [1989]. Credit Philippe Tauzin).

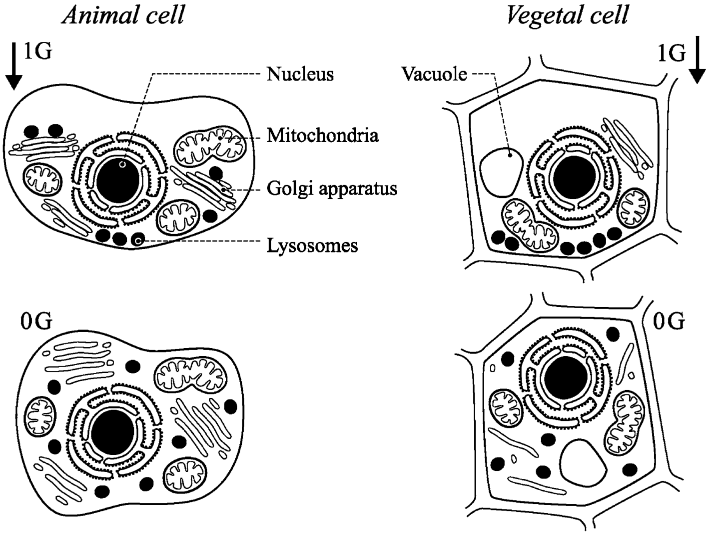

Figure 2.7. Decrease in Pressure and Loss of Sedimentation in Microgravity Compared to Normal Gravity. *Above* (1 g): in Both Animal and Plant Cells, the Denser Items have Sedimented to the Lower Part of the Cell. *Below* (0 g): The Cell Elements Are Almost Evenly Distributed in the Cell Volume. In Addition, the Physical Pressure and Strain on Structures Is Reduced. (Adapted from Cogoli et al. [1989]. Credit Philippe Tauzin).

structures and organelles or by its absence, respectively. Indirect effects are those caused by changes in the cell microenvironment under altered gravitational conditions. Indirect effects may be due to the absence of convection and sedimentation at 0 g that causes a change of the distribution of nutrients and of waste products around the cells [Cogoli, 2006].

In a world of molecules embedded in fluids and loaded with electrical charges dominated by viscosity and electrostatic forces, gravity is an extremely weak force. However, the impact of gravity may not be negligible in biological systems that are not static, but in a non-equilibrium status. In a biological process consisting of many subsequent steps, the principle of "small cause/large effect" applies, by which a small perturbation of one of the steps is sufficient to provoke dramatic changes downstream, as predicted by the bifurcation theory described Tabony et al. [2002].

All living systems react in one way or another to changes of the environmental parameters such as temperature, illumination, pressure, concentrations of nutrients, or activators/inhibitors. Gravity is a mechanical force. Change of the gravitational environment, i.e., changes of the forces acting on the cell, is a significant environmental change. It should therefore be no surprise that single cells also react and adapt to changes from 1 to 0 g conditions [Cogoli, 2006].

Important changes such as the loss of sedimentation, density-driven convection and hydrostatic pressure are occurring in a weightless cell culture. For a cell immersed in a fluid, as it is the case in a culture, this is a completely new situation. First, in 1 g, mammalian cells sediment within a few minutes to the bottom of the flask, where many of them may spread and adhere. In 0 g, instead, cells remain in suspension. Going from 1 to 0 g is a change from a two – to a three-dimensional environment and has a remarkable impact on cell interactions, cell movements, and, due to the lack of a substratum on which to spread and adhere, on cell shape.

Second, density-driven convection, which is due to changes in the concentration of nutrients and waste products in the medium, does not occur in microgravity, thus preventing mechanical diffusion. Thermodynamic diffusion is not affected, however.

Third, a new convection, predicted at the beginning of the twentieth century by Marangoni and not detectable at 1 g, becomes relevant in micro-gravity. The lack of buoyancy prevents gas bubbles, like the CO_2 bubbles developed by the metabolism of cells, to rise to the surface of a culture, thus favoring the formation of larger bubbles in the middle of the liquid phase rather than a separation of the liquid and gas phases.

The physiology of the cell may also be influenced by gravity. While passive transport of small molecules through the lipid bilayer is governed by diffusion (a gravity-independent process), active transport of ions and charged molecules, in which protein channels and transient membrane invaginations are involved, may be influenced by gravity. The balanced exchange of ions and molecules through cell membranes might be sensitive to gravity. The same may hold for membrane turnover, a basic process in cell life, and for intercellular diffusion of substances of varying molecular weight.

Gravity may also play a role in intercellular transport processes. In fact exothermic metabolic processes generate continuously warmer micro-regions that are less dense than the neighborhood. Thus, thermal convections are produced by gravity with consequent ultra-structural rearrangements. Such convections are obviously absent in microgravity.

Also, the energy turnover in the cells can be influenced by gravity. Gravity causes an uneven distribution of the organelles that gives rise to a torque capable to modify the shape and the structure of the cell. Energy is required to maintain its shape against gravity. In microgravity, such energy may be saved for other processes, such as proliferation or biosynthesis.

Finally, free-swimming cells consume energy to swim against gravity to avoid sedimentation. Such energy is not required at 0 g.

To investigate these phenomena, research programs in the biological sciences and biotechnology have focused on three primary areas of interest: (a) separation physics aimed at providing improved resolution and sensitivity in preparative and bioanalytical techniques; (b) cell biology, cell function, and cell-cell interactions; and (c) physical chemistry of biological macromolecules and their interactions, including studies of protein crystal growth directed at supporting crystallographic structure determinations.

In the field of biotechnology, for example, the absence of convection and sedimentation can help the separation and isolation of biological specimens. The increase in surface tension will improve transport processes, and consequently secretion and growth. The objective is to cultivate proteins (hormones, enzymes, antibodies) and cells that secrete a medically valuable substance. The purified product would be returned to Earth for medical use, product characterization, or improvement of ground-based separation techniques. However, this process is now challenged by ground-based computer graphics models, and by genetic-engineering techniques, like the cloning process, that are much less expensive than experiments in space.

2.2.2. Results of space experiments

When gravity is altered, biological changes are observed even when cells are isolated from the whole organism and grown in culture (*in vitro*). Physical scientists predicted this would not occur because gravity is an extremely weak force compared with the other fundamental physical forces acting on or within cells. However, spaceflight results suggest that microgravity may alter the characteristics of cultured cells. Most cells flown in space have either been suspended in an aqueous medium or attached to an extra-cellular matrix bathed by an aqueous medium.

2.2.2.1. Suspended cultures

Many space missions have flown bacteria in experimental cultures. The first cultures of *Escherichia coli* flew on board the U.S. *Biosatellite-2* in 1967. Mattoni et al. [1971] reported that after a 45-h orbital flight, the flight populations grew significantly faster than the ground controls. Another bacteria, Bacillus subtilis, was found to exhibit an increased duration of exponential growth, and an approximate doubling of final cell population density compared to ground controls [Klaus et al., 1997] (Figure 2.8).

Planel et al. [1994, 2004] discovered an increased resistance of E. coli and Staphylococcus aureus to antibiotics when cultured in several experiments in space. The effect was attributed to an increase of the thickness of the cell membrane, observed in electron micrographs, with consequent decrease in the membrane permeability. These results suggest that humans are at greater risk in space, given that there may be larger populations of bacteria in a confined environment, which are, moreover, less sensitive to antibiotics.

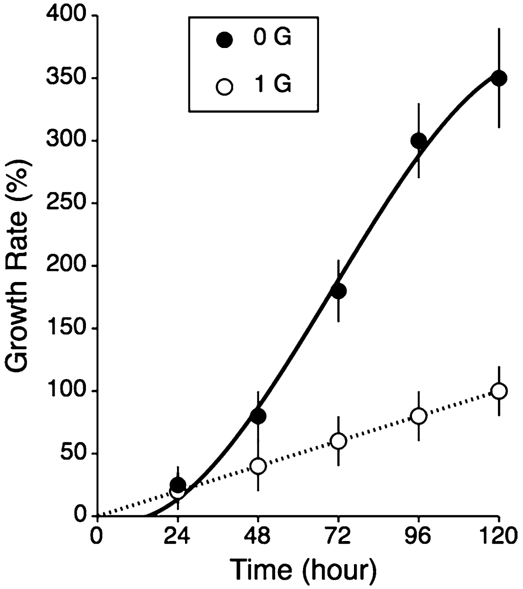

Figure 2.8. Diagram Showing the Increase in Growth Rate of Bacteria (*Bacillus subtilis*) Cultured Aboard Skylab (0 g) by Comparison with the Same Bacteria Grown in Ambient Conditions as Skylab, But on Earth (1 g).

These effects may simply reflect the fact that when challenged with a new environment, the first response of bacteria is to increase growth rate until new mutations appear that are better adapted. However, these differences may also be related to the lack of convective fluid mixing and lack of sedimentation, both processes that require gravity. We already mentioned that the major effect of reduced gravity environments is a reduction in gravitational body forces, thus decreasing buoyancy-driven flows, rates of sedimentation, and hydrostatic pressure. Under such conditions, other gravity-dependent forces, such as surface tension, assume greater importance. These alterations in fluid dynamics in a reduced gravity environment have significant implications. For example, in cell culture experiments, the diffusion of nutrients, oxygen, growth factors, and other regulatory molecules to the plasma membrane, as well as the diffusion of waste products and CO_2 away from the cell, will be reduced in the near absence of convection unless countered by stirring or a forced flow of the medium.

It is thought that, in reduced gravity, the more uniform distribution of suspended cells may initially increase nutrient availability compared to the sedimenting cells at 1 g that concentrate on the container bottom away from available nutrients remaining in solution. This phenomenon would increase growth rate. However, if waste products build up around cells in the absence of gravity, then after some time they could potentially form a pseudo-membrane that decreases the availability of nutrients or directly inhibits cell metabolism. It is suggested that inhibitory levels of metabolic byproducts, such as acetate, may be formed when glucose is in excess within the medium. Therefore, although perhaps somewhat counter-intuitive, a reduction in glucose availability actually may be beneficial to cell growth. Also, local toxic byproducts could become concentrated on the bottom of the 1-g container with cells in increased proximity to each other. Such a process could limit cell growth. Thus, changes in bacteria and possibly other cells during spaceflight may be related to alterations in the microenvironment surrounding non-motile cells, e.g., the equilibrium of extra-cellular mass-transfer processes governing nutrient uptake and waste removal. Such changes appear to be typical *indirect* effects of gravity caused by changes of the microenvironment of the cells.

The current view is that a “cumulative” response resulting from reduced gravity may be responsible for the observed effects at the level of the single cell. Earlier predictions suggesting that no effect of spaceflight should be expected were more focused on the physical inability of gravity to elicit an immediate or “direct” response from organisms of such small mass. Rather than a “direct” response, reduced gravity is suspected to initiate a cascade of events: the altered physical force leads to an altered chemical environment, which in turn gives rise to an altered physiological response [Klaus, 1998].

Saccharomyces cerevisiae, the yeast used to bake bread and cakes, is a highly appreciated organism in the study of several aspects of eukaryotic cell, like signal transduction, genetic expression, and adaptation to environmental stress. It has the great advantage of being resistant to rough environmental conditions like freezing or lack of nutrients. It also has biological properties and behavior analogous to those of mammalian cells that are, by contrast, much more sensitive to the environment and therefore much more difficult to keep alive in space experiments. The analogy with mammalian cells permits the investigation of crucial biological processes, including cancer in yeast cells. In addition, yeast is widely used in biotechnological processes, in particular in genetic engineering. Therefore, it is not surprising that yeast cells have been extensively chosen for experiments in space.

With the increasing interest in bioprocessing in space the requirement for sophisticated cell culture and tissue engineering facilities, also known as bioreactors, to be installed in space laboratories was obvious. Space bioreactors were first developed using yeast cells that are easy to cultivate and to preserve instead of delicate and sensitive mammalian cells. Now that the instrumentation has proven adequate, the experimentation with mammalian cells and tissue can begin.

2.2.2.2. Attached cells

Early results with cultured cells from muscles or bones suggest that spaceflight induces a wide variety of responses. For example, delayed differentiation and changes in the cytoskeleton, nuclear morphology, and gene expression have been reported for bone cells [Hughes-Fulford and Lewis, 1996]. Muscle fibers cultured in space were 10–20% thinner (i.e., atrophied) compared with ground controls due to a decrease in protein synthesis rather than an increase in protein degradation [Vandenburgh et al., 1999]. Interestingly, the atrophy of isolated muscle fibers in culture was very similar to the amount of muscle atrophy reported in flight animals (see Chapter 5, Section 5.3). These data from bone and muscle cells suggest that spaceflight affects adherent cells and tissues even when isolated from systemic factors. The same results were obtained during ground-based studies using clinostats (Figure 2.9).

Figure 2.9. The Clinostat Is a Simple Device that Places a Plant, a Small Organism, or Cell Growing in Culture on a Rotating Platform. The Rotation Causes the Biosystem Under Test to be Subjected to the Gravity Vector from All Directions. From the System's Point of View, the Rotation Cancels the Gravity Vector by Continuous Averaging, thus Approximating the Highly Reduced Vector Found in the Actual Space Environment. (Credit CNES).

Changes in the physical environment surrounding cells, *in vivo* or *in vitro*, can lead indirectly to changes within the cell. Cellular structures that might oppose mechanical loading are only beginning to be defined. Exciting research on the interaction of the cell cytoskeleton with membrane components and the extra-cellular matrix is shedding light on possible "force sensors" at the cellular level that might be essential for the differentiation process [Wayne et al., 1992]. Ingber [1998, 1999] has applied the concept of "tensional integrity", which is a tension-dependent form of cellular archi-tecture that organizes the cytoskeleton and stabilizes cellular form, to cells. This architecture may be the cellular system that initiates a response to mechanical loading as a result of stress-dependent changes in structure that alter the mechanical load on extra-cellular matrix, cell shape, organization of cytoskeleton, or internal prestress between cell and tissue matrices.

The consensus of physical chemists prior to this decade was that forces exerted between molecules within a cell were far greater than gravitational forces. Thus, they concluded that gravity should not be perceived at the cellular level [Brown, 1991]. However, at that time very little was known about how cells interacted with components of the extra-cellular environment. These interactions might function to either suppress or amplify signals generated by gravitational loading. Defining the cellular connections that might sense and transduce mechanical signals into a biochemical response may also shed light on the events initiating cell maturation. As a cell matures, it stops dividing and begins to express characteristics of a mature cell type. However, if a cell does not mature, it will continue to divide. This is the definition of a cancer cell.

The maturation process may be triggered by multiple factors, including loads placed on the extra-cellular matrix during different phases of development.

In summary, flight experiments suggest that gravity, quite likely, is perceived by cells through physical changes both in the aqueous medium surrounding cells in culture and in cellular structures that oppose or sense mechanical loads. Exactly how the gravity signal is then transduced to cellular functions is yet to be determined. The answer to this question is not only relevant to understanding the fundamental processes in normal cell physiology, but also in the patho-physiology of certain diseases, such as age-related bone loss, cancer, or immune disorders [Bouillon et al., 2001].

2.2.2.3. Threshold for gravity perception

The changes in the swimming behavior of ciliates and flagellates, which presumably compensate part of the changes in the cell physical properties in 0 g (e.g., sedimentation, thermal convection) can be measured for calculation of the sensitivity to gravity perception [Machemer et al., 1991]. In 1992, a sophisticated slow rotating centrifuge microscope, called NIZEMI (for *Niedergeschwindigkeit Zentrifuge Mikroskop*) developed by the German Space Agency, measured the minimal in-flight acceleration that was able to induce a graviceptive response in microorganisms. The following acceleration threshold were obtained: Paramecium, 0.35 g; Euglena, 0.16 and 0.12 g; and Loxodes, less than 0.15 g. Interestingly, the results were similar when the cells were subjected either to increasing or decreasing accelerations, and the effect was independent of the previous exposure to microgravity up to 12 days, although the cells underwent several division cycles.

Because the organelles used for gravity-sensing mechanisms in these organisms show some analogy to the statoliths in plants and the otoliths in humans and other vertebrates, the results of these studies on threshold for gravity perception are of fundamental importance for determining the optimal level of artificial gravity for long-duration human missions.

2.2.2.4. Human blood cells

Although the reports to date are conflicting, some indicate that a microgravity environment may compromise the immune system function. These investigations are carried out on cultures of lymphocytes prepared on the ground and tested in space, and with whole-blood samples taken from the crew and tested in-flight, respectively (Figure 2.10). Cogoli et al. [1980] reported that cultures of human lymphocytes subjected to microgravity responded to concanavalin A, a lymphocyte stimulating agent, 90% less than ground-based controls. This is a standard test used to evaluate the competence of peripheral blood lymphocytes to multiply when stimulated with this agent. Studies on the astronauts of the first four space shuttle flights revealed that the lymphocyte responses to photohemagglutinin, another lymphocyte stimulating agent, were reduced from 18% to 61% of normal following spaceflight. It has been suggested that the above changes were due to stress-related effects, but this should be studied further.

These studies are important because, as was discussed earlier, the concentrations of microorganisms in space vehicles may be significantly higher than normal. The conditions associated with space travel, space stations, and planetary colonies raise

Figure 2.10. A Crewmember Insert Blood Test Samples in a Refrigerated Centrifuge in the Columbus Laboratory of the International Space Station. (Credit NASA).

many new and important problems concerned with host-parasite interactions involving humans and animals. Rotation of crewmembers on the ISS will introduce different strains of fungi, bacteria, and viruses that could contribute to the emergence of "new" strains of opportunistic pathogens through mutation and genetic exchange.

Clearly, spaceflight is associated with a significant increase in the number of circulating white blood cells, including neutrophiles, monocytes, T-helper cells, and B cells. In contrast, the number of natural killer cells is decreased. Plasma norepinephrine levels are increased at landing and are significantly correlated with the number of white blood cells [Mills et al., 2001]. These data suggest that the stress of spaceflight and landing may lead to a sympathetic nervous system-mediated redistribution of circulating leukocytes, an effect potentially attenuated after longer missions. Whether hematopoesis, or the maturation of lymphocytes, is compromised is yet to be established. The multiple stresses of spaceflight may also lead to hormonal imbalances, and corticosteroid release may lead to immuno-suppression. Oogenesis and spermatogenesis, i.e., the formation of female and male sexual gametes, may also be compromised. In any case, additional research is required to confirm or reject the presence of these problems.

On the other hand, there is a significant reduction in the percent of whole blood that is comprised of red blood cells (hematocrit) in some astronauts. The hematocrit is a compound measure of red blood cells number and size. This reduction in the number of red blood cells in astronauts is often referred as the space anemia. This reduction may be due to several factors. While in space, the overabundance of fluids in the upper part of the body causes the kidneys to remove this excess fluid, part of which is plasma (see Chapter 4, Section 4.3.2). This reduction in plasma volume causes an over-abundance of oxygen-carrying capability, which, in turn, would reduce the production of erythropoietin and consequently decrease red blood cell production.

This process would be favored by the fact that muscles lose mass and thus require less oxygen. However, it is also possible that the over-abundance of oxygen-carrying capacity in the blood is responsible for an increase in the destruction rate of red blood cells. Finally, as we will see in Chapter 5, as astronauts lose calcium in their bones, the structure and function of the bone and its marrow may change and may result in a decrease in red blood cell production.

2.2.3. Bioprocessing in space

Research in biotechnology relies on the manipulation of cells of living organisms. The purpose of these manipulations is to produce useful molecules, natural or artificial, in useful quantities, to develop new organisms or new biological molecules for specific uses, or to improve yields of plant and animal products through genetic alteration. Recombinant techniques, for example, make it possible to produce natural or artificially mutated versions of proteins exhibiting a wide range of activities and uses, scientific and medical, in large quantities. The techniques essential to these manipulations are applied in aqueous environments and are subject to fluid dynamics and transport processes.

Gravity affects biological systems through its influence on the transfer of mass and heat, particularly in the area of fluid dynamics and transport, as well as its impact on cell structure and function (Figure 2.11). Consequently, microgravity may lead to new knowledge about biological systems, to improvements in current experimental techniques, and to the development of new experimental approaches. Examples include fermentation processes, compartmental targeting of expressed products within the cell, and the ultimate purity, structural integrity, and activity of a protein product.

Particle sedimentation under the influence of gravity, for example, can interfere with aggregation processes such as those mediating cell-cell interactions, cell fusion, cell agglutination, and cellular interactions with substrates.

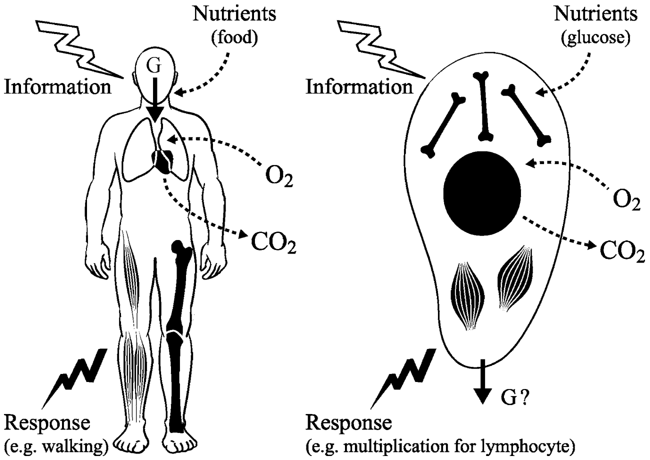

Figure 2.11. Schematic Comparison Between Body (*Left*) and Cell (*Right*) Functions, Showing that Biological Processes That Occur at Cellular Level Are Similar to Those at Organism Level. (Credit Philippe Tauzin).

A detailed knowledge of the three-dimensional architectures of biological macromolecules is required for a full understanding of their functions, and of the chemical and physical effects that they manage to achieve these functions. To be able to synthesize new proteins, whether for medical uses or as complex biomaterials, it is necessary to be able to relate molecular structure and function. Protein crystallography, currently the principal method for determining the structure of complex biological molecules, requires relatively large, well-ordered single crystals of useful morphology. Crystals with these qualities may be difficult to produce for a variety of reasons, some of which may be influenced by gravity, through density-driven convection and sedimentation. Protein crystal growth experiments conducted on board the space shuttle (Figure 2.12) have provided persuasive evidence that improvements can, in fact, be realized for a variety of protein samples.

There are two types of biological materials for which commercial bioprocessing in space could offer advantages over production on Earth: proteins and cells. The proteins include hormones, enzymes, antibodies and vaccines. The cells with medical prospects are: (a) those that when cultivated, secrete a medically-valuable substance that can be isolated either in space or on Earth; (b) those that can be implanted in man for therapeutic purposes; and (c) those that, through cell fusion, can yield antibody-producing hybrid cells [Bonting et al., 1989].

How does space bioprocessing work? The raw material, whether a protein mixture or a mixture of living cells, is brought into space and separated in microgravity; the purified product is then returned to Earth for medical use, product characterization, or improvement of a ground-based processing technique. Table 2.2 lists some of the medical products that could be obtained through bioprocessing in space.

However, the continuous production of such biological materials on a commercial scale in space proved not compatible with the cost for access to space, and space

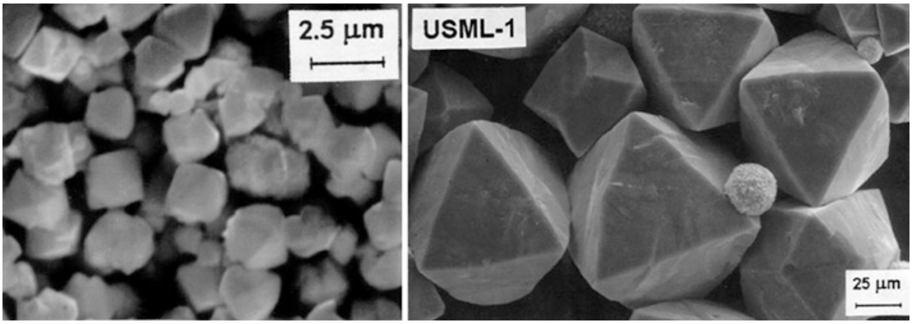

Figure 2.12. Zeolites Have a Rigid Crystalline Structure with a Network of Interconnected Tunnels and Cages, Similar to a Honeycomb. Zeolites Have the Ability to Absorb Liquids and Gases Such as Petroleum or Hydrogen, Making Them the Backbone of the Chemical Processes Industry. Industry Wants to Improve Zeolite Crystals so that More Gasoline can be Produced from a Barrel of Oil. The Zeolite Crystals Grown on the Ground (*Left*) Are Smaller Than Those Grown in Space (*Right*). The Zeolite Crystal Growth Furnace Unit Aboard the ISS Allows to Grow Zeolite Crystals and Zeo-Type Materials in Space. (Credit NASA).

Table 2.2. Some Candidate Biological Materials for Space Processing and their Medical Prospects [Bonting et al., 1989].

Materials	Condition
• Alpha-1-antitrypsin	• Emphysema
• Antihemophilic Factor	• Hemophilia
• Beta cells Pancreas	• Diabetes
• Epidermal Growth Factor	• Burns
• Erythropoietin	• Anemia
• Granulocyte Stimulating Factor	• Wound Healing
• Growth Hormone	• Growth Problems
• Immunoglobulins	• Immune Deficiency
• Interferon	• Viral Infections
• Transfer Factor	• Multiple Sclerosis
• Urokinase	• Thrombosis

bioprocessing remains marginal today. Furthermore, ground-based genetic engineering in mammalian or human embryo cells is now a very strong alternative to space bioprocessing, together with purification methods such as affinity or immuno-affinity chromatography and high-pressure liquid chromatography. Also, alternatives to X-ray crystallography are emerging, using physical and mathematical models and computer graphics, that are equally useful in determining the three-dimensional structure of proteins.

2.3. Development biology

The major goal for developmental biology is to determine whether any organism can develop from fertilization through the formation of viable gametes (reproductive cells) in the next generation, i.e., from egg to egg, in the microgravity and radiation environment of space. In the event that normal development does not occur, the priority is to determine which period of development is most sensitive to microgravity.

2.3.1. Questions

Can higher plants and animals be propagated through several generations in the space environment? Although many embryos orient their cleavage planes relative to the gravity vector, we do not understand whether gravity, per se, is essential to gametogenesis, fertilization, implantation in animals, organogenesis, or development of normal sensory-motor responses. Given the effects of microgravity exposure on bone, muscle, and vestibular function, there is some doubt whether vertebrates can develop normally in space.

The amphibian has been used as a model for many experiments on embryonic development in space [Souza et al., 1995]. In Xenopus laevis, the South African three-clawed frog, for example, the unfertilized egg has a polarized structure because of an unequal distribution of the yolk: the animal pole is poor in yolk, whereas the vegetative pole contains large quantities. Before fertilization, the egg, surrounded by a layer of jelly, is oriented randomly. After fertilization, the whole egg detaches itself from this layer and rotates, so that the heavier vegetative pole moves downwards, in the direction of gravity. Very roughly, the animal pole corresponds to the head, and the vegetal pole corresponds to the dorsal side (Figure 2.13). An hour or so after fertilization, a second rotation occurs: the cortex rotates by 30 relative to the cytoplasm. This rotation establishes the dorso-anterior axis of the animal. The egg then begins to divide and form the embryo that, after an appropriate time, emerges from the jelly-like egg as a tadpole.

The cortex rotation depends on a transient array of parallel microtubules at the vegetal cortex. A kinesin-like protein is associated with the microtubules and is thought to move the cortex along the microtubules, anchored in the cytoplasm [Elinson et al., 1990]. The cortex rotation can be influenced by gravity in several ways. First, extremes of gravity, caused by centrifugation, can overcome the microtubule mechanism and produce a dorso-anterior axis on the centripetal side [Black and Gerhart, 1985]. Second, gravity alone can produce a dorso-anterior axis in the absence of the microtubule mechanism [Scharf and Gerhart, 1980]. Third, gravity alone can orient the microtubules prior to their formation, thereby directing where the dorso-anterior axis will form [Zisckind and Elinson, 1990]. Gravity in these cases acts by moving the heavy yolk-rich cytoplasm downward, producing a cytoplasmic rearrangement.

These gravity effects have led to repeated attempts to place frog eggs in space in order to see how they develop in microgravity. In the most successful of such experiments, there was little or no perturbation of the dorso-anterior axis [Souza et al., 1995]. A normal head formed, indicating that some form of cytoplasmic rearrangement had occurred. This arrangement was likely due to the functioning of the parallel

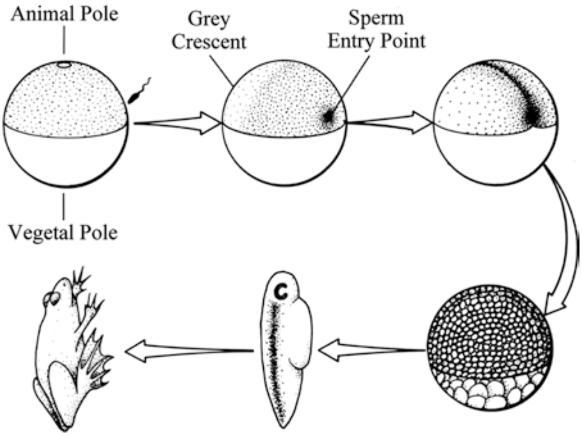

Figure 2.13. The Fertilized Egg of a Common Amphibian Is Shown as It Develops from Single Cell to Larva and Adult. Cell Constituents of the Egg Are Segregated by Density – the Dark, Less Dense Material Rises to the Upper Half of the Sphere, While the Denser Light-Colored Material Settles to the Bottom. Continued Development of the Embryo Follows This Orientation. (Credit NASA).

microtubule mechanism. One possibility is that gravity-induced rearrangement is an evolutionarily primitive mechanism, which substitutes for the microtubule mechanism. If there were any frogs lacking the microtubule mechanism, their eggs would be interesting objects to put in space: the hypothesis is that the dorso-anterior axis would be altered in the resulting space tadpoles.

Developmental biology also includes all aspects of the life span of an organism, from fertilization through aging. Topics of research include gamete production, fertilization, embryogenesis, implantation (in mammals), the formation of organs (organogenesis), and postnatal development (changes after birth). The role of gravity in these processes is entirely unknown. For example, we don't know if cell division (mitosis) and the orientation of bilateral symmetry are influenced by gravity.

It is known that at some point after fertilization, different in diverse organisms, cells become committed to developing along a certain pathway. This restriction in fate is called determination. During early cell divisions in most animal embryos, there are gradual restrictions in developmental potentiality. This is not the case in plants. Sooner or later in all animals the cells in the embryo can usually give rise only to a certain tissue or organ. They have lost their plural potentialities. This second process of development is differentiation, a term that designates the processes whereby the differences that were "determined" become manifest. The mechanisms by which the determination and differentiation occur at the right time to produce the normal organisms is called the formation of pattern, i.e., not only do they realize their fates, but they do so in the correct place at the correct time.

The formation of the various tissues and organs, or organogenesis, not only spans several developmental stages, but also continues after birth or hatching and into the natal period. For each organ system, there appears to be a *critical period* during which development can be disrupted by relatively small environmental stresses. The systems affected by weightlessness in the adult, e.g., vestibular apparatus, bone metabolism, and the formation of blood cells, might suffer more severe and more permanent effects if the gravity stimulus were withdrawn during the appropriate stage of organogenesis. This would be similar to the results of the experiments indicating that the receptors of the visual system, their neural connections, and the visual cortex develop abnormally in animals raised in complete darkness [Imbert, 1979].

Further, the transition from the neonatal period to adulthood is marked by fundamental developmental events, such as cell specialization, cell-cell interactions, the development and integration of many physiological and biochemical functions, and growth (Figure 2.14). For example, radical changes in the structure and connections of neurons occur during the development of the nervous system. From tissue layers found in embryonic animals, cells increase in number and eventually differentiate and migrate to their appropriate function and position in the developing nervous system. In all, up to 75% of neurons are lost by the process of *apoptosis*, or programmed cell death during development. Those that remain must form synapses with communicating neurons. Because these processes are regulated by both chemical and mechanical factors, gravity may play a crucial role as a stimulus for proper development.

Regenerative processes are also fundamental developmental responses to postnatal tissue loss and injury. In many situations, these processes are simply responses to changes in the environment to which the individual is exposed. Understanding the

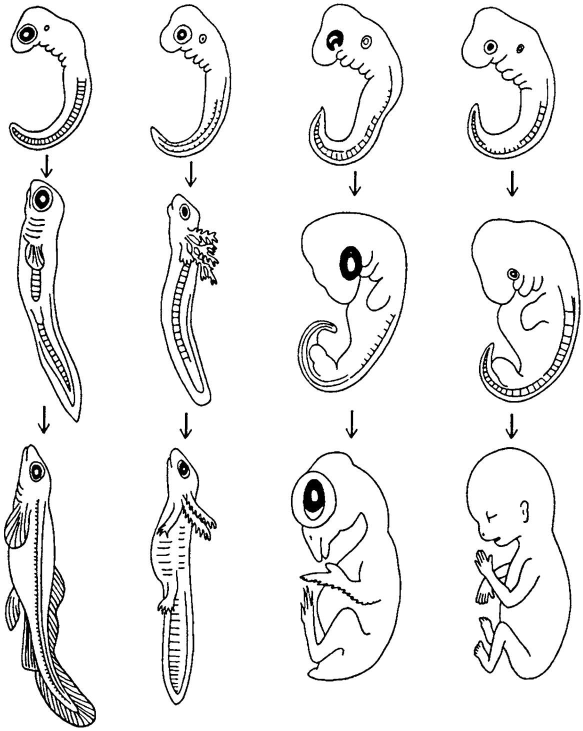

Figure 2.14. Comparison Between the Embryonic Development of Fish, Salamander, Chick, and Human (from *Left to Right*, Respectively). The Early Stages (Drawn to Scale) Are Closely Similar Among Species. The Later Stages (Not Drawn to Scale) Are More Divergent. (Source Unknown).

role of gravity not only in ontogeny, the development of the individual, but also in phylogeny, which is the evolution of species, justifies the studies on various species in space for successive generations over long periods of time. By acting on this external factor, would it then be possible to modify the blueprints contained in the genome and change some characters of the species? In other words, would we all become boneless, jellyfish-like organisms, after many generations in space?

2.3.2. Results of space experiments

Diverse organisms have been subjected to microgravity for varying periods of time. The results of these studies have been inconsistent. Both normal and abnormal developments have been observed, depending on the organism and the stage of development at which the material was subjected to microgravity. Moreover, in the study of embryonic material in particular, most experiments have by necessity been performed with eggs that were fertilized on the ground, well before orbital flight, so that the critical g-sensitive time period immediately after fertilization was spent at 1 g. Also, in many experiments, the other environmental factors, such as launch and re-entry forces, atmosphere, and radiation level, were not adequately controlled.

2.3.2.1. Invertebrates

Because aquatic species normally live in a neutrally buoyant environment, they should be less susceptible to microgravity than terrestrial species. However, it has been shown that the formation of skeletal hard parts (shells, spicules) that involve calcium carbonate is altered during development in microgravity. By studying the sea scallop calcification process, for example, scientists hope to learn more of the mechanics behind bone density loss in humans during long-duration spaceflight (see Chapter 5, Section 5.5.2), a problem closely related to osteoporosis here on Earth.

Sea urchins are a long-standing, widely used model for studying the biology of fertilization. Common genetic origins, or homologies, between the sea urchin system and mammalian systems make the sea urchin a good model for obtaining basic information that can point to important questions to be addressed by studying mammalian systems. Sea urchin sperm also provides the added benefit of survivability; these animals are able to tolerate delays that sometimes occur with flight research. A series of experiments carried out in space using the ESA BioRack facility indicated that microgravity caused an increase in sperm motility. However it has not been demonstrated if this increase in motility allows the sperm to get to the eggs more quickly and fertilize better [Tash et al., 2001].

Jellyfish serve as excellent subjects for research on gravity-sensing mechanisms because their specialized gravity-sensing organs have been well characterized by biologists. Jellyfish *Ephyrae* that developed in microgravity had significantly more abnormal arm numbers as compared with 1-g flight (centrifuged) and ground controls. As compared to controls, *Ephyrae* that developed in space showed abnormalities in swimming behavior when tested postflight. However, the mean numbers of statoliths and pulses per minute as determined postflight did not differ significantly from controls. *Ephyrae* that were flown after developing on Earth tended to show changes in their gravity-sensing organs too. Studies on gravity threshold conducted in the onboard centrifuge revealed that more than 50% of the animals convert to Earth-like swimming behavior upon exposure to 0.3 g. The swimming behavior of both *Ephyrae* hatched on Earth and in microgravity showed that they had difficulty orienting themselves in space [Souza et al., 2000].

Experiments on the fruit fly *Drosophila melanogaster* during a 4-day *Vostok* mission revealed that mating is possible without gravity, and that developmental processes and morphogenesis were normal in microgravity. Nematodes *Caenorhabditis elegans* successfully reproduced twice in space and generated thousands of offspring [Nelson et al., 1995]. However, the mating activity of males of the parasitic wasp *Habrobracon* was severely disrupted, and the capability for their eggs to hatch in orbit was decreased. Studies on gypsy moth have been performed to study the effect of microgravity on the diapause cycle. Diapause is the dormant period in an insect life cycle when it is undergoing development into its next phase. Results show that microgravity shortens the diapause cycle of gypsy moths and leads to the emergence of larvae that are sterile. The capability to produce sterile larvae may lead to the development of a natural form of pest control.

According to the laws of aerodynamics, insects cannot produce enough lift pressure to fly. The mechanism whereby they achieve flight must involve unsteady flows interacting with the dynamically changing wing surfaces. Interestingly, experiments carried out on insects in space have shown that larvae of fruit fly that developed in space did not learn to fly and preferred to float without beating their wings. Wing abnormalities and mutations have also been reported in floor beetle when examined after spaceflight. Similarly, honeybees were unable to fly normally and tumbled in weightlessness with no wing beat.

Perhaps the most famous space experiment using invertebrates is the one carried out on *Skylab* in 1973 to ascertain whether two common cross spiders (*Arachnous diadematus*) spin webs differently in microgravity. Because the spider senses its own weight when constructing the web to determine the required amount of silk to make the web, it was thought that gravity played an important role in the construction of the web. Studies were carried out in space during *Skylab*, Spacelab, and ISS missions. Results showed that during their first attempt in space, the webs were different from ground controls, but later the webs were nearly identical [Summerlin, 1977]. However, although the spiders did not spin their web patterns differently (Figure 2.15), it seems that the threads themselves were different.

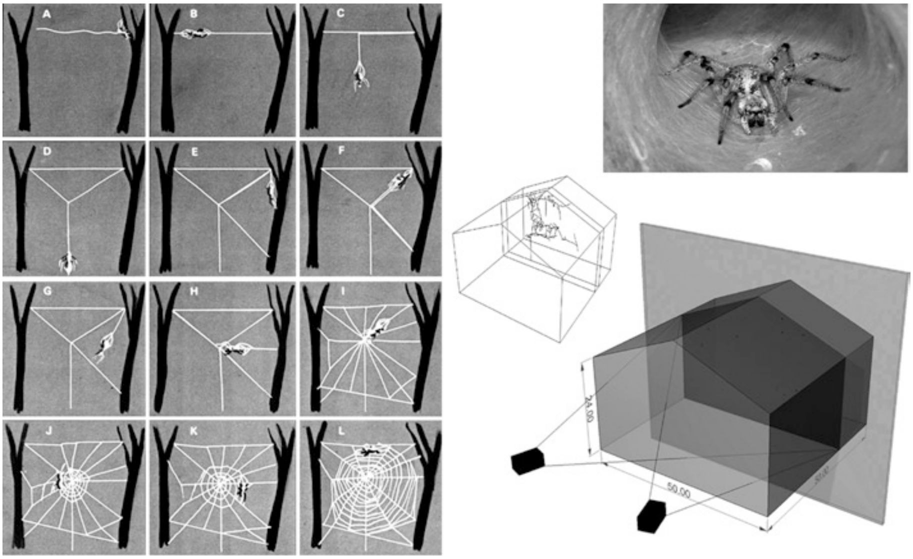

Figure 2.15. ***Left*: The Common Spider Produces a Web of Nearly Concentric Circles Each Day at Approximately the Same Time. The Web Is Constructed in a Very Orderly Fashion, Starting with a Bridge and Frame (a–d), and Axial Threads (e–i). Spiral Emanating from the Hub Is Constructed Next (j–l) [Summerlin, 1977]. *Right*: We Proposed an ISS Experiment Using Agelena Labyrinthica, Which Produces a Sheet Web with a Three-Dimensional Funnel Shaped Retreat Spun Above It. Each Segment of the Spider Housing Will be Illuminated by a Sheet Laser and Recorded by Dual Cameras for Three-Dimensional Analysis. The Spider Housing Will be Mounted on Rails and Will Automatically Move Toward the Cameras After Each Picture Is Taken.**

The spiders used in these previous space studies were orb-weavers, whose webs were mostly two-dimensional, i.e., the upper and the lower part in orb-webs differ only in shape and not in fundamental structure, as it is the case in three-dimensional webs. We have proposed an ISS experiment in which spiders that build three-dimensional web structures would be flown. Based on recent discoveries that perception of depth and height is altered in microgravity and that there is an alteration in the mental representation of physical space when the gravitational reference is removed [Clément and Reschke, 2008] we hypothesize that the spiders will behave like astronauts during exposure to microgravity. Consequently, the shape and the speed for building three-dimensional webs should be affected during early exposure to microgravity. But after longer exposure the animals should use other strategies to build the same three-dimensional webs as they do on Earth. In fact, it is even possible that the webs built in space after complete adaptation would be the most perfect of three-dimensional structures. A detailed analysis of the strategies used by the spiders to build these perfect webs and their final design will be extremely useful for arachnologists, architects, artists, and engineers.

There is a strong interest on the part of industry in advanced composite materials. Spider silk is an ultra-lightweight fiber that combines enormous tensile strength with elasticity. Each fiber can stretch 40% of its length and absorb a hundred times as much energy as steel without breaking. Spiders have specialized rear legs, which are capable of applying the sticky silk without adhering to it. Engineers would like to develop systems that mimic the action of these legs, which are known in engineering as an “end-effector”.

An experiment is also planned to use scorpions onboard the ISS. It is known that the circadian patterns in animals and humans are also influenced by activities such as food intake and locomotion. The exposure of scorpions to microgravity will help to analyze entraining and coupling mechanisms of biological clocks and will contribute to the analysis of disturbances of clock systems in humans, by fully automatic measurement of physiological parameters with circadian patterns, which include locomotion, eye movements, O_2 consumption and cardio-vascular activity. Scorpions represent an interesting animal model because they can tolerate a complete lack of food and water for more than 6 months without nutritional care. The animals will be connected to sensors and electrodes and exposed to microgravity, 1-g, and different light regimes [Wilson, 2003].

Snails *Biomphalaria glabrata* also flew on several occasions onboard space shuttle and ISS missions. On orbit video recording revealed that the snails were easily dislodged from the aquarium wall, while on Earth they spent most of their time attached to the walls. Once separated from the wall they floated through the water, which gave them the chance to contact other snails in orbit. As these snails are hermaphrodites, mating pairs were often seen floating attached to one another. After the spacecraft landed, embryos of all developmental stages were present [Marxen et al., 2001].

2.3.2.2. Lower vertebrates

No vertebrates have ever been raised from conception to sexual maturity in the absence of gravity. No birds or reptiles have bred on orbit, although fertilized chicken and quail eggs have flown on several occasions. Young chick embryos have survived. Quail eggs that were fertilized on the ground have hatched on the *Mir* space station, but yielded hatchlings that were disoriented[1] and would not or could not spontaneously feed [Jones, 1992].

Studies of sea urchins, fish, frogs, and newts [Dournon et al., 2001; Moody and Golden, 1999] indicate that fertilization can occur in space, but in these cases the gametes had been developed while the organism was on Earth. In most of these studies, however, mating and insemination was performed on the ground before launch. Inseminated females store the sperm in a compartment of the body called spermatotheca and use the sperm cells at the moment of egg deposition. The advantage of this approach is that the time of fertilization and therefore the age of embryos can precisely be determined by the experimenter.

This type of fertilization was successfully performed in salamanders (*Pleurodeles waltl*) and newts (*Cynops pyrrhogaster*) onboard *Spacelab*, *Mir*, and the ISS [Izumi-Kurotani and Kiyomoto, 2003]. The female newts keep spermatozoa in their cloacae ready to fertilize eggs after hormonal stimulation of ovulation. Egg laying then occurs within 24–48 h. The presence of spermatozoa in the perivitelline space and of spermatic spots on the surface of the eggs in microgravity can be considered as a proof that the development of embryos is not based on parthenogenesis. During these experiments, about 56% of eggs were successfully fertilized. By comparison, the ground experiments revealed a ratio of 51%, suggesting that occurrence of egg fertilization was not affected by microgravity [Aimar et al., 2000]. Using the same method, in-flight fertilization in house crickets *Acheta domesticus* was performed onboard the ISS in 2005. After the flight, embryos were recovered, suggesting that eggs could develop for 8 days in microgravity.

Female frogs were sent into space and induced to shed eggs that were then artificially inseminated. As already mentioned, the eggs did not rotate, even though the cortex did, and yet, surprisingly, the tadpoles emerged and appeared normal. There were abnormalities noted at the cellular level though. After returning to Earth, the tadpoles metamorphosed and matured into normal frogs. Subsequent embryonic studies revealed that the cleavage rhythm during development appeared normal, yet some morphological changes occurred in frog embryos and tadpoles (Figure 2.16). The embryo had a thicker blastula roof that should have created abnormalities in the tadpole, but no deformations appeared, suggesting plasticity of the embryo [Souza et al., 1995; Duprat et al., 1998].

Another interesting finding was that the tadpoles did not inflate their lungs during spaceflight. Earth or 1-g space (centrifuged) tadpoles swam to the surface, gulped air, and expanded their lungs within 2–3 days of hatching. Air bubbles were present in the

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[1] When a cosmonaut took a hatchling from its habitat, the chick appeared content as long as it was held. But once released, the bird first flapped its wings for orientation and began to spin like a ballerina, then kicked its legs, causing it to tumble like a spinning ball. The cosmonaut noted that the chick would fix its eyes on the cosmonaut while trying to orient in space. When placed in their habitat, the chicks had difficulty flying to their perch to eat, and, unlike the adults, had difficulty grasping the perch for stability when eating. The hatchlings ate normally only when held by the crew and, thus, did not survive. By contrast, adult quails adapted quickly to the space environment. They soared, rather than flapping their wings, and held onto their perch for stability when eating.

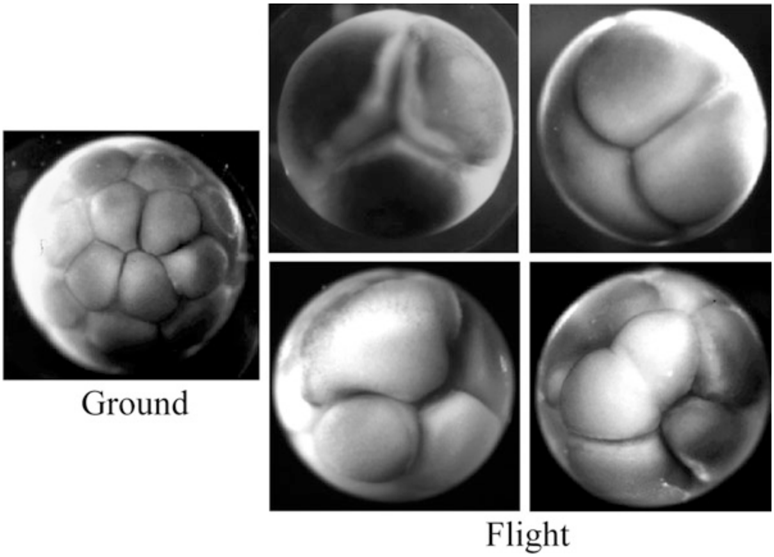

Figure 2.16. Comparison in the Development of Amphibian Eggs from Pleurodele Newt on Earth and in Space. There Are Clear Abnormalities in Orbit, Such as Larger Sillons and Odd Number of Cells, in the Flight Specimens by Comparison with the Ground Controls. (Adapted from Gualandris-Parisot et al. [2002]).

tadpole aquatic habitat on orbit, yet the tadpoles did not inflate their lungs while in microgravity. Two possible explanations for these flight findings include lack of directional cues and increased influence of surface tension that may make it more difficult for an orbit-born tadpole to burst through a bubble and gulp air. The tadpoles returned to Earth within 2–3 days of emerging from the egg, and the lungs appeared normal by the time the tadpoles were 10-day old [Wassersug, 2001]. One investigation has suggested that gametes formed in space are normal [Ijiri, 1997]. In this experiment, *Medaka* fish mated freely in microgravity and the subsequent developmental steps were similar in flight and ground-control fish. Newly laid eggs formed a cluster on the belly of the female fish (Figure 2.17). After detachment from the female's body, young fish hatched in microgravity and swam normally both in space and after returning to Earth. Back on the ground, the offspring produced healthy second-generation animals.

These studies produced multiple important findings. They show that vertebrates can be induced to ovulate in space and that rotation of fertilized eggs is not required for normal development in space. Long-duration microgravity exposure studies on the ISS revealed that larvae were able to regulate the morphological changes that occur during developmental in microgravity. The vertebrate embryo is very adaptive and the system is plastic, yet the long-term fate of the animal throughout its life in space remains unknown.

2.3.2.3. Mammals

When investigations address human adaptation to spaceflight and its health implications, the use of other mammalian species often becomes necessary. The rat is the

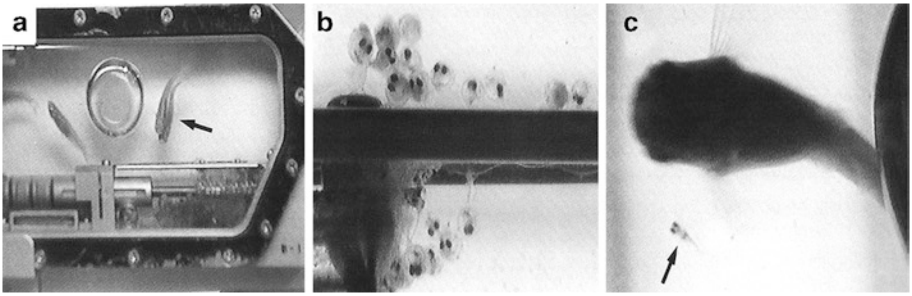

Figure 2.17. In the Summer of 1994, Four Japanese Killifish (Medaka) Flew for 15 days on Board the Space Shuttle Columbia (IML-2; STS-65). These Fish Mated in Space for the First Time Among Vertebrate Animals (**a**) and Laid Eggs (**b**), Which Developed Normally and Hatched as Fry (**c**). (Adapted from Ijiri [1997]).

mammal employed most frequently for space research. Its well-demonstrated biochemical and structural similarity to humans makes the rat an appropriate subject with which to test new drugs and investigate many disorders experienced by astronauts during and after spaceflight. Within a 2-week period, which corresponds to a space shuttle flight, the rat neonates go through a critical development period, during which rapid neural and motor development occurs (Figure 2.17). Also, because of their phylogenetic proximity to humans, non-human primates, such as rhesus monkeys, have occasionally served as research subjects in space biology, but only when the need has been clearly demonstrated [Souza et al., 2000].

Fertilization events have been studied in several species for which fertilization occurs externally, such as newt or fish. As previously discussed, the data indicate that for these animals, production of a zygote and early cleavages are mostly normal in the space environment. Fertilization events in mammals have not been studied, primarily because they occur internally. On several occasions, however, pregnant rats flown in space gave birth to normal neonates after flight. It was observed that during postflight delivery, flight dams have twice as many abdominal contractions as the ground controls, suggesting that more extended exposure to spaceflight could still have a detrimental effect on pregnancy, or at least the birthing process [Ronca and Alberts, 2000]. In addition, male rats mated 5 days after flight to non-space experienced females produced offspring with growth retardation and many abnormalities such as hydrocephaly, out of place kidneys, and enlargement of the bladder. Mating two and a half to 3 months after the spaceflight produced healthy and viable offspring [Tou et al., 2002].

Fertilization might also be affected by mobility changes in sperm. In fact, it is known that bull sperm swim with higher velocity in microgravity. This increased velocity is coupled to changes in phosphorilization of specific flagellar proteins [Tash and Bracho, 1999]. Altered gravity changes mammalian male and female reproductive systems in a rather complex manner. For example, a transient but dramatic reduction in testis weight and testosterone has been reported in male rats in orbit. However, the pituitary responded in a physiological manner to changes in plasma testosterone, indicating that the hypothalamic-pituitary-gonadal axis was not impaired by spaceflight. So, spermatogenesis was not reduced. Examination of the ovaries of postpartum rats flown in space during 9–20 days of gestation showed no effect on ovarian weight or number follicles [Tou et al., 2002]. The physiological mechanisms for reproduction are obviously intact in microgravity, despite of modifications of some components of the complete system.

As for the early period of development, the effects of microgravity on nervous system development were considered in only a few animal species and specific tracts. While these effects on the early formation of the nervous system were mainly based on studies in the aquatic animals, axonal growth and dendritic morphology related to functions such as equilibrium control and control of circadian activity, respectively were also studied in rats.

Rat embryos exposed to microgravity during the period when the vestibular system starts to become functional, showed delayed development compared to controls. In particular, 3 h after shuttle landing, central projections from the gravisensing organs receptors to the medial vestibular nucleus were more immature than in the controls [Bruce, 2003]. This result suggests that gravity is required for appropriate synaptic development and fine-tuning of the projections from the gravity sensing receptors to the central nervous system. These observations were supplemented by studies of neonate rats during the 16-day *Neurolab STS-90* mission, which revealed an absence of connections into the vestibular nuclei from the cerebellum, the main control center for balance and coordination of movement [Raymond et al., 2003]. Recent studies have also revealed that microgravity affected the retinas of neonatal rats, probably by degeneration of cells or parts of individual cell types [Tombrain-Tink and Barnstable, 2005].

The force of gravity may influence events underlying the postnatal development of motor function in rats, similar to those noted in hatchling quail. Such effects most likely depend on the age of the animal, duration of the altered gravitational loading, and the specific motor function. The effect of microgravity on muscle mass and function occurs in less than 1 week [Tischler et al., 1993]. The ossification of skeletal bones of fetuses of female rats flown in space during their pregnancy was arrested. However, during the 1-g re-adaptation period, the reduced ossification of the embryos was over-compensated, and newborns from this mission were ahead of the controls. Exposure of bone and bone cell cultures originating from mammals to microgravity is a widely used tool for understanding the underlying mechanisms of bone formation. Nevertheless, the basic mechanisms of the modifications in developing bones in microgravity are poorly understood. Isolated fetal mouse long bones experience no change in relative length increase and collagen synthesis induced by microgravity. Instead, a decreased mineralization, as well as a decrease in glucose consumption and an increase in calcium release is seen [Van Loon et al., 1995].

Like morphology, all physiological functions in organisms, as well as their behavior, experience modifications during development. The righting response from a supine posture to a prone posture is a good experimental model to test maturation of vestibular function. Beside the vestibular system, tactile cues from contact with a solid surface, as well as proprioceptive cues from muscle spindles and tendons contribute to a successful righting response. To separate the contribution of vestibular from other sensory inputs, the righting response can be studied during water immersion, i.e., the

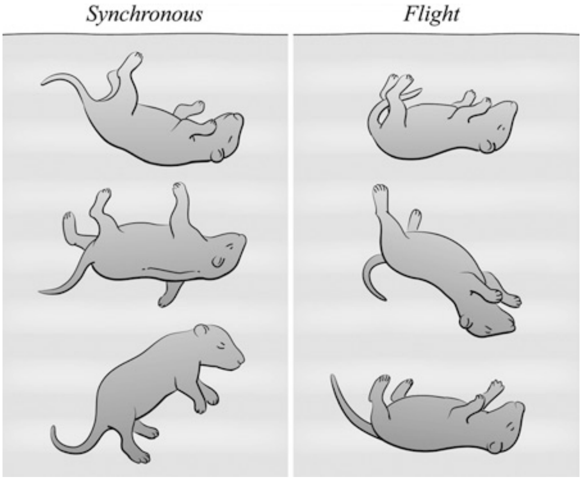

Figure 2.18. This Cartoon Shows the Sequence of Body Movements During the Righting Response in Water by Neonatal Rats Raised on Earth (Synchronous) or Exposed to Microgravity (Flight). (Credit Philippe Tauzin).

animal is positioned in the supine position in a water-filled container and then released. Righting behavior in the absence of tactile cues revealed clear response deficits in neonates that underwent prenatal development in space (Figure 2.18). Exposure to microgravity during postnatal periods of life significantly retarded the development of this righting behavior [Ronca, 2003].

Walton [1998] also reported differences in swimming behavior and locomotion in neonatal rats when the musculo-skeletal system did not bear weight during critical times of development. The results from the 17-day Neurolab shuttle mission showed that neonatal rats flown in space exhibited altered locomotor behavioral development that persisted for the 1-month recovery period, and that righting reflex strategies were still abnormal 5 months after return to Earth.

One interesting feature of sensory, neuronal, and motor systems is the existence of critical periods during their development. The concept of critical period during development goes back to studies performed by Nobel prizes laureates Hubel and Wiesel [1962] on the visual system in kitten. Deprivation is the preferred scientific method to study the existence and duration of critical periods. Consequently, every long-lasting change in the environment may have its specific critical period. In general, three criteria must be fulfilled to define a development period as "critical": (a) the developing system must be susceptible to a specific environmental modification; (b) the extent of modification must be related to age, and in particular to a well-defined period of development; and (c) the modification must persist for long periods of postnatal life or even permanently. In space studies, only the first two criteria were observed; indeed, long-duration effects of irreversibility were rarely noted.

Other results from space studies indicated delayed development of certain nerve connections to muscles. The connections returned to normal after return to Earth, yet fibers in hind limb muscles did not reach normal size even after a month back on Earth. The data suggest that biomechanical loading of limbs during early development may be essential for innervation of muscles. Another mechanism, however, may be at work: besides the lack of loading during critical times, there is also the possibility that adaptive changes in the vestibular system, particularly the reduction in descending otolith input required to maintain muscle tone (see H-reflex data in Chapter 3, Section 3.3.2), modify the nerve-to-muscle connections [Ronca and Alberts, 1997].

To date, relatively little neurobehavioral research has been done in microgravity with vertebrates, juvenile or adult. This is partly because the habitats for raising them in space did not exist and because the study of vertebrates up to sexual maturity requires longer exposure to microgravity [Wassersug, 2001]. The ISS will now provide both capabilities. Physiological experiments using implanted electrodes in fish, rats, or rhesus monkeys have provided interesting data on the adaptive changes in the neuro-vestibular system, for example (see Chapter 3, Section 3.2.1). However these experiments are limited to constrained or caged animals, which do not experience motion in microgravity, making it difficult to draw a comparison with adaptive changes in astronauts. The response of animals to free-fall is astonishingly diverse, as shown by the observations made on frogs, lizards, and snakes in parabolic flight [Wassersug, 2001]. Other observations of animals placed in microgravity after vestibular lesions prove interesting for understanding the role of gravity in the process of recovery of balance function.

In conclusion, short-duration exposure to the space environment does not significantly affect the embryonic development, although interesting and unexplained changes occur during embryogenesis and early development. However, because the animals in most of these studies were only partially adapted to the space environment due to the short duration of the flight, it is possible that long-duration exposure will have more significant effects. The opportunity to conduct development studies onboard the ISS will leave room for much investigation.

2.4. Plant biology

2.4.1. Questions

On Earth, plant roots as a rule grow downward toward gravity, while stems grow up and away from gravity, a phenomenon known as gravitropism (see Figure 1.3). Circumnutation, i.e., the successive bowing or bending in different directions of the growing tip of the stems and roots, might also due in part to gravity. By studying plants in microgravity on board spacecraft, biologists seek to understand how plants respond to gravity at microscopic and macroscopic levels. Also, plants respond to environmental stimuli such as light, temperature, and magnetic or electric fields. These responses are masked on Earth by the overriding response of plants to gravity. In addition, any exploration strategy that includes a long-term sustained human presence in space absolutely requires the ability to continuously grow and reproduce various plant species over multiple generations for food production and closed environmental life support system.

2.4.2. Results of space experiments

A large variety of plants with short life spans have flown in space: algae, carrots, anise, pepper, wheat, pine, oat, mung beans, cress, lentils, corn, soybeans, lettuce, cucumbers, maize, sunflowers, peas, cotton, onion, nutmeg, barley, spindle trees, flax, orchids, gladiolas, daylilies, and tobacco. Because of this wide variety, for the most part, observations on plants exposed to microgravity have been anecdotal. It has been demonstrated repeatedly that plants do grow in microgravity. However, whether plants can grow and develop normally over several generations remains to be determined.

2.4.2.1. Graviception

For research purposes, the gravitational response, as with any stimulus response, has been divided into three steps: (a) stimulus perception: how a plant senses gravity; (b) signal transduction: how the plant transfers this knowledge into action; and (c) the response or resulting action: differential cell elongation or differential growth that results in the root or shoot bending in a new direction.

Where does the response occur? In roots we have already seen that perception occurs in the root cap (see Figures 2.5 and 2.6). The sensing mechanism underlying a plant's ability to orient its organs in a gravitational field seems to involve the sedimentation of intracellular particles known as statoliths. The statoliths each consist of a number of starch grains surrounded by two membranes, the structure being termed an *amyloplast*. With the movement of statoliths, the cell receives a mechanical stimulus. How a cell transfers this mechanical stimulus into a chemical signal is still of great debate. One hypothesis is that as the statoliths "fall", they come to rest on other organelles such as the endoplasmic reticulum or plasma membrane, thus exerting pressure on the organelle that results in the opening of ion channels and the release of ions such as calcium that initiate the signal transduction pathway [Perbal et al., 1997].

Transmission of the stimulus to the reaction zone, i.e., the bending of the root, could occur because of a change in the flow of the plant hormone auxin. How gravity regulates auxin transport remains unknown. Nevertheless, auxin typically flows in a fixed direction, from the shoot towards the root. After flowing down to the root tips, auxin begins to flow in the opposite direction, as if making a U-turn, along the roots. If the root is tilted relative to gravity, the concentration of auxin increases in the lower part of the elongation zone in the root, causing a differential growth between the lower part and the upper part.[2] As a result, the root bends downward (Figure 2.19).

In microgravity, statoliths do not settle within the root cap cells (Figure 2.20), so gravity is not perceived, nor is asymmetric auxin distribution induced. Microgravity experiments on board sounding rockets, the space shuttle, and the ISS have shown that growth direction was indeed uncontrolled in microgravity, and some roots even extended in the same direction as the aerial stems (Figure 2.21).

Onboard centrifuge experiments have demonstrated that seedlings grown in space required a dose of 20–30 g s (gravity time seconds), or less than 0.1 g for 200–300 s,

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[2] Interestingly, phototropism in shoots seems to obey to the same mechanism. Light would stimulate the movement of auxin away from the light source. The increased supply of auxin to cells opposite the light source would cause them to elongate more than the cells on the same side as the light source.

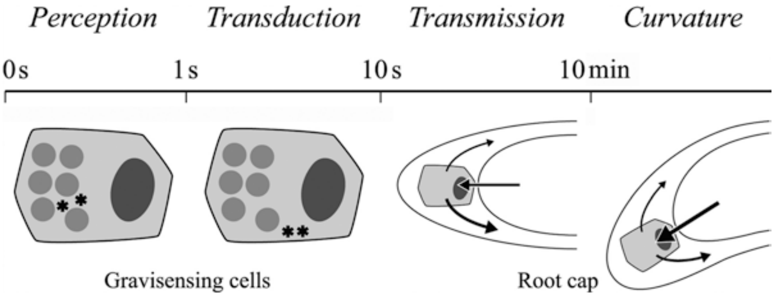

Figure 2.19. The Different Phases of the Gravitropic Curvature of the Root. Four Phases Are Generally Distinguished. The Perception Is the Physical Phase of the Gravitropic Reaction and Corresponds to the Movement of the Statoliths in the Gravisensing Cells Located in the Root Cap. It Is Followed by the Transduction of the Stimulus, i.e., the Transformation of the Mechanical Effect of Gravity into a Biochemical Factor. Both Phases Occur Within the Gravisensing Cells. The Transmission of Gravistimulus to the Reaction Zone Consists in an Asymmetrical Hormonal Message (Downward Transport of Auxin). It Is Responsible for a Differential Growth (Curvature) that Occurs Far Away from the Perception Zone. Note the Time Scale. (Credit Philippe Tauzin).

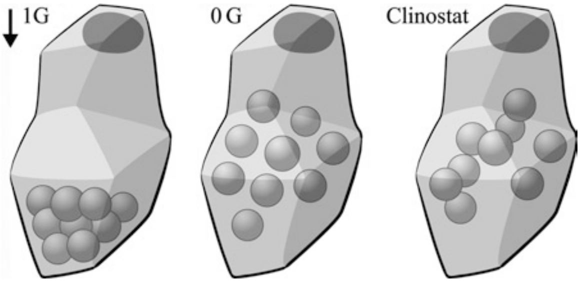

Figure 2.20. Comparison of the Position of the Statoliths in Roots Grown in the Vertical Position (1 G), in Microgravity (0 G) or on a Clinostat. The Limits of the Protoplasm, the Statoliths, and the Nucleus Are Represented. (Adapted from Smith et al. [1997]. Credit Philippe Tauzin).

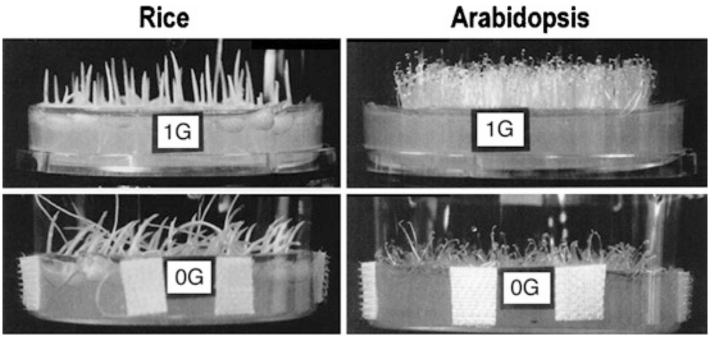

Figure 2.21. Photographs of Rice and Arabidopsis Seeds Cultivated on Earth and in Microgravity. (Credit Takayuki Hoson, Osaka City University).

to elicit a gravitropic (root bending) response [Perbal and Driss-Ecole, 1994]. Studies had revealed that the minimum force that is sensed by plant organs is in the range of 5×10^{-4} g for roots and 10^{-3} g for shoots [Shen-Miller et al., 1968], but these values were obtained on clinostats with a background of 1 g. These thresholds have not been confirmed in space studies yet, as the lowest g level generated by onboard centrifuges is 0.01 g, i.e., 20 times more that the supposed threshold acceleration of 5×10^{-4} g. However, in-flight experiments indicated that the root is able to perceive its orientation with respect to a linear acceleration vector and to generate a signal of curvature in less than 30 s.

Another interesting observation is the fact that the statoliths are more sensitive in 0-g grown plants than plants grown in 1-g [Perbal et al., 2004]. In microgravity, the amyloplasts are situated near the nucleus, whereas in 1 g they are sedimented on the endoplasmic reticulum. When a centrifugal force is applied to the organs, the probability of having contacts between amyloplasts and the reticulum tubules is much less in 0 g than in 1 g, although the response is greater in 0 g than in 1 g. Thus, experiments performed in space brought a strong argument against the hypothesis based on a role of the endoplasmic reticulum in the transduction of gravity stimulus [Perbal, 2006].

To some extend the transduction pathway of the gravity sensing mechanisms could be analyzed in space by using transgenic plants. One experiment currently ongoing on board the ISS examines calcium redistribution in *Arabidopsis* plants harboring a depletion of auxin in some areas.

Even on Earth, the shoot apex of a plant may not grow directly upwards, but it may exhibit continuous helical and spiral movements as it grows so that seen from the side it appears to oscillate. This circumnutation movement may be a constant seeking of the apex for perfect alignment along the line of the gravitational force and be determined by constant adjustments in the levels of hormones produced in response to gravity perception. Experiments using sunflower seedlings, 4–5 days old, grown in space revealed that circumnutation takes place in microgravity, albeit with some reduction in the amplitude of oscillation, indicating that gravity is not essential [Brown et al., 1990].

Peg formation on cucumbers, melons, and squash is also influenced by gravity. A peg is a small protuberance that develops immediately after germination in the transition zone between root and stem, which helps the cucurbitaceous seedlings shed their seed coats. On Earth, the downward growth (gravitropism) of the roots results in a curvature at the transition zone. When seeds germinate in a horizontal or inclined position, a peg develops on the lower, concave side of the bending transition zone at an early stage of seedling growth. As such, it had been presumed that peg formation was regulated by gravity. It was recently discovered that when cucumber seeds germinate in space, a peg forms on each side of the transition zone, indicating that pegs develop with or without gravity. However, on Earth, the seedlings suppress peg formation on the upper side of the inclined transition zone in response to gravity, which causes unilateral placement of the peg in cucumber seedlings, but in space the second peg remains [Takahashi et al., 2000]. Experiments are currently being conducted on board the ISS to investigate the consequences of the presence of more pegs on the plant.

2.4.2.2. Development of plants

The questions raised by growing plants in the space environment are the following: How will space affect seed viability and germination? Is plant development normal in space? Will plants be able to reproduce in space? Significantly, results of studies on the German *Spacelab-D1* mission, which incorporated onboard 1-g centrifuge controls, indicated that single plant cells behave normally or even exhibited accelerated development. In contrast, the roots of seedlings germinated in microgravity grew straight out from the seed, and the same roots contained statoliths that were more or less randomly distributed in their cells. Control roots centrifuged at 1 g in-flight, were normally gravitropic (Figure 2.22).

Many species of plants have grown in microgravity. In 1972 the first plant, *Arabidopsis thaliana*, was successfully grown from seed to flowering plant and to next generation of seeds on *Salyut-7*. This was repeated for the first potential crop plant, super dwarf wheat, on *Mir* in 1996. It appears that the absence of gravity has no real effect on germination. For example, 12 million tomato seeds remained in space for 6 years, as part of an experiment embarked on the Long Duration Exposure Facility (LDEF), a satellite the size of a school bus that was placed in orbit by the space shuttle and retrieved by another crew 6 years later. Postflight measurement of germination showed no difference with ground controls, indicating that seeds remain viable in space.

Cytological studies of roots flown under a variety of conditions in space have consistently revealed reduced cell divisions as well as a variety of chromosomal abnormalities. Reduced amounts of cellulose and lignin were also found in space-grown mung bean, oat, and pine. Early space experiments exhibited poor plant growth

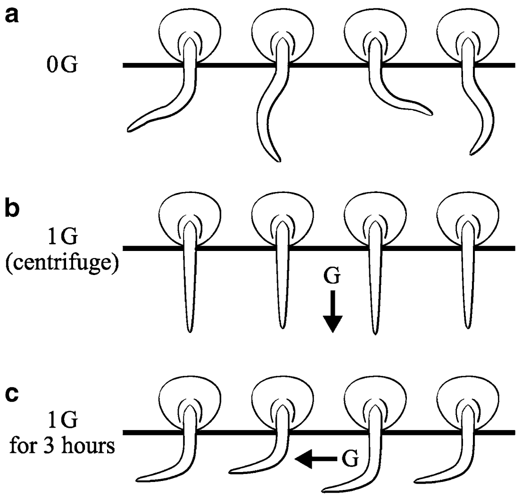

Figure 2.22. Experiments Carried Out on the German Spacelab-D1 Mission Showing that Roots May Grow Randomly in Microgravity (a), But Can be Reoriented Uniformly on Exposure to 1 g on a Centrifuge (b, c) for as little as 3 h. (Adapted from McLaren [1989]. Credit Philippe Tauzin).

and altered development: plants died in transition from vegetative to flowering stage or plants flowered, but were abnormal. Beginning in 1993, a series of experiments on the *space shuttle* and then on *Mir* was initiated to examine this problem. It now appears that early abnormalities in plant reproduction could be caused by the toxic effect of ethylene, rather than spaceflight factors, and that seed size was diminished possibly because storage and utilization of reserves are modified in absence of gravity [Musgrave et al., 1997].

Arabidopsis thaliana has been successfully grown from seed-to-seed on ISS (see Figure 2.21). During a 2-month growth period, the plants progressed from seed hydration to germination, vegetative, and reproductive stages, producing mature seeds. Ninety percent of the seeds germinated in space, although only 70% of the plants grew to maturity. Some of the seeds that were harvested from the plants that were grown in microgravity were planted in a ground study. These seeds produced typical plants without any visible abnormalities [Link et al., 2003]. Soybeans were also grown from seed to seed for the first time in space. Biomass production in the space seeds was approximately 4% larger than ground controls. Flight and grounds controls produced nearly identical numbers of seeds, but the space seeds were larger on average. Scientists found that the seeds that were produced in space were healthy, the germination rates were comparable to those on Earth, and no major morphological differences were evident.

Brassica rapa (field mustard) and *Triticum aestivum* (super dwarf wheat) plants were germinated and grown in a plant growth chamber over several growth cycles on ISS. By the end of the experiment, the plant growth chamber produced a total of eight harvests, seven primings, and a plant tissue archive of more than 300 plants. In-flight progress of plant growth is monitored through image collection; harvested plants are frozen or fixed for later analysis on the ground [Morrow et al., 2004]. Seed protein was significantly lower in the ISS material. Also, microscopy of immature seeds fixed on ISS showed embryos to be at a range of developmental stages, while ground control embryos had all reached the same stage of development. These differences could be attributable to differences in water delivery or reduced gas exchange due to lack of convection (Figure 2.23).

Plants continue to conduct photosynthesis and transpiration in space. However, some studies indicate a decreased ability to do so. Chloroplasts can have their internal structure disorganized, and their starch stores depleted. When plants were able to produce seeds in space, either additional light was needed versus on Earth or it was noted that oxygen production from photosynthesis was reduced. These results suggest that the microgravity environment may affect the flavor and nutritional quality of produces grown in space [Musgrave et al., 2005].

The growth and development of the dwarf wheat plants on the ISS was similar to the growth and development of plants on Earth. Analysis of the plants indicated that the microgravity-grown plants were 10% taller than plants grown on Earth. In 0 g, by comparison with 1-g control, the growth of the primary root and its apical (up-down) dominance over the secondary roots were reduced (Figure 2.24). Also, the growth of plant organs in space seems characterized by changes in the orientation of stem and leaves and secondary roots, more adventitious roots, and faster growth of secondary roots. The morphology of the primary root is not strongly modified. Experiments in

Figure 2.23. Astronaut Peggy A. Whitson Displays a First Crop of Soybeans Growing Inside the Advanced Astro-Culture Unit on Board the ISS. This Experiment Is Used to Determine Optimal Time for Cross-Pollination and Harvesting. (Credit NASA).

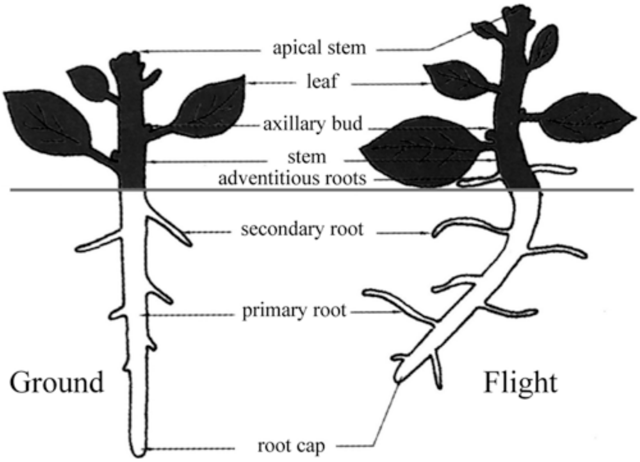

Figure 2.24. Summary of the Effects of Microgravity on the Development and Growth of Plant Roots and Shoots. (Adapted from Perbal [2001]).

space should be done to confirm that the reduced apical dominance results from a change in the hormonal content in roots. Once again *Arabidopsis* harboring a gene responsible for auxin depletion will be useful to analyze auxin distribution in space grown seedlings.

The cell cycle has been intensively studied in plants in the last decade [Inzé, 2005]. Plant molecular biologists now have the opportunity to use many molecular tools to analyze plant growth in space [Paul and Ferl, 2002]. We are close to understanding the causes of the changes in the development of plants in space. Many pioneering experiments have been done in space without monitoring gas composition, temperature, humidity, so that the conclusion of their authors must be questioned since plants are very sensitive to external factors. More clear-cut results have been obtained on board the ISS, because dedicated facilities providing onboard 1-g controls and better culture conditions have been developed. We know that the reproductive phase is complete in microgravity when the culture conditions (gas and liquid exchanges) are adequate. However, whether or not a seedling growing from the beginning in microgravity and across multiple generations can flower and produce normal seeds that can lead to normal plants remains a matter of debate. The experience gained from the past studies will be useful for the future.

2.5. Radiation biology

The broad spectrum of radiation encountered in space goes from extreme ultraviolet radiation, X-rays and high-energy particles such as electrons, neutrons, protons, to heavy ions such as iron. This section will be limited to a description of the ionizing radiation encountered in LEO and its biological effects as revealed by the biology experiments performed during space missions to date. A more complete description of the space radiation environment can be found in Eckart [1996]. The issues of radiation from the medical perspective will be discussed in greater detail in Chapter 8.

2.5.1. Ionized radiation in space

The sources of radiation during space missions are diverse:

(a) Cosmic radiation includes galactic radiation from supernova explosions as well as radiation of solar origin associated with solar flares (Figure 2.25). The primary galactic radiation present outside the Earth's atmosphere is composed of about 85% protons (with a hydrogen nucleus), 12% alpha particles (with a helium nucleus), and 1.5% of heavy ion particles with high charge and energy. These high-energy particles interact with the nuclei of the nitrogen and oxygen atoms of the atmosphere, resulting in a highly complex secondary radiation, which irradiates the whole surface of the globe.

(b) The solar particle radiation consists of 95% protons. High surface doses may be experienced, but dosage levels rapidly decline with the depth of material penetrated.

(c) Space missions that include travel within or through the Van Allen belts also add a third source of radiation. The Van Allen belts consist of protons and electrons trapped by the geomagnetic field. A phenomenon of special importance for missions in LEO is the South Atlantic Anomaly, in which the particles are drawn closer to the Earth than at other regions of the globe due to the asymmetry of the geomagnetic field.

(d) Finally, additional radiation is created in high-energy collisions of primary particles with spacecraft materials (Figure 2.26).

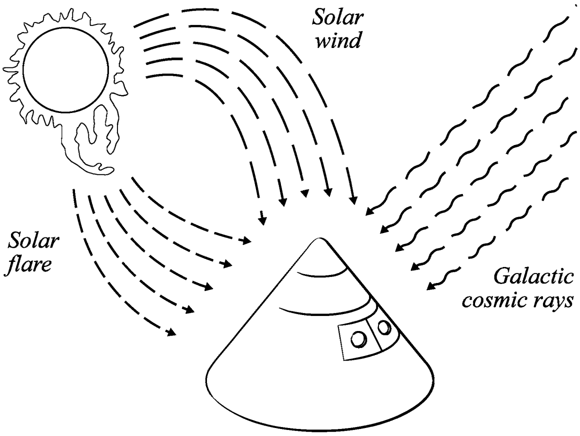

Figure 2.25. The Three Main Sources of Ionizing Radiation in Space. (Credit Philippe Tauzin).

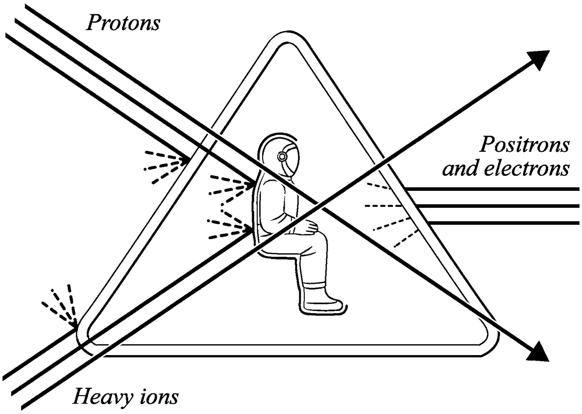

Figure 2.26. This Diagram Illustrates the Secondary Radiation Generated by the Collision of Various High-energy Primary Particles with the Spacecraft Materials. (Credit Philippe Tauzin).

The first evidence of the effects of space radiation on human crew are the "light flashes" first observed by Apollo and *Skylab* astronauts.[3] During most of the *Skylab-4* mission, these flashes averaged 20/h; however, flashes increased to 157/h when the

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[3] During the debriefing of the *Apollo-12* mission, Pete Conrad reported the following: "We all did see these corona discharges. [...] Most of the time (we saw them) during our sleep periods when we were lying in our bunks. [...] They appeared as either a bright round flash or a particle streaking rapidly across your eyeball in a long thin illuminated line. I could determine whether it was my left eye or my right eye that did it at the time." Alan Bean also reported: "If I was thinking about watching for them, I would see one every minute or somewhat less. One of them would be a flash, and about 1 min later there would be a line. It did not appear to make any difference whether we were in lunar orbit, translunar, transearth, or anything else. If you just wanted to look for them, you could see them going by" [Godwin, 1999].

Skylab orbit passed over the center of the so-called “South Atlantic Anomaly”. The flashes are believed to be due to high-energy heavy particles of cosmic rays and have been reproduced in humans on Earth by exposure to high-energy ionizing particles. Three explanations have been proposed to explain the phenomenon of light flashes seen by crewmembers: (a) an emission of photons by high-energy particles slowed by fluid in the eye (Cerenkov radiation); (b) a light generated by these particles ionizing fluid in the eye; or (c) an artificial light stimulus caused by these particles impacting retinal sensors in the eye [Pinsky et al., 1975].

2.5.2. Biological effects of radiation

All space agencies agree that the effects of space radiation, especially on the non-dividing cells of the retina and central nervous system, must be assessed before long-duration human missions beyond Earth’s magnetosphere are attempted. However, most of the biological effects of radiation remain largely unknown. The mechanisms of ionizing radiation impacts on cells are either direct, with particles impacting a vital target molecule and directly transferring their energy, or indirect, with particles impacting other molecules (e.g., water) to yield longer-lasting, very-reactive free radicals (with unpaired electron).

The biological effects of protons are fairly well understood. Through bombardment of spacecraft material, protons produce neutrons. These neutrons, upon colliding with a hydrogen nucleus, liberate their energy. Because living organisms contain many hydrogen-rich compounds, such as proteins, fat, and water (70%), they are most likely to be affected. However, the half-life of neutrons is only 11 min, after which they decay naturally to protons and electrons. Early dosimetry performed on *Skylab* and Russian space stations indicates that the flux of neutrons is probably not significant. The major space hazard comes from the highly charged energetic particles.

From ground-based experience (such as radiotherapy or nuclear explosion) it is known that the early, acute effects of radiation include skin effects (burns), eye lens opacification (cataract), graying of hair, immune system suppression (higher risk of infection), and the loss of non-dividing cells. Late effects include cancer in blood-forming organs (bone marrow, thyroid, lung, stomach, colon, and bladder) and genetic effects, which arise from, cell transformation (chromosome aberrations and translocations).

At the cellular level, when DNA strands break, non-rejoined breaks can lead to cell death, whereas incorrectly rejoined breaks can lead to mutation. The temporal and spatial characteristics of the radiation energy determine the quantity and quality of damage. Single-strand breaks can normally repair. However, double-strand breaks with close single hits or a high-density energy hit do not repair. Cells in mitosis are the most vulnerable. High-energy particles, with a high capacity to transfer their energy along the path, can generate significant percentage of double-strand DNA breaks. The effects are widespread and can lead to the death of numerous cells along the path. In addition, it is difficult to protect the vehicle and its inhabitants from these particles, even with shielding [Tobias and Todd, 1974].

Most results in space radiology have been obtained during short-duration space missions in LEO However, some observations were made on specimens flown on board free-flying satellites for several years, as well as on the ISS. The biological systems investigated include bacterial spores, plant seeds, and animal eggs, which were alternately sandwiched between nuclear track detectors allowing both a precise determination of the biological region penetrated by the particles and a determination of the charge and energy of each particle passing through. Chromosome damage and abnormalities were seen. In general, seeds are less sensitive than developing embryos or growing plants, which may be because their cells are not actively dividing. It is difficult to determine if these effects in lower organisms will lead to tumor induction, shortening of life, or chromosome aberration in organisms with longer life spans [Planel et al., 1994].

Several studies have been performed to try and determine which radiation is the most damaging, or even whether the damage was solely due to radiation at all. Some studies show that standard radioprotectant chemicals like cysteine, aminoethyliothiourea, and 5-methoxytryptamine don't stop the damage. This might indicate that the low-energy, indirect radiation is not primarily at fault. However, on some of the flights for which damage was found, the duration was short enough that galactic cosmic radiation dosages were rather low. Of course high-energy particles remain a possible threat, but some of the chromosomal damage and abnormalities could also be attributed to other environmental factors, like microgravity. On the other hand, experiments with protozoa and bacteria suggest that small doses of radiation may actually be beneficial because small doses elicit stress responses and have been shown to increase DNA repair [Planel et al., 1987; Hammond et al., 1999].

Microlesions of cultured retina cells induced by single heavy ions were first discovered via spaceflight experiments. These findings initiated biological investigations using particle accelerators on Earth. However, the results of ground – and space-based studies are often conflicting. For example, a higher number of mutations were observed in biological systems (e.g., larvae of *Drosophila*) exposed to an "artificial" radiation source while in orbit compared to ground controls. This difference suggests the possible existence of a combined effect of radiation and microgravity, the repair of radiation-induced lesions being altered in space [Planel et al., 1985].

This illustrates the difficulty of differentiating between the effects of the several factors inevitably present during spaceflight. For this reason, some biological effects, and their protection, can be studied only in space. An experiment on board the ISS utilizes a phantom torso, i.e., part-dummy, part-dosimeter-imbedded mock-up of a human's upper body, minus a set of arms, built to determine the effects of radiation on the human body (Figure 2.27). Dosimeters are mounted at critical organ-tissue locations within the dummy where critical organs are located: the head, the heart, the liver and kidneys. The dosimeters record the level of radiation received as a function of time. Other instruments mounted on the outside of the ISS measure the spectrum of particles that first hit the ISS shielding. As they go through the station wall and the dummy, the radiation is modified. The secondary radiation may have a different effect on tissue than the primary radiation. So the radiation spectrum is measured before and after it hits the dummy. The information gained from this and subsequent experiments (see Chapter 8, Section 8.3.5) will help determine the best types of materials and methods for shielding human crew.

For human mission to Mars, considerably better quantitative data on low-energy transfer radiation dose rates beyond the magnetosphere are still required. In particular,

Figure 2.27. ISS Astronauts Display the Phantom Torso That Monitors the Radiation Level at Various Depths Within Its Tissues When Placed Inside or Outside the ISS. (Credit NASA).

better predictability of the occurrence and magnitude of energetic particles from solar flares is needed, given that radiation from solar flares can be life threatening in relatively short time periods.

2.6. Facilities for space biology

2.6.1. Laboratories on board the ISS

Inside the *Columbus* module is the dedicated Biological Laboratory (BioLab). This double-sized rack developed by ESA is used to perform space biology experiments on microorganisms, cells, tissue cultures, small plants, and small invertebrates BioLab includes an incubator, a microscope, and spectrophotometer. Two centrifuges provide artificial gravity. It also has a glovebox and a combination of cooler and freezer units. The Japanese counterpart of BioLab is the *Saibo* (meaning "living cells") Experiment Rack, which is comprised of a clean bench, a glovebox with microscope, and a cell biology experiment facility with incubators, a centrifuge, and sensors to monitor atmospheric gases (Figure 2.28).

On the external surfaces of the *Zvezda* service module and the *Columbus* module is the *Expose* facility, which allows short – and long-duration exposure of experiments to space conditions and solar UV radiation. The *Expose* facility can accommodate experiments in photo processing, photobiology, and exobiology.

The ISS is also equipped with growth chambers and animal habitats where temperature, illumination, and atmospheric composition are controlled independently. They have the capability to maintain and monitor microbial, animal, aquatic, and plant cell and tissue cultures for up to 180 days. The aquatic habitat accommodates

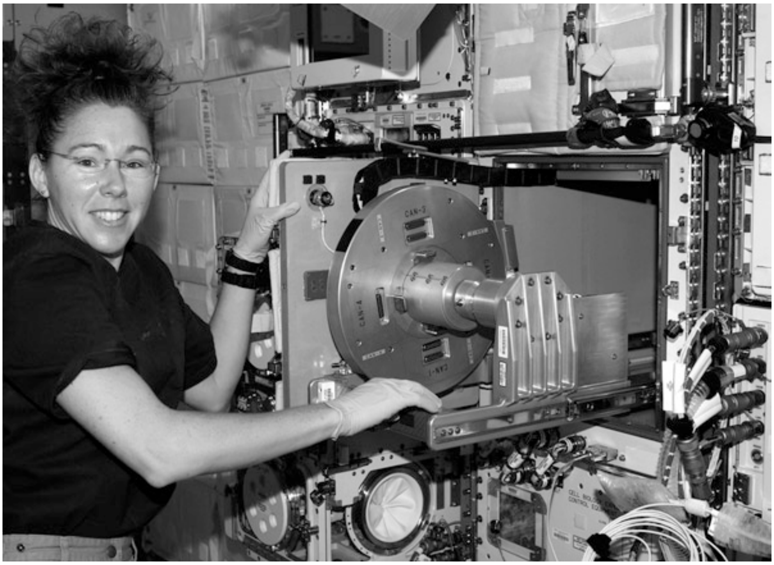

Figure 2.28. A Crewmember Conducts a Biology Experiment Facility in the Saibo rack in the Kibo Laboratory of the ISS. (Credit NASA).

small fresh water organisms to support egg generation studies for examination at all life stages. Animal habitats are capable of housing up to six rats or a dozen mice. These habitats are compatible with another compartment accommodating pregnant mice and subsequently their offspring from birth through weaning. Plant units are able to support plant specimens of various heights through all stages of growth and development. The insect habitat supports drosophiles and other insects for multigenerational studies and radiation biology. Egg incubators support the incubation and development of small reptilian and avian eggs prior to hatching.

These units include:

(a) The NASA Advanced Biological Research System (ABRS) has two chambers to grow a variety of biological organisms, including plants, microorganisms, and small arthropods (insects and spiders).
(b) The Biotechnology Specimen Temperature Controller (BSTC) can grow and maintain mammalian cell cultures in microgravity.
(c) The European Modular Cultivation System (EMCS) is being used for multi-generation experiments and studies of gravitational effects on early development and growth in seeds and plants and other small organisms, such as worms and fruit flies.
(d) The Eosteo Bone Culture System of the CSA provides the right conditions to grow bone cells in microgravity.
(e) With two aquariums, automatic feeding systems, LED lights to generate day/night cycle, and CCD cameras for observations, the Japanese Space Exploration Agency (JAXA) Aquatic Habitat (AQH) enables a variety of breeding experiments in space with small freshwater fish, such as *Medaka* or zebrafish.

(f) For studies on organ function to embryonic development of mammals is the Mice Drawer System (MDS) developed by ASI and NASA. Research conducted with the MDS is an analog to the human research program, but allowing better focus at microscopic level.

(g) Finally, the LADA Greenhouse is used for growing plants in the Russian segment of the ISS. Since its launch in 2002, it has supported a series of experiments on fundamental plant biology and space farming, growing multiple generations of sweet peas, wheat, tomatoes, and lettuce (for the enjoyment of the crew!).

2.6.2. Bioprocessing

The NASA Commercial Generic Bioprocessing Apparatus (CGBA) provides programmable, accurate temperature control – from cold stowage to a customizable incubator – and can be used in a wide variety of biological studies, such as protein crystal growth, small insect habitats, plant development, antibiotic-producing bacteria, and cell culture studies.

ESA also uses the Protein Crystallization Diagnostics Facility (PCDF) to study the protein crystal growth conditions by way of non-intrusive optical techniques like Dynamic Light Scattering (DLS), Mach-Zehnder Interferometry (MZI), and classical microscopy. Understanding how crystals grow in purely diffuse conditions helps define the best settings to get organic crystals as perfect as possible. These crystals are then preserved and analyzed on Earth or on-board to deduce the three-dimensional shape of proteins.

2.6.3. Storage and operations

2.6.3.1. Freezers

Freezers allow freezing storage, and transportation of samples collected on ISS for later return to Earth. There are three ESA-built and NASA-operated freezers called Minus Eighty-Degree Laboratory Freezer for ISS (MELFI) which each have a volume of 175 L of samples stored at temperatures ranging from +4°C to as low as −80°C. A NASA General Laboratory Active Cryogenic ISS Equipment Refrigerator (GLACIER) also serves as an on-orbit ultra-cold freezer (as low as −165°C) and has a volume of 11.4 L. These freezers have special “damping” mechanisms that ensure that this microgravity level is undisturbed by human or machine activity. Smaller devices, with a volume of 4.2 L and temperatures ranging from −20°C to 48.5°C, can be used either as a freezer, refrigerator, or incubator. The Kriogem-3 M is a Russian refrigerator-incubator for stowage of biological samples.

2.6.3.2. Gloveboxes

Periodic sampling is performed automatically or by the onboard crew, in such a way as to leave the remaining material undisturbed. Sampling is obviously carefully planned and minimized to preclude vibrations and other unwanted gravitational forces. Gloveboxes provide an enclosed workspace used for performing experiments and handling research organisms. They provide containment of experiments, and a safe environment for research with liquids, combustion, and hazardous materials on board the ISS (Figure 2.29). The laboratory-fixed ESA/NASA Microgravity Science

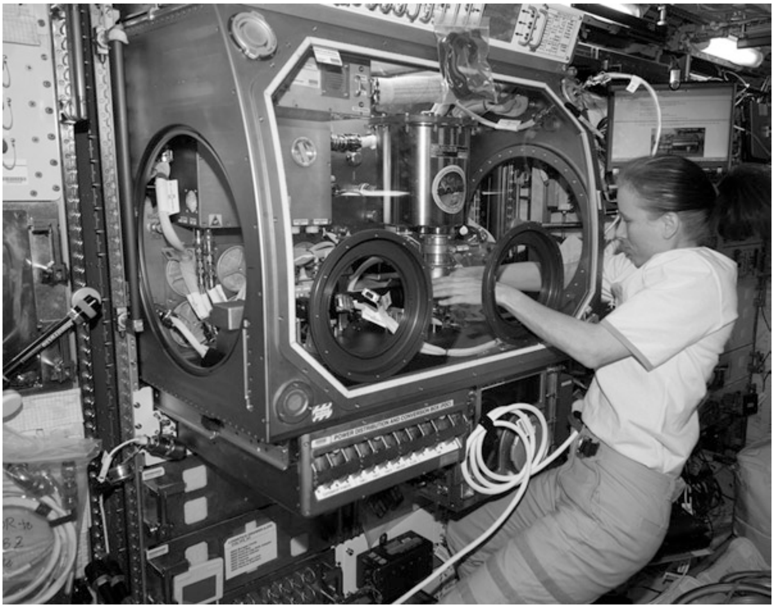

Figure 2.29. An Astronaut Works on a Biology Experiment Inside the Microgravity Science Glovebox (MSG) in the Columbus Laboratory of the ISS. (Credit NASA).

Glovebox (MSG) ensures that hazardous materials do not float about the cabin. Crewmembers access the work area through ports equipped with rugged, sealed gloves. A video system and data downlinks allow for control of the enclosed experiments from the ground. A Portable Glove Box (PGB) is a smaller glovebox that can be transported around ISS and used to provide two levels of containment for experiments in any laboratory module. Three levels of containment can even be achieved by placing the PGB inside the larger volume of the MSG.

2.6.3.3. Centrifuges

Several on-board centrifuges are provided within the facilities described above. These centrifuges provide a 1-g control for microgravity experiments. However, a missing tool for space biology on board the ISS is a multi-purpose centrifuge that would provide the capability to explore a range of gravity levels between 10^{-6} and 1 g in order to study gravity thresholds for certain phenomena. This multi-gravity research facility would help determine the optimal parameters for artificial gravity in humans.

A Centrifuge Accommodation Facility (CAF) was originally designed planned for flying on board the ISS. Although the flight model was built and ready to launch, the project was cancelled. This NASA-JAXA facility could provide artificial gravity ranging from 10^{-6} to 2 g. Appropriate incubators and growth chambers were provided for cells, simple organisms, plants, and animals. Some habitats would have had the experimental capability of selectable gravity levels of up to 2 g by being mounted on a 2.5-m diameter centrifuge. Other habitats were equipped with internal centrifuges, which provided selectable gravity levels from 0.01 to 1.5 g. should provide unique opportunities for space biology research during long-duration exposure to microgravity. It is unfortunate that the research community has forever lost the opportunities that the CAF would have provided.

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Chapter 3

The Neuro-Sensory System in Space

To be aware of the environment, one must sense or perceive that environment.[1] The body senses the environment by the interaction of specialized sensory organs with one aspect or another of the environment. The central nervous system utilizes these sensations to coordinate and organize muscular movements, shift from uncomfortable positions, and adjust properly. One relevant question is "what is the relative contribution of gravity to these sensory and motor functions?" This chapter reviews the effects of microgravity on the functioning of the sensory organs primarily used for balance and spatial orientation. Disorientation and malaise so frequently encountered during early exposure to microgravity and upon return to Earth are described. Theories and actual data regarding the role of the central nervous system in the adaptation of sensory-motor functions, including the control of posture, eye movements, and self-orientation, to changing environmental gravity levels are explored. For a comprehensive review of space research conducted in this area since the beginning of spaceflight, the reader is referred to the book *Neuroscience in Space* [Clément and Reschke, 2008] (Figure 3.1).

3.1. The problem: space motion sickness

The neuro-vestibular system consists of organs sensing the acceleration environment, nerves transmitting this information to the spinal cord and brain, and the central nervous system (CNS) that integrates this information so that we can determine our position and orientation relative to the environment. The vestibular organs in the inner ear detect and measure linear and angular accelerations. These responses, already complex, are further integrated with visual and proprioceptive inputs (Figure 3.2). In microgravity, some of these signals are modified, leading to misinterpretation and inadequate responses by the brain. One of these responses is space motion sickness (SMS) (Figure 3.3).

SMS is a special form of motion sickness that is experienced by some individuals during the first several days of exposure to microgravity. The syndrome may include such symptoms as depressed appetite, a nonspecific malaise, lethargy, gastrointestinal discomfort, nausea, and vomiting. As in other forms of motion sickness, the syndrome

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[1] The words "sense" and "perceive" are from Latin words: "sense" means "to feel", whereas "perceive" means "to take in through", i.e., to receive an impression of the outside world through some portion of the body.

G. Clément, *Fundamentals of Space Medicine*, Space Technology Library 23,
DOI 10.1007/978-1-4419-9905-4_3,

Figure 3.1. Astronauts on Board the ISS Wear Different Colors and Patterns of Polo Shirts for Ease of Identification of Crewmates When They Are Not Right Side Up. (Credit NASA).

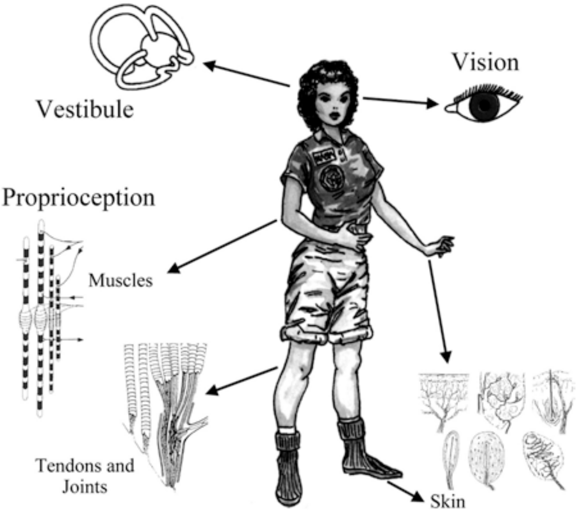

Figure 3.2. The Eyes, the Inner Ear and the Special Receptors in the Skin, Muscles and Joints All Participate in Maintaining Posture and Balance, and Assist in Our Movements.

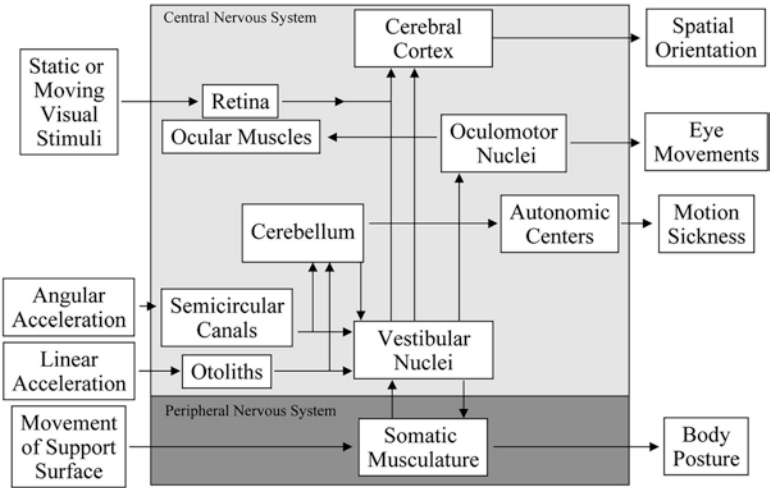

Figure 3.3. Inputs and Outputs of the Neuro-Vestibular System. The Information from the Various Sensory Organs First Reaches the Brainstem and Cerebellum. We Are Not Consciously Aware of What Is Going on in Our Busy Body When We Sit, Stand, Walk, or Run. However, Certain Sensations Do Eventually Reach the Cerebral Cortex, and Through Them We Remain Consciously Aware of the Relative Positions of Our Body Parts. Motion Sickness Might Be Caused by a Conflict Among Sensory Inputs Through Connections with the Autonomic Nervous System.

may induce an inhibition of self-motivation, which can result in decreased ability to perform demanding tasks in those persons who are most severely affected. Gastrointestinal symptoms have their onset from minutes to hours after orbital insertion. Excessive head movement early on-orbit generally increases these symptoms. Symptom resolution usually occurs between 30 and 48 h, with a reported range of 12–72 h, and recovery is rapid.

Even if someone doesn't literally get sick to their stomach, they may feel a less dramatic motion sickness effect known as "sopite syndrome", characterized by lethargy, mental dullness, and disorientation. Many astronauts have noticed this effect, which they call "mental viscosity," "space fog," or "the space stupids."

There were no reports of SMS in the Mercury and Gemini programs, while 35% of the Apollo astronauts exhibited symptoms. The incidence during the *Skylab* missions increased to 60%. About two-thirds of the space shuttle astronauts and *Soyuz* cosmonauts experienced some symptoms of SMS. There are no statistically significant differences in symptom occurrence between pilots versus non-pilots, males versus females, different age groups, or novices (first time flyers) versus veterans (repeat flyers.) An astronaut's susceptibility to SMS on his/her first flight correctly predicted susceptibility on the second flight in 77% of the cases [Davis et al., 1988]. In other words, one astronaut who has been sick during his or her first flight is likely to be sick again during subsequent flights.

SMS affects a similar percentage of both U.S. and Russian crews. Symptom recurrence at landing, also called “Mal de Débarquement,” reportedly afflicts 92% of Russian cosmonauts returning from longer missions [Gorgiladze and Bryanov, 1989]. No reports of *mal de débarquement* were noted in the space shuttle program. However, many astronauts returning to Earth after long-duration stay on board the ISS now experience this syndrome. The severity of the symptoms and the functional recovery after the flight seem to be directly proportional to the time on orbit.

Microgravity by itself does not induce space sickness. There were no reports of motion sickness during the Mercury and Gemini spaceflights. As the volume of spacecraft has increased, allowing for more mobility, the incidence of SMS has increased as well. Movements that produce changes in head orientation seem necessary to induce SMS symptoms. In particular, many crewmembers report that vertical head movements (rotation in the pitch or roll planes) are more provocative than horizontal (yaw) head movements [Oman et al., 1990]. However, once sickness has been well established, head movements in any plane are generally minimized by the affected crewmember. Indeed, movement of any kind is frequently restricted until the astronaut is on the road to recovery.

Head or full body movements made upon transitioning from microgravity to a gravitational field less than that on Earth, and vice versa, may not be as provocative. It is interesting to note that of the 12 Apollo astronauts who walked on the Moon, only 3 reported mild symptoms, such as stomach awareness or loss of appetite, prior to their EVA. None reported symptoms while in the one-sixth gravity of the lunar surface, and no symptoms were noted upon return to weightlessness after leaving the Moon surface [Homick and Miller, 1975].

There are considerable individual differences in susceptibility to SMS, and currently it is not possible to predict with any accuracy those who will have some difficulty with sickness while in space. Although anti-motion sickness drugs offer some protection against SMS, some drugs (i.e., scopolamine) may interfere with the adaptation process, and symptoms controlled by these drugs are experienced again once treatment ceases.

Symptoms have rarely occurred during extravehicular activity (EVA). Because most space sickness has abated by the third day of flight, mission rules restrict EVAs until the third mission day. Nevertheless, some astronauts medicate prior to space walking. The minimum flight duration for the space shuttle was also 3 days, to reduce the probability for astronauts, in particular the pilots, to be incapacitated by SMS symptoms prior to re-entry and landing [Davis et al., 1988]. The fact that the shuttle and *Soyuz* dock to the ISS only after having spent 2 days in orbit reduces the occurrence of SMS in the crew when arriving in a large open space such as the ISS.

Other issues related to the adaptation of the central nervous system through the vestibular pathways include: (a) the perceptual effects and illusions of free-falling, visual reorientation illusions, and acrophobia episodes (fear of height) during EVA; (b) decreased sensorimotor performance and visual scene oscillation (oscillopsia) during re-entry; (c) disequilibrium and ataxia when standing and walking after landing; and (d) g-state flashbacks during unusual stimulation of the vestibular system during the re-adaptation period following landing.

3.2. Vestibular function

The gravity vector is a fundamental factor in human spatial orientation, which results from the integration of a complex of sensory inputs coming from the vestibular organs in the inner ear, the eyes, mostly from peripheral retina, and tactile and proprioceptive receptors located in the skin, joints, muscles, and viscera.

3.2.1. The vestibular system

3.2.1.1. The vestibular end organs

The vestibular system's main purpose is to create a stable platform for the eyes so that we can orient to the vertical – up is up and down is down – and move smoothly. The inner ear contains two balance-sensing systems: one is sensitive to linear acceleration, the other to angular acceleration (Figure 3.4).

The linear acceleration sensing system sends messages to the brain as to how the head is translated or positioned relative to the force of gravity. It contains two tiny sacs filled with fluid, the saccule and the utricle, lined along their inner surface with hair cells of various lengths. Overlying the hair cells is a gelatinous matrix (the otoconia) containing solid calcium carbonates crystals (the otoliths, meaning "ear stone" in Greek). During linear acceleration, the crystals, being denser than the surrounding fluid, will tend to be left behind due to their inertia. It has been demonstrated that the resultant bending of the cilia causes cell excitation when the bending is toward the kinocilium (the longest hair cell), and inhibition when away from the kino-cilium. During head motion, the weight and movement of the otoliths stimulate the nerve endings surrounding the hair cells and give the brain information on motion in a particular direction (up, down, forward, backward, right, left) or tilt in the sagittal (pitch) or the frontal (roll) plane.

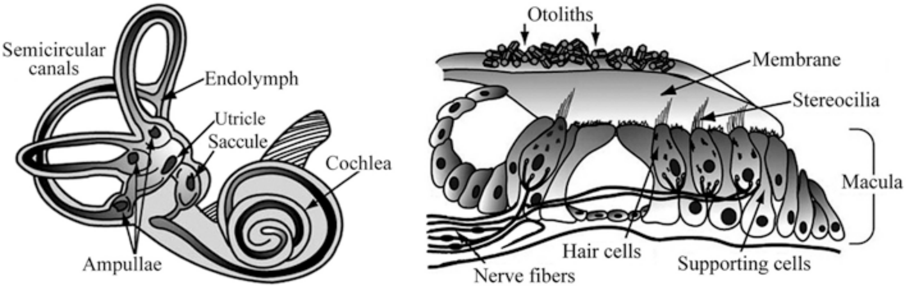

Figure 3.4. ***Left*: Schematic of the Vestibular System in the Inner Ear Showing the Three Semicircular Canals (Anterior, Posterior, Horizontal) and the Two Otolith Organs (Utricle and Saccule). *Right*: Otoliths Are Small Particles of Calcium Carbonate in the Gel-Like Membrane Layer Situated Over the Sensory Hairs (Stereocilia) of the Utricles and Saccules.** When the Head Moves or Is Tilted Relative to Gravity, the Membrane Exerts a Shear Force on the Cilia, Which in Turn Stimulates the Hair Cells. The Hair Cells Signal the Corresponding Information Via the Nerve Fibers to the Central Nervous System, Where the Sensation of Motion or Tilt Results.

The angular acceleration sensing system comprises three semicircular canals. The system detects angular acceleration through the inertial movement of the liquid (the endolymph) within each canal and provides the brain with information about rotation about the three axes: yaw, pitch, and roll. The semicircular canals do not react to the body's position with respect to gravity. They react to a change in the body's position. In other words, the semicircular canals do not measure motion itself, but change in motion. Not surprisingly, the semicircular canals are not affected by spaceflight, as shown by the absence of changes in the perception of rotation or in the compensatory eye movements in response to rotation both in-flight and after flight (see Section 3.3.5 below).

3.2.1.2. Linear acceleration and gravity

When our head is horizontal the hair cells in the utricles are not bent and this stimulation is interpreted as signifying "normal posture". If our head is tilted forward, the otoliths shift downward under the action of gravity, bending the hair cells. If we translate backward, again there is a shift of the otoliths forward due to the inertial forces. Thus, an equivalent displacement of the otoliths (and consequently the same information is conveyed to the central nervous system) can be generated when the head is tilted 30° forward, or when the body is translating at 0.5 g backward (Figure 3.5). This example simply illustrates Einstein's principle stating that, on Earth, all linear accelerometers cannot distinguish between an actual linear acceleration and a head tilt relative to gravity.[2]

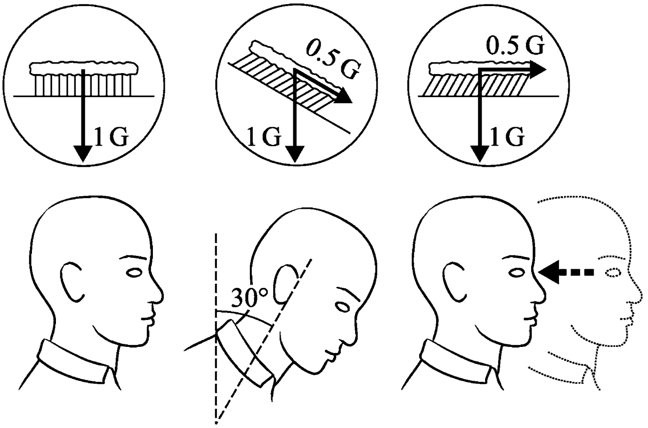

Figure 3.5. The Otoliths Bend the Hair Cells of the Utricles the Same Way When the Head Is Maintained at a Constant Tilt Angle of 30° Relative to Gravity and When the Whole Body in Translated Backwards at 0.5 g.

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[2] In a normal situation, the brain would easily distinguish between a tilt of the head relative to gravity and a head translation by comparing the sensory information from the otolith organs with that from the eyes or muscle proprioceptors. But in complete darkness, there could be a conflict between the proprioceptive input (e.g., signaling that the head is tilted) and the otolith input (e.g., signaling that the head translates).

On Earth, otolith signals can be interpreted as either linear motion (translation) or as tilt with respect to gravity. Because stimulation from gravity is absent in weightlessness, interpretation of otolith signals as tilt is inappropriate (Figure 3.6). Therefore, it is possible that during adaptation to weightlessness, the central nervous system reinterprets all otolith signals to indicate translation. This hypothesis is known as the Otolith Tilt-Translation Reinterpretation (OTTR). This central reinterpretation would persist following return to Earth, and be at the origin of spatial disorientation, until re-adaptation to the normal gravity environment occurs [Parker et al., 1985; Young et al., 1986].

Evidence for the OTTR hypothesis comes from subjective reports by astronauts returning from spaceflight who have a sense of body translation when they voluntarily pitch or roll their head. For example, many experience a backward translation when they pitch their head forward, or a rightward translation when they roll their head to the left. The utricle and the saccule are not located at the axis of head rotation during roll or pitch head movements. Therefore, this movement must evoke otolith stimulation, which could readily be perceived as translation during and immediately after landing. Such a misleading interpretation of otolith signals might be responsible for the staggering posture of the astronauts as soon as they land. The astronauts tend to lean to the outside of the turn when walking and turning corners immediately after landing, also suggesting a misevaluation of the apparent vertical from otolith signals.

The OTTR hypothesis has been the theoretical basis of much space research on the neuro-vestibular system for the past 15 years. I was fortunate enough to be able to perform a space experiment that tested this hypothesis in 1998. This experiment, which flew on board the Neurolab *STS-90* mission, used a human-rated centrifuge constructed by ESA [Buckey and Homick, 2003]. On Earth, when an individual is rotated in a centrifuge in darkness, he/she senses the direction of the resultant gravito-inertial force and regards this as the vertical. If a centrifugal force equivalent to 1 g is directed sideways, the gravito-inertial force is displaced 45° relative to the upright body, and the subject has a sense of being tilted by 45° to the outside (Figure 3.7). In microgravity, however, the gravitational component is negligible and the gravito-inertial force is equivalent to the centrifugal force. This force could be interpreted

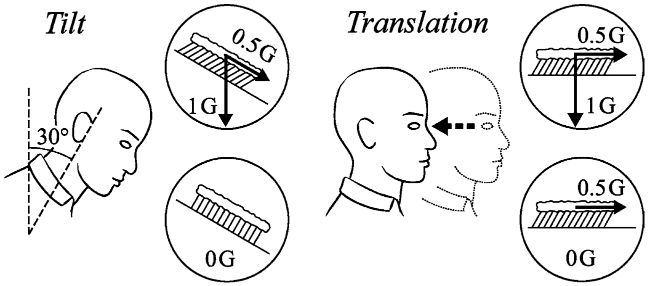

Figure 3.6. In Microgravity, the Otoliths Are Stimulated by Head Translation, but Not by Head Tilt. Consequently, It Is Hypothesized that, After a Period of Adaptation, the Brain Reinterprets All Otolith Signals as Signaling Head Translation. (Credit Philippe Tauzin).

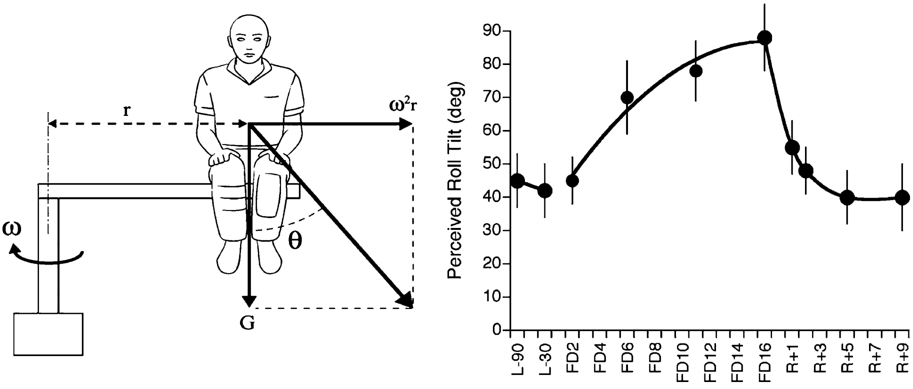

Figure 3.7. On Earth, a Subject Sitting at the End of a Centrifuge Arm in Darkness Adopts the Direction of the Gravito-Inertial Force (GIF) as the New Direction of "Gravity". In Microgravity, the GIF Is Equivalent to the Centrifugal Force and the Subject Could Perceive Either a Body Tilt or a Body Translation, Depending on the Interpretation of the Otolith Signals by the Central Nervous System.

either as a 90° tilt of the body, or a whole body translation in the opposite direction. During the Neurolab mission, four astronauts were asked to report their perceived angle of tilt during steady-state centrifugation in darkness throughout the flight and during the postflight re-adaptation period. Centrifugation was always perceived as tilt, not translation. Therefore the findings do not support the OTTR hypothesis. Despite the fact that the otoliths do not respond to head tilt in orbit, the brain continues to sense a steady-state linear acceleration applied to the otoliths as the upright in all circumstances.

The debate regarding the OTTR hypothesis is still raging. Some have proposed that the OTTR only occurs during voluntary head movements, or only during rotational head movements, or that OTTR must be frequency dependent. Centrifugation, by applying very low frequency passive linear acceleration to the entire body, would thus not elicit OTTR. I am currently conducting follow-up studies on astronauts returning from spaceflight, by spinning them about a tilted axis or tilting them in roll or in pitch while translating at various frequencies to further address this hypothesis.

The Neurolab centrifuge experiment, however, brought another interesting result. At the beginning of the flight, during a 1-g centrifugation in darkness, the astronauts perceived a 45° tilt to the side, very much like on Earth. However, as the mission progressed, they felt more and more tilted, until they felt a 90° tilt to the side on flight day 16 (Figure 3.7). This simple result indicates that the brain does not continuously calculate the direction of gravity, but uses an internal estimate of gravity whose weighting changes during spaceflight. The internal estimate normally used on Earth carries over to the early period of exposure to weightlessness, and therefore the astronauts continue to perceive a 45° tilt, despite the absence of sensed gravity. After a period of adaptation, the internal estimate declines to zero and the astronauts perceive a full body tilt to the side [Clément et al., 2001, 2003].

3.2.1.3. Changes in the vestibular receptors

Although it is difficult to measure changes in the vestibular end organs directly, several attempts have been made to examine the question "Is there anatomical and physiological changes in the vestibular end organs and their primary afferents after exposure to microgravity?"

Experiments on frogs have revealed no alteration of the sensory epithelium of the vestibular organ of adults returned from an 8-day stay aboard *Mir*, or following larval development in microgravity. However, changes in the structure of the otolith crystals in rats had been observed during an earlier *Cosmos-782* mission. A degeneration of the otolith crystals could occur because of changes in body calcium, protein metabolism, and calcium exchange. In addition, it is unclear how many of these changes were due to the high accelerations experienced by the animals during take-off and landing.

More recent Spacelab experiments indicated no deleterious effects in the otoliths of rodents who flew as compared with the ground controls. However, an unexpected change found during the Spacelab *SLS-1* mission, and later confirmed during the Neurolab mission, was an increase (by a factor of 12) in the number of synapses in hair cells from the in-flight maculae as compared with the control data. These findings suggest that mature utricular hair cells retain synaptic plasticity, permitting adaptation to an altered environment. Consistent with these results is data that show a decrease in synapse activity in centrifuged rats. These data suggest that the maculae adapt to g-forces changes in either direction by up- or down-regulation of synaptic contacts in an attempt to modulate neural inputs to the CNS [Ross and Tomko, 1998]. Recent morphometric studies of the utricular area performed in tadpoles following stays on board the ISS confirmed a vestibular sensitization in microgravity.

Primary afferent fibers of the vestibular nerve are relaying the information originating at the hair cells to the brainstem. Within each nerve are also efferent fibers from the CNS that provide neural feedback to modulate the activity of the peripheral organs. The resting activity of single otolith afferents and their response to centrifugal forces were found to be different in microgravity compared to the ground condition in frogs. Recently, a study recording the vestibular nerve impulse data from the oyster toadfish during the Neurolab mission confirmed these results. On the other hand, the spontaneous firing rate of single horizontal semicircular canals afferents did not change postflight relative to preflight in two flight monkeys. However, these monkeys were restrained in a laboratory chair, thus preventing any movements of the head during the flight. It is known that movement and interaction with the environment are necessary factors to drive adaptive changes. For example, vestibular patients show a faster recovery when moving around after vertigo crisis or unilateral surgery.

Few experiments addressing the early development of the vestibular system have been carried out in space. This is an interesting research topic given that in all species the vestibular system begins to respond to linear or angular acceleration prior to hatching or birth, in contrast to hearing or vision, which can be postnatal in some species. Mammalian offspring emerge from the birth canal in a species-typical orientation, which, for rats and humans, is headfirst. Fetuses typically achieve the appropriate orientation via active, in-utero behavior. Perhaps the vestibular system is employed for this early task. Indeed, many infants born in the breach position are born with vestibular disorders. Also, the so-called "righting response," by which the newborn mammals actively adjust from a supine to a prone position, is disrupted by induced vestibular disorders during development.

In the development of the visual system, activity in the retinal pathway influences the specification of those connections that determine how visual information is processed in the cerebral cortex. In every other sensory system known, especially those that make up the neural space maps in the brainstem, sensory stimulation has been implicated in the initial specifications of the connections and physiological properties of the constituent neurons. Only in the utricle and saccule gravitational pathway has it been impossible to study the role of sensory deprivation, because there is no way to deprive the system of gravitational stimulation on Earth. For this reason, experiments in microgravity should be planned to test the hypothesis that gravity itself plays a role in the development and maintenance of the components of the vestibular system. These components include both the vestibular receptors of gravity (i.e., the sensory hair cells in the utricle and saccule, vestibular ganglion cells that form synapses with vestibular hair cells, and vestibular nuclei neurons) and the motor neurons. The latter receive input from axons of the vestibular nucleus neurons composing the vestibular reflex pathways. The vestibular system also receives inputs from the proprioceptive system, involved in the control of muscle length and tension, and from the visual system, involved in the control of eye movements. Little is known about the exact nature of these interactions and virtually nothing concerning the development of these connections.

3.2.2. The other senses

In common speech, five different senses are usually recognized: sight (vision), hearing, taste, smell, and touch. Of these, the first four use special organs – the eye, ear, tongue, and nose, respectively, whereas the last uses nerve endings that are scattered everywhere on the surface of the body, as well as inside the body (visceral sensations). Proprioceptive sensations arise from organs within the body, from muscles, tendons, and joints. To what level these five senses are affected by spaceflight is uncertain.

3.2.2.1. Vision

The visual environment in space is altered in several ways. First, objects are brighter under solar illumination. Earth's atmosphere absorbs at least 15% of the incoming solar radiation. Water vapor, smog, and clouds can increase this absorption considerably. In general, this means that the level of illumination in which astronauts work during daylight is about one-fourth higher than on Earth. Second, there is no atmospheric scattering of light. This causes areas not under direct solar illumination to appear much darker (Figure 3.8).

Early anecdotal reports that orbiting astronauts were able to see objects such as ships, airplanes, and trucks with the naked eye suggested improved visual acuity in space. Extensive testing of Gemini astronauts was performed using a small, self-contained binocular optical device containing an array of high- and low contrast rectangles. Astronauts judged the orientation of each rectangle and indicated their response by punching holes in a record card. Another method, taking into account the particularity of the visual environment of space described above, also used large rectangular patterns displayed at ground sites in Texas and Australia. Astronauts were required to report the orientation of the rectangles. Displays were changed in orientation between passes and

Figure 3.8. An Astronaut Uses a Still Camera to Photograph a View of Earth from a Window in the Cupola of the ISS. (Credit NASA).

adjustments for size were made in accordance with slant range, solar elevation, and the visual performance of astronauts on preceding passes. Results with both measurement methods indicated that visual performance was neither degraded nor improved during spaceflight. The astronauts' reported ability to detect moving objects (airplanes and ships) was probably based on the detection of turbulence or waves behind the vehicles. Also, the color contrast might improve the ability to identify features, as Astronaut William Pogue described it during his *Skylab* mission "We were able to see icebergs about a hundred yards in diameter quite easily because of the higher contrast of white ice with the dark blue sea [Clément and Reschke, 1996]."

More refined visual testing has been performed on several shuttle flights using a specially-designed visual test apparatus to assess contrast sensitivity, phoria, eye dominance, flicker fusion frequency, stereopsis, and acuity (Figure 3.9). With the exception of reduced contrast sensitivity, no significant changes due to weightlessness were found. These changes were too small to impact operational performance. However, if contrast sensitivity continues to change during longer exposure to weightlessness, the decrement could become operationally significant.

An interesting observation is that some astronauts have described a decrease in their ability to see clearly at close range when in space. Interestingly enough, most of the astronauts experiencing this change were in their early forties and could see clearly without reading glasses when they were on the ground. One theory as to why this might happen is that the eye is like a water balloon. Rest it on a table and it gets longer as it flattens out (which is the normal condition on Earth). Put that balloon in space and it shortens, becoming more round. The eye could do the same thing and when it shortens it becomes farsighted, causing more difficulty seeing objects up close.

Recent studies revealed that optic disc edema, globe flattening, choroidal folds, hyperopic shifts, and raised intracranial pressure have been observed in approximately 20% of astronauts on long-duration missions both during and after spaceflight. In some cases, these changes were transient and in others, the changes were persistent with varying degrees of visual impairment. Furthermore, there are indications that

Figure 3.9. Near-Visual Acuity Test Performed by an Astronaut on Board the Space Shuttle. (Credit NASA).

visual alterations and changes to the eye (disc edema) have occurred in astronauts on space shuttle flights, but the condition is not well defined and lacks consistent data. These alterations could have profound mission impacts and long-term health impacts for the individual, such as a permanent loss of vision. One hypothesis for these changes is intracranial hypertension, due to the headward shift of body fluids following orbital insertion. Microgravity is known to produce a headward shift of 700–1,400 mL of fluid (see Chapter 4, Section 4.3.2). Photographic studies show a significant decrease in the size of the retinal vasculature after flight. Intraocular pressure rises during flight and drops below pre-flight levels after landing. The relationship between intracranial pressure and changes in visual acuity could also be due to excessive CO_2 exposure. Operational data from ISS and *Mir* is being mined and studies are planned to determine if there is indeed a relationship, but no definitive information is currently available.

It is also worth noting here that the light flashes perceived by the astronauts in the absence of normal visual stimulation were caused by heavy ionized cosmic particles passing through retinal cells (see Chapter 2, Section 2.5.2). Although no performance disturbance has been associated with these light flashes, it is likely that the flashes mask transient visual stimuli.

Many astronauts have reported impairment in evaluating distances, both on the Moon[3] and during orbital flights. The collision of the *Progres*s spacecraft with the *Mir*

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[3] The following quotes are exerted from the postflight debriefings of the astronauts who walked on the Moon during the *Apollo-12* mission [Godwin, 1999]:

"Everything looked a lot smaller and closer together in the air than it turned out to be on the ground. When we were on the ground, things that were far away looked a lot closer than they really were. The thing that confused me was that we were so close to the Surveyor crater. I didn't realize we were as close to it as we were." —Pete Conrad.

station in 1996 could have been due to a misevaluation by the *Mir* cosmonauts of the actual distance between the two vehicles. I have a personal interpretation for these changes in distance perception [Clément and Reschke, 2008]. I think that perception of absolute distances is altered after a long exposure in a confined environment where there is only a short distance sighting. It is known that distances between objects and the observer are altered when there are no objects with familiar sizes, such as trees, people, or vehicles, in the background. This is the case on the Moon, inside a space vehicle, or any other confined place. People who spend a long time in enclosed chambers, such as divers or submariners, have trouble evaluating distance when they get out. For this reason, submarine crewmembers are not allowed to drive immediately after returning from long tour of duty in the confined space of a submarine.

The objects seen inside the ISS are within distances of several cm to a few meters, whereas the objects outside (Earth or the stars) are very far away. There is no intermediate distance range. It is therefore possible that the perception of the distances to objects is altered in this intermediate range.

Even when objects of a familiar size are present, our perception of distances is different when we look in the vertical direction. For example, when we look down from the top of a 100-m tall building, the people and the vehicles below look noticeably small. But when we look 100 m "down" the street at ground level, we don't comment on how small the people and vehicles look. The reason is that we have learned the "rules" for scaling people at a distance, but not from a height. In the absence of a vertical gravitational reference, the perception of distance might be distorted in the same way as when we look down or up [Clément and Reschke, 2008].

An experiment currently in progress on board the ISS seems to indicate that the astronauts underestimate distance for the intermediate range of 100–1,000 m (Figure 3.10). Also, the perception of distance in the vertical direction, which is clearly overestimated on the ground (e.g., when on top of a building, the people in the streets look small), become as accurate as in the horizontal direction after 1 month in orbit. It is unclear if these illusions are direct effects of reduced gravity on the neuro-vestibular system, as seen in vestibular patients on Earth [Clément et al., 2008b, 2009] or due to other factors of the space environment, such as high contrast, confinement to cramped quarters, and the absence of known landmarks in the crewmember's intermediate space. Nevertheless, these errors in visual perception and misperceptions of size, distance and shape could represent potentially serious problems. For example if a crewmember does not accurately gauge the distance of a target, such as a docking port or an approaching vehicle, then the speed of this target could also be misevaluated. In addition, disturbances in the mental representation of objects and the surround may influence the ability of astronauts to accurately perform perceptual-motor and perceptual-cognitive tasks such as those involved in robotic control.

"In appearances, it took us a long time to convince ourselves that some of the craters which looked so close were really much farther away." —Alan Bean.

"When we were at the ALSEP site, it looked as if we were about 450 feet west and 50 feet north of the position of the LM. It was a pretty good level site. Later when I got back to the LM and looked back, I noticed it didn't look as if the site were that far away. This was the continual problem we had, trying to judge distances." —Alan Bean.

Figure 3.10. ESA Astronauts During a Training Session for the 3D-SPACE Experiment. This ISS Experiment Uses a Head-Mounted Visual Display, a Trackball, and a Digitizing Tablet. The Subject Is Presented with Depth-Related Visual Illusions, or 3D Objects That He Can Adjust So That They Look “Normal”, or Natural Scenes in Which He Has to Judge the Distance Between Identified Landmarks. The Digitizing Tablet Is Used for Neuropsychological Testing of Writing Horizontally and Vertically and Drawing Geometrical Figures with the Eyes Closed. (Credit ESA).

Suspicions are that daylight is not bright on the surface Mars. The sunlight on Mars is about one-half of the brightness of that seen on Earth. The sky of the Red Planet does not appear blue, but pink due to suspended dust, which means that the surface of Mars is, in fact, darker than what is experienced on Earth [Online source: http://quest.arc.nasa.gov/mars/ask/atmosphere/].

Also, on Mars, the terrain may be more sloped than that explored by the *Apollo* astronauts. The astronauts may be traversing areas of deep shadow, possibly requiring the use of lights. Scientists are also investigating options for EVA sensory supplementation. Although vibrotactile and electrodermal cueing systems have been demonstrated in patients, these techniques appear encumbering and impractical, and require that the suit also incorporate a capable inertial attitude and heading reference system. Night vision sensor imagery, an artificial horizon, and a navigation display could also be incorporated into an add-on external heads-up display [Hirmer and Clément, 2011].

3.2.2.2. Hearing

“In space, no one can hear you [scream].” This cliché, which is commonly used in science fiction movies, has apparently not attracted the interest of scientists for studying hearing during spaceflight, since very little data is available yet.

The ISS is a noisy place. To better characterize the acoustic environment, a sound measurement survey is performed once every 2 months to measure the acoustic spectral levels at specified locations. An acoustic engineering evaluation is performed to diagnose acoustic abnormalities, investigate crew complaints, and evaluate effectiveness of newly installed noise reduction measures. Noise exposure levels are measured by crew-worn dosimeters complemented by dosimeters deployed at fixed locations to determine work, sleep, and 24-h noise exposure levels (with a microphone on the shirt collar). Recent data indicate that noise levels on the ISS, even during sleep periods, can average more than 70 dBA,[4] and that the recordings have "maxed out" at over 90 dBA during scheduled sleep intervals.

Several aspects of spaceflight can have an impact on hearing capability: (a) life support equipment is continuously running (ranging from 64 dBA for the air conditioning to 100 dBA for some vent relief valves) and the noise reverberates through the spacecraft's structure; (b) astronauts spend 24-h a day in the office, always close to noise sources; and (c) there is no privacy, with a constant interaction with other crewmembers. Thus quietness periods such as on Earth do not exist: earplugs can reduce noise but not vibrations.

Spaceflight raises a spectrum of noise questions: its effect on perception and performance, adaptation effects, the fatiguing and annoying aspects of noise, and individual sensitivity differences. The degree to which noise and environmental disturbances affect sleep during spaceflight missions remains to be determined. Because certain minimum noise levels are always present, spaceflight potentially constitutes a more stressful noise environment than a simple consideration of decibel levels would imply (Figure 3.11).

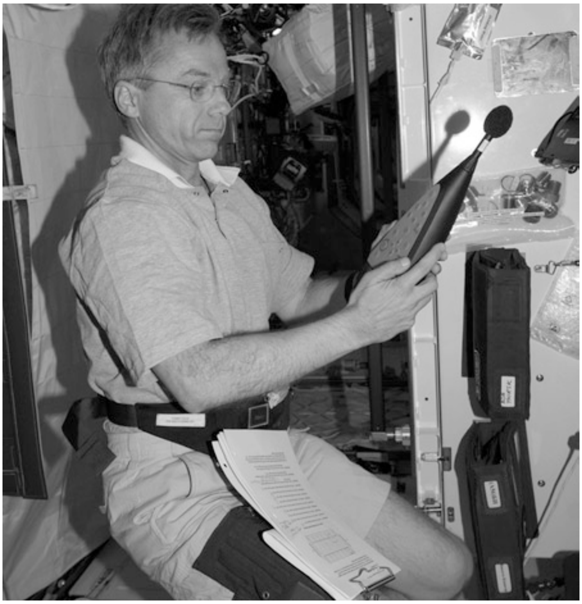

Figure 3.11. Canadian Space Agency Astronaut Robert Thirsk Works with a Sound Level Meter for an Acoustic Survey in the Destiny Laboratory of the ISS. Note the Procedure Documents on His Lap. (Credit NASA).

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[4] The threshold for hearing is defined as 0 dBA, corresponding to corresponds to 0.00000003% of atmospheric pressure (1/30 billionth). The threshold for pain is 0.03% of atmospheric pressure, or approximately 120 dBA. For comparison, a circular saw creates noise levels from 91 to 99 dBA. Even what we call "silence" on Earth is in fact a background noise of about 40 dBA.

Although very stringent noise requirements for ISS result in a noise environment comparable to home and office, intelligibility of hearing as noise increases may vary across individuals. For example, it is known that both the lack of language proficiency and the reverberance in a room impair hearing. The performance of a native English speaker on board the ISS at 60 dBA therefore must to be compared with that of a non-native English speaker at 68 dBA! In addition, low noise levels can also be annoying and affect individual and group (communication) behavior.

The investigation of hearing in astronauts is difficult to conduct during spaceflight because classical hearing assessment techniques do not work in the noisy environments often found in spacecraft (no soundproof laboratory). Because crewmembers are at risk for hearing loss due to noise levels often encountered during spaceflight, techniques and investigation to track this loss are needed during and after the mission.

Auditory brain stem response recordings were investigated during shuttle flights. No significant differences were observed between mean latency values for any potential on the ground or during flight, suggesting that the auditory function is not altered in microgravity [Thornton et al., 1985]. Another experiment performed on *Mir* showed that the localization of a sound source in microgravity was within the same range as on Earth, i.e., between 1° and 2°. Since the faculty of localizing sound sources depends on normal binaural hearing, it was concluded from this study that hearing was not altered in cosmonauts.

3.2.2.3. Smell and taste

It is well known that during spaceflight, astronauts ask for more spices and condiments to add taste to the prepared food. Diminished sensitivity to taste and odor could result from the passive nasal congestion reported in conjunction with the headward shift of fluid. Taste, particularly the non-volatile component mediated by the taste buds, may be susceptible to threshold shifts in microgravity, because of a reduced mechanical stimulation as a result of changes in the convection process.

Evaluation of olfactory recognition using paper impregnated with lemon, mint, vanilla, or distilled water, and taste recognition using solution of solutions of sucrose, urea, sodium chloride, and citric acid, demonstrated no subjective changes in smell or taste function postflight. However, there were large differences among individuals. Some of them could have been due to the reminiscence of space motion sickness symptoms!

Materials used in spaceflight are subjected to testing for odor as well as for flammability and toxicity. Odor evaluations are made by panels of test subjects who rate materials on a scale from 0 (undetectable) to 4 (irritating) with a score of 2.5 (falling between "easily detectable" and "offensive") considered as passing. Nevertheless, because particulate matter does not settle out in weightlessness, odor problems in a space habitat may be more severe than under similar terrestrial conditions.[5]

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[5] An astronaut onboard the ISS reported: "I had the pleasure of operating the airlock for two of my crewmates while they went on several space walks. Each time, when I repressed the airlock, opened the hatch and welcomed two tired workers inside, a peculiar odor tickled my olfactory senses. At first I couldn't quite place it. It must have come from the air ducts that re-pressed the compartment. Then I noticed that this smell was on their suit, helmet, gloves, and tools. […] The best description I can come up with is metallic, a rather pleasant sweet metallic sensation. It reminded me of my college summers where I labored for many hours with an arc-welding torch repairing heavy equipment for a small logging outfit. It reminded me of pleasant sweet smelling welding fumes. That is the smell of space" [Pettit, 2003].

Also, responses to odors can be accentuated by the presence of visual cues. For example, during the earlier Spacelab missions, crewmembers complained of disturbing odors, which they attributed to the primates and test rats which shared their facilities and which were in view [Connors et al., 1985]. In later missions, the animal cages were placed in visually separated areas and no odor problems were mentioned.

3.2.2.4. Proprioception

The absence of gravity modifies the stimuli associated with proprioception and impact spatial orientation, including knowledge of position in the passive limb, difficulty of pointing accurately at targets during voluntary limb movement, modification of tactile sensitivity, and changes in the perception of mass. However, the nature of proprioceptive changes in microgravity has been poorly studied. There is almost no space study of neck and joint angle sensors, and on the role of localized tactile cues in the perception of body verticality.

When crewmembers point at remembered target positions with their eyes closed, they make considerable errors and tend to point low. When they are asked to reproduce from memory the different positions of a handle, the accuracy of setting the handle to a given position is significantly lower with an error towards a decrease of handle deflection angle. Also, when trying to touch various body parts, they usually note that their arms are not exactly where expected when vision is restored. The problem is that these examples are suggestive of either degradation in proprioceptive function, or an inaccurate external spatial map, or both [Watt, 1997; Young, 1993].

An elegant way to evaluate changes in the proprioceptive function is to measure the subjective sensation generated by the stimulation of proprioceptive receptors. A classic technique consists in vibrating a muscle tendon to elicit illusory limb movement. Using this technique, it was observed that the illusion of body tilt forward or backward was less pronounced in-flight than postflight during vibration of lower leg muscles. One interpretation of this result is that the utricles and saccules are unloaded in microgravity and decrease their descending modulation of alpha and gamma motoneurons, resulting in decreased tonic vibration reflexes.

A nice illustration of an alteration of proprioceptive inputs during the early exposure to microgravity is the impossibility for an astronaut to maintain a “vertical” posture, perpendicular to the foot support, in absence of visual information (Figure 3.12). The large body tilt observed in these conditions reveals an inaccuracy in the proprioceptive signals from the ankle joint (or in their central interpretation). After flight day three, however, the astronauts are able to maintain an upright posture, suggesting that adaptive processes take place quite rapidly [Clément and Lestienne, 1988].

Among the somato-sensory systems projecting to the neuro-vestibular system, the position receptors of the cervical column (neck receptors) play an important role. During the Spacelab-*D1* mission, the trunk of a crewmember was passively bent sidewards or forwards, while keeping his head fixed to the floor of Spacelab, thus stimulating the neck receptors. The crewmember reported an illusory rotation of a head-fixed target cross seen in the monitor of his helmet, which was entirely due to the stimulation of the cervical position receptors, since the otoliths were not stimulated.

Another interesting feature of microgravity is that it allows separation between two distinct physical concepts, mass and weight, which both produce similar sensations of heaviness. On Earth, weight can be judged passively through the pressure receptors in

Figure 3.12. An Astronaut with the Feet Attached to the Floor of the Space Shuttle and Placed in Darkness Using an Occluding Goggle Is Instructed to Maintain an "Upright" Posture on Flight Day Two. In the Absence of Gravitational and Visual Inputs, His Body Is Tilted Forward, Suggesting a Recalibration of the Proprioceptive Inputs from the Ankle Joint. (Credit NASA).

the skin, if the object is placed upon a supported limb. Weight can also be judged actively, if the object is held against the force of gravity by the muscular effort, or is repeatedly lifted. Mass can only be judged actively, derived from the force required to produce a given acceleration, or from the acceleration produced by imparting a given force. Thus, active weight perception usually includes mass perception. It is therefore difficult to investigate weight without mass during active movement, except in weightlessness. Using balls of various masses that the astronauts shook up and down moving their arms, it was found that the process of discriminating the mass of objects in microgravity was less accurate than in normal gravity. Weight discrimination was impaired for 2 or 3 days postflight, while crewmembers felt their bodies and other objects to be extra heavy. The impairment in-flight was partly due to the loss of weight information (a reduction in the pressure stimulation), and probably also to incomplete adaptation to microgravity. The increase in apparent heaviness of objects reported for static weight judgment after the flight suggests that some central re-scaling of the static pressure systems had occurred [Ross et al., 1986].

3.3. Posture and movement

Postural activity is the complex result of integrated orientation and motion information from visual, vestibular, and somato-sensory inputs. These inputs collectively contribute to a sense of body orientation and, additionally, coordinate body muscle activities that are largely automatic and independent of conscious perception and voluntary control.

3.3.1. Rest posture

Human factor studies, after investigating photographs taken during *Skylab* missions, have led to the Neutral Body Posture model (Figure 3.13). This model is characterized by a forward tilt of the head (with the line of sight 25° lower than the body-centered horizontal reference), shoulders up (like a shrug), and arms afloat, up and forward with hands chest high.

Recent investigations, taking into account body size, gender, and mission duration suggest, however, that the neutral body posture model is too generalized, and should be modified with additional data to provide more representative spaceflight crew postures. However, it is unclear how the direction of the line of sight has been evaluated from the *Skylab* photographs. Also, the downward deviation of gaze in microgravity in this model is in contradiction with the results of several space experiments that actually measured the eye deviation during spaceflight (see Section 3.3.5).

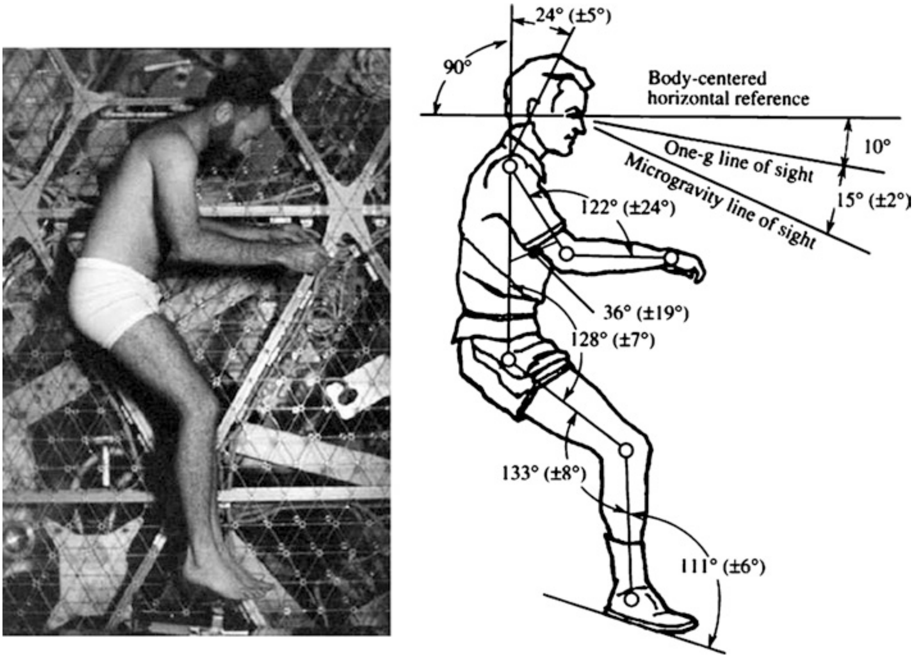

Figure 3.13. The Neutral Body Posture and the Rest Position of Foot, Leg, Hip, Elbow, Shoulder, and Neck Joints in Microgravity, as Well as the Direction of the Line of Sight, Were Modeled Based on the Photographs of Skylab Astronauts. (Adapted from NASA [1995]. Credit NASA).

3.3.2. Vestibulo-spinal reflexes

Two of the more dramatic responses to orbital flight have been postural disturbances and modified reflex activity in the major weight-bearing muscles. For example, monitoring the Hoffman reflex (or H-reflex), which takes advantage of the anatomical pathways that link the otoliths and spinal motoneurons, has been selected as a method of monosynaptic spinal reflex testing to assess otolith-induced changes in postural muscles. In contrast to a doctor tapping a patient's knee to produce the proverbial "knee jerk" reflex, during H-reflex the stimulus is an electrical shock to sensory fibers coming from stretch receptors in the calf (*Soleus*) muscle, and the response is the electrical activity recorded from the muscle. Each time a subject is tested, the number of motoneurons that have been excited by a standard volley of sensory impulses is counted. That number is an indicator of spinal cord excitability. Interestingly enough, this number fell in ISS crewmembers, quite quickly at first and then more gradually over many days. A return to normal was observed within days after landing [Watt, 2001].

When performed in conjunction with linear acceleration, such as "falls" simulated by bungee cords, the H-reflex amplitude is low in-flight, but very large postflight. Interestingly, sudden drops are perceived as falls or drops on Earth, and were felt in-flight much as they were preflight. Later in-flight as well as postflight drops were perceived as more sudden, fast, and hard. During those drops, the subjects did not have a falling sensation, but rather a feeling that "the floor came up to meet them".

Second, extensive dynamic postural testing with a moving platform was performed before and after space missions. Balance control performance has been systematically tested before and after the flight using a computerized dynamic posturography system widely employed for evaluation of balance disorders [Paloski et al., 1993]. This system consists of a platform and a visual surround scene, both of which are motorized to simulate motion. Subjects complete multiple tests before and after the flight to establish stable individual performance levels and the time required recovering them. Two balance control performance tests are administered. The first test examines the subject's responses to sudden, balance-threatening movements of the platform. Computer-controlled platform motors produce sequences of rotations (toes-up and toes-down) and translations (backward and forward) to perturb the subject's balance. The second test examines the subject's ability to stay upright when visual or ankle muscle and joint information is modified mechanically (Figure 3.14).

Postflight measurements revealed significant deviations from the results obtained before flight. The strategy used by the individuals for balancing on the moving platform is modified, and their behavior indicates a decrease in their awareness of the direction and magnitude of the motion. On landing day, every subject exhibited a substantial decrease in postural stability. Some had clinically abnormal scores, being below the normative population 5th percentile. After flights ranging from 5 to 13 days, postflight re-adaptation took place in about 8 days and could be modeled as a double-exponential process, with an initial rapid phase lasting about 2.7 h, and a secondary slower phase lasting about 100 h. The effects of demographic factors like age, gender, and longer mission duration on these responses are currently being evaluated.

Information obtained from these investigations is promising for ground-based clinical research. A relatively large number of individuals on Earth suffer from prolonged, frequently life-long, clinical balance disorders. Disorders like Ménière's disease and

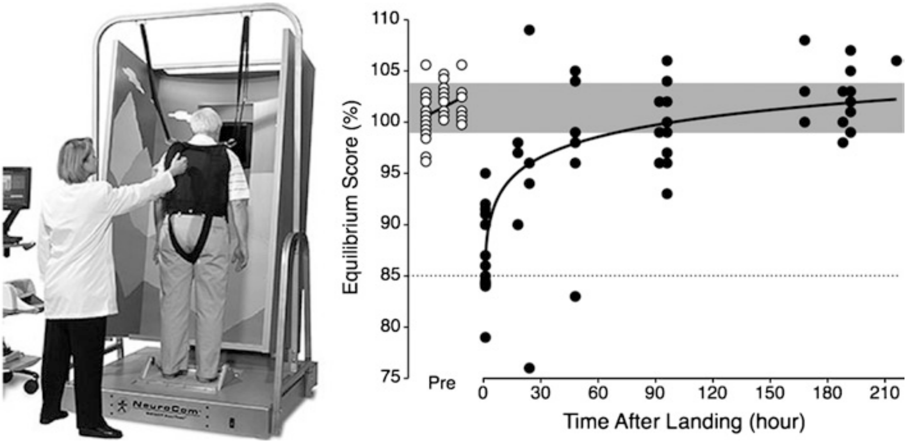

Figure 3.14. Subjects' Ability to Stand as Still as Possible Is Investigated Using a Computerized Force Platform Inside a Visual Booth. The Platform and the Booth Are Designed to Isolate the Multiple Sensory Information Used in Balance – Visual, Vestibular, and Proprioceptive. An Equilibrium Score Is Calculated from Various Sensory Tests, E.g., with the Eyes Open or Closed, the Platform Still or Translating, the Visual Environment Still or Tilting. The Graph Compares the Data for 13 Crewmembers Before (Pre) and After Landing (in Hours Following Shuttle Wheel Stop), Compared with a Large Normative Database. A Few Hours After Landing, the Average Returning Crewmember Was Below the Limit of Clinical Normality (*Dashed Line*). Preflight Stability Levels Were Achieved by 8 Days After Landing, Following a Double Exponential Time Course. (Adapted from Paloski et al. [1993]).

traumatic injuries to the inner ear can severely influence quality of life. Falls are the leading cause of injury-related deaths in the elderly and these numbers continue to increase. Inner ear disorders are thought to account for 10–50% of falls among senior citizens. Currently, human spaceflight is the only means available for studying the response to sustained loss and recovery of inner ear information. Comparison between data from astronaut-subjects and similar data from patients and elderly subjects demonstrates similarities between these balance disorders. One sensible difference is that the posture problems recover in a few days for the astronauts, whereas it can take weeks in the patients, some of who never recover. It is hoped that a better understanding of the strategies used during the recovery process in the astronauts, and of the plasticity of this system in general, will help to improve rehabilitation treatments for patients with balance disorders on Earth.

3.3.3. Locomotion

The cautious gait of astronauts descending the stairs of the "white room" docked with the space shuttle and walking on the runway[6] is an obvious example of changes in

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[6] The ritual of the crew walking on the runway and inspecting the vehicle immediately after landing is called a "walk-around" in NASA jargon. While the astronauts are "kicking the tires," the scientists are impatiently waiting to collect postflight data in the Flight Clinic. It is well known that re-adaptation to Earth gravity is very rapid and the possibility of testing this process at its earlier stage is fundamental for a full understanding of its mechanisms.

sensory-motor coordination. Typically, locomotion in microgravity poses no problem and is quickly learned. However, adaptation continues for about a month. The astronauts who pay a short visit to the ISS note that the long-duration crewmembers move more gracefully, with no unnecessary motion. They can hover freely in front of a display while the new comers would be constantly touching something to hold their position.

When locomoting in space, the astronauts stop using their legs. Instead they use their arms or fingers to push or pull themselves. For clean one-directional movements, a push must be applied through the center of gravity, i.e., just above the hips for a stretched-out body. When translating though, the natural place for the arms is overhead to grab onto and push off from things as they come whizzing by. This is the worst possible place from the physics of pushing and pulling for clean movements, for by exerting forces with arms overhead, some unwanted rotations will inevitably occur, which must be compensated with ever more pushes and pulls, giving an awkward look to the whole movement. "To cleanly translate, the best is to keep the hands by the hips when exerting forces and boldly go headfirst. This way the pushing and pulling is directed through the body's center of gravity and gives nice controlled motions without unwanted rotations." [Pettit, 2003].

Movement in a weightless environment obeys to the Newton's laws of motion. Friction forces are negligible and the angular momentum is always conserved unless acted on by an outside torque. Filmed sequences of astronauts performing a number of gymnastic moves in space were analyzed frame-by-frame. The principle of conservation of angular momentum was demonstrated as the astronauts tumbled, twisted and rotated in space. Throughout their motion and up until they entered in contact with the wall, the angular momentum was constant at 35.7 ± 1.2 kg × m^2/s while rotating freely.[7]

Since legs are used less for locomotion, new sensory-motor strategies emerge in microgravity. Some of this newly developed sensory-motor program "carries over" to the postflight period, which leads to postural and gait instabilities upon return to Earth. Both U.S. astronauts and Russian cosmonauts have reported these instabilities even after short-duration (5–10 days) spaceflights. Subjects experienced a turning sensation while attempting to walk a straight path, encountered sudden loss of postural stability especially when rounding corners, perceived exaggerated pitch and rolling head movements while walking, and experienced sudden loss of orientation in unstructured visual environments. In addition, oscillopsia and disorienting illusions of self-motion and surround-motion occurred during head movement induced by locomotion.

The beginning of the stance phase of locomotion, when initial foot-ground contact occurs, is characterized by a rapid deceleration of the foot. The forces created by the heel strike impact travel through the body and reach the head. The head-neck-eye complex then operates to minimize angular deviations in gaze during locomotion

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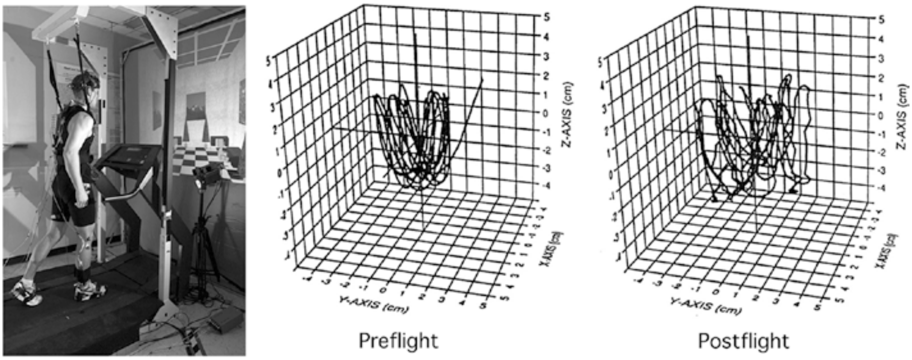
[7] Dan Barry, an astronaut of the *STS-96* Shuttle mission, got stranded in the middle of an ISS module, with the help of two fellow crewmembers. He then tried to kick himself over to the wall. He recalled later: "When I reached out an arm, my body moved back and my center remained in the middle of the room. I instinctively tried moving fast, then slow, and then bicycled my legs. None of it helped. I just had to wait for the air currents to drift me to the wall. Sneezing and spitting didn't do much good either. On the other hand, throwing clothing as fast as I could produced enough reaction to send me to the opposite wall.

[Pozzo et al., 1990]. After spaceflight, however, changes have been documented in both head-trunk and lower limb patterns of coordination. Bloomberg et al. [1997] reported changes in head pitch variability, a reduction of coherence between the trunk and compensatory pitch head movements, and self reports from crewmembers that indicated an increased incidence of oscillopsia (the illusion of a visual surround motion) during postflight treadmill walking (Figure 3.15). A number of characteristics of walking also appear to be changed after spaceflight. For example, during the contact phase of walking, the foot "thrusts" onto the support surface with a greater force than that observed before flight.

The alterations in locomotion seen after spaceflight raise some concern about the crew capability for unaided egress from the *space shuttle* or the *Soyuz* in a case of emergency. As discussed earlier, many crewmembers experience marked vertigo when making head movements during re-entry, landing, and afterwards. This vertigo could be a major obstacle to successful egress if vision were impaired, as with a smoke-filled cabin. An interesting investigation was performed by Bloomberg et al. [1999], in which the ability for crewmembers to repeat a previously seen trajectory without vision was examined. When attempting to walk a triangular path after flight, blindfolded subjects showed both under- and over-estimations of the distances walked, but a correct estimation of the angle turned. These results suggest a difficulty for reconstructing motion cues from the otoliths, but not from the semicircular canals. However, the changes found could also be related to the lower walking velocity during postflight testing. These results imply that mechanisms like computing self-displacement and updating spatial information (both of which being also called navigation) are disturbed by spaceflight and have to be reacquired after return to Earth.

Apollo astronauts fell frequently on the surface of the Moon. In particular, the high and rearward center of gravity of the Apollo suit influenced upslope walking, and the stiffness of the inflated suit strongly influenced gait, and made it impossible to squat to retrieve dropped objects. New requirements for suit center of gravity and biomechanical properties of various motions on the Martian surface must be defined.



Preflight

Postflight

Figure 3.15. Head Movements Along the Fore-Aft (*X*), Lateral (*Y*), and Vertical (*Z*) Directions in One Crewmember During Walking on a Treadmill Before Spaceflight and on the Day Following Landing of the Space Shuttle. (Adapted from Bloomberg et al. [1999]).

It is highly desirable to reduce the incidence of falls not only to reduce the residual medical risks, but also because falls cut into EVA efficiency, and regaining one's feet requires physical effort. Once tired, an astronaut might be expected to fall more frequently – a phenomenon very familiar to any beginner skier. Preflight sensorimotor locomotion training might help to expand the repertoire of automatic motor responses to locomotor disturbances [Paloski et al., 2008].

3.3.4. Body movement

On Earth's surface, gravity significantly affects most of our motor behavior. It has been estimated that about 60% of our musculature is devoted to opposing gravity. For example, when making limb movements during static balance, anticipatory innervations of leg muscles compensate for the impending reaction torques and the changes in location and projection of the center of mass associated with these movements. Similar patterns of anticipatory compensations are seen in-flight, although they are functionally unnecessary. Also, rapidly bending the trunk forward and backward at the waist is accompanied on Earth by backward and forward displacements of hips and knees to maintain balance. The same compensatory movements of hips and knees are made in weightlessness. Because the effective gravity torques are absent during spaceflight, the innervations necessary to achieve these synergies in weightlessness are different from those needed on Earth. Consequently, these in-flight movements must reflect reorganized patterns of muscle activation.

During the first space experiments in which I participated in 1982, which were conducted on board the *Salyut-7* space station, we found that dorsi-flexor muscles, e.g., the *Tibialis anterior* leg muscle, assume a larger role in space than on Earth in regulating the orientation of the individual relative to his/her support. This is in contrast with the general use of muscle extensors on Earth, which are used to counteract gravity. This transfer of motor strategies from one muscle group to another explains the forward tilted posture of crewmembers placed in darkness when instructed to maintain a posture perpendicular to the foot support (see Figure 3.12).

Using a simple ball catching experiment in weightlessness, it has been elegantly shown that the central nervous system uses an internal estimate of gravity in the planning and execution of movements. During the act of catching a ball on Earth, the brain estimates the trajectory of the ball, accurately taking into account its downward acceleration due to gravity. In space, a seated astronaut was required to catch a ball traveling at a constant velocity, in contrast to the constant acceleration that would occur on Earth (Figure 3.16). The ability to anticipate and predict is one of the nervous system's basic functions. When we catch a ball, the brain does not wait for it to touch the hand before stimulating arm flexor muscle contraction to compensate for the impact. About one third of a second before impact, the brain elicits just the right amount of contraction to counteract the force exerted, which itself depends on the weight of the object combined with the acceleration of its fall. The experiment led to the conclusion that the brain works by anticipating the effects of gravity on the ball rather than by making direct measurements of its acceleration. This anticipation ability remains even in conditions of weightlessness. Thanks to childhood experience, the brain possesses internal models of the gravity laws governing the behavior of a falling object, and perhaps more generally, Newton's law of mechanics. We see here the beginnings of

Figure 3.16. Ball Catching Experiment During the Neurolab STS-90 Mission. A Ball Was Thrown at the Subject at a Constant Velocity. The Trajectory of the Subject's Arm and the Activity of His Forearm Muscles Were Recorded as He Was Trying to Catch the Ball. (Credit NASA).

an adaptation to new laws. A longer period in weightless flight would now be needed to assess how such an adaptation might develop [McIntyre et al., 2001].

Likewise, the analysis of astronauts' writing or drawing showed that such fine movements are not altered in microgravity. When cosmonauts were asked to draw "horizontal" ellipses in the air without the aid of vision, results indicated minimal changes as a function of microgravity, suggesting that the body (egocentric) reference system was not disturbed. The subjects were capable of maintaining a sense of verticality despite disappearance of the main factor contributing to verticality on Earth, i.e., the gravitational force [Gurfinkel et al., 1993]. However, bending the head over the trunk causes the cosmonauts arm movement pattern to be more aligned with the head vertical axis, indicating that the head axis could also be used as a reference frame.

3.3.5. Eye movement

Eye movement is probably the response of the vestibular system that has been the most studied during spaceflight. For several decades, the study of eye movements has been a source of valuable information to both basic scientists and clinicians. The singular value of studying eye movements stems from the fact that they are restricted to rotations in three planes and the eyeball offers very little inertia to the eye. This facilitates accurate measurement (for example using video eye recording in near infrared light), a prerequisite for quantitative analysis.

Eye movements must continuously compensate for head movements so that the image of the world is held fairly steady on the retina, and thus appears clear and stationary. During head movements, the vestibular apparatus measures head velocity and relays this information to those centers controlling eye position to generate compensatory eye movements; this reflex behavior ensures that vision is not blurred. When performed in darkness, this leads to a pattern of rhythmic eye movements known as nystagmus, consisting of slow phases in the direction opposite to the head and fast phases that bring the eye back when it reaches the extreme of its travel. The nystagmus response to a rapid head movement outlasts the changes in signals in the semicircular canals, through the activation of a velocity storage mechanism located in the brainstem.

This so-called “vestibulo-ocular reflex” has been studied systematically in orbital flight, both during active (voluntary) and passive movements of the head [Clément, 1998]. With my co-investigators, we were the first to report that the amplitude of vertical eye movements was decreased during the first 3 days of weightlessness compared to normal value on Earth, but not the horizontal eye movements. In this experiment, the eye movements of an astronaut were recorded when he voluntary moved his head while either fixating a visual target or imagining that target in darkness. During the first few days in orbit, the vestibulo-ocular reflex was less efficient in stabilizing the visual image. This response recovered quickly, but subsequent investigations confirmed that after spaceflight, the pattern of eye and head movements was again significantly altered when subjects moved their head in an attempt to fixate a visual target (Figure 3.17).

Problems in hand-eye coordination and blurriness of the visual scene when re-entering in normal gravity have also been reported after long-duration missions. Tracking of moving visual targets seems to be altered, especially in the vertical direction. After landing, subjects have difficulties following a vertically moving visual dot. When the target moves up, the eyes try to catch-up the visual target with fast saccades rather than smooth pursuit. The vestibular nuclei located in the brain stem are part of a system that allows one to fix the gaze on a stationary target during voluntary head motions as well as to track moving targets. This system appears to be disturbed during spaceflight, presumably as a consequence of altered vestibular receptor function due to the absence of gravity. These deficits might pose a problem for piloting tasks during landing on Mars.

One problem in studying eye movements by asking subjects to perform voluntary head movements is that the CNS is “aware” of the movement to be performed. A copy of the motor command (the so-called efference copy) is presumably sent to the eye-head coordination control system, and this helps to achieve the adequate, compensatory eye movements. For this reason, scientists also use passive rotation generated by servo-controlled rotating chair or sled to generate unpredictable inertial stimulation of the vestibular system and to study the resulting responses. Several of these devices have flown on board the Spacelab. In 1985, a 4-m linear sled generated sinusoidal oscillations in subjects sitting either facing the track, or perpendicular to it, or lying

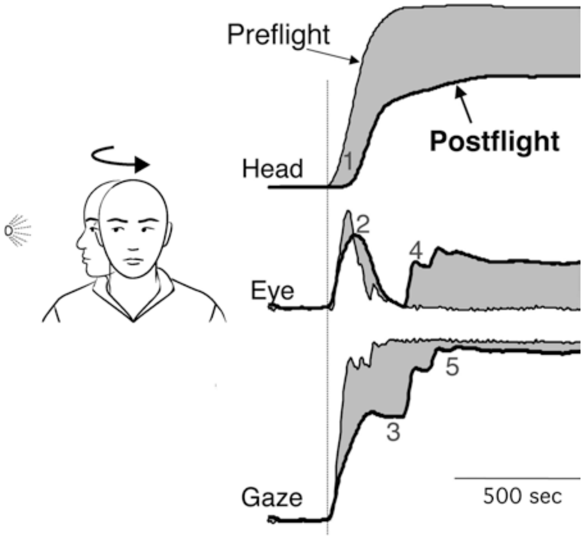


Figure 3.17. The Ability to Maintain Visual Fixation on Targets While Turning the Head Is Diminished Immediately After Landing. Compared with the Preflight Response, the Head Movement Is Delayed and Its Amplitude Is Reduced Postflight (1). As a Consequence, the Vestibulo-Ocular Reflex Is Initiated at an Inappropriate Time (2), Pulling Gaze from Target (3). Large Eye Saccades (4) Are Then Required to Direct Gaze Back on Target (5).

on their back. The peak linear acceleration was 0.2 g. Absolute thresholds for the perception of linear acceleration in-flight and postflight were found to be elevated in some astronauts and lowered in others for some axes, relative to ground-based controls. Another measure of linear acceleration sensitivity, the time elapsed from acceleration onset to reports of self-motion, which varies inversely with magnitude of acceleration, have been more consistent. Results indicate an elevation of the sensitivity when linear accelerations are exerted along the body longitudinal axis, and a decrease in sensitivity for the other axes. It is, however, difficult to rule out a contribution of the somato-sensory sensation in these results.

In 1992, a rotating chair flew on board the Spacelab *IML-1* mission, allowing the evaluation of the vestibulo-ocular reflex evoked by passive rotation of four crewmembers about the yaw, or pitch or roll axis, during the course of a 7-day spaceflight. Results showed that the responses generated by rotation in pitch and roll were the most affected in space.

More recently, in 1998, a human-rated centrifuge flew on the Neurolab mission, in which crewmembers were both exposed to angular and linear acceleration (see Figure 1.23) One objective of this experiment was to study the adaptation of the CNS by measuring the eye movements in response to angular and linear acceleration in space. Eye rotations can compensate for both the rotational and the translational components of head motion. On the Earth's surface, two major sources of linear acceleration are normally encountered. One is related to the Earth's gravity: the gravitational force pulls the body toward the center of the Earth, and the body opposes this force to maintain an upright standing posture. The other sources of linear acceleration arise in the side-to-side, up-down, or front-back translations of the head, which commonly occur during walking or running, and from the centrifugal force sensed when turning or going around corners. The body responds by tending to align the longitudinal body axis with the resultant linear acceleration vector. Put in simple terms, we have to exert an upward force such as to balance gravity when standing upright and to tilt into the direction of the turn when in motion. As mentioned above, in microgravity, the otoliths are not stimulated by head tilt, and therefore the eye movements in response to head pitch or roll are likely to be altered during and after spaceflight. The results of the centrifuge experiment have not confirmed this hypothesis, though: the torsional (along the line of sight) eye movement elicited by the linear acceleration (known as ocular counter-rotation) was unchanged in-flight and postflight relative to preflight. More investigations are therefore necessary to fully understand the adaptation of the compensatory eye movements during spaceflight.

New tests of the otolith function are currently introduced to evaluate the re-adaptation of eye movements in response to body tilt after spaceflight. Recently, we investigated the eye movements and the perception of crewmembers exposed to body rotation about an axis tilted from Earth's vertical (Figure 3.18, left). This off-vertical axis rotation (OVAR) causes, when rotation is in darkness at a constant low velocity, the perception of being successively tilted in all directions. Consequently, both a counter-rotation of the eyes and a perception of moving along the edge of an inverted cone, appear. At higher rotation rates the illusion is that of being upright, but moving along the edges of a cylinder (hence more translational motion), and eye movements are predominantly horizontal. Astronauts returning from space missions generally experience a larger

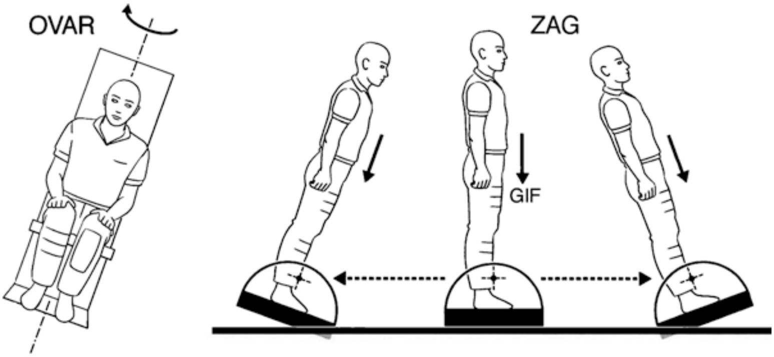


Figure 3.18. ***Left*. A Subject Rotating at Constant Velocity About an Axis Tilted Relative to the Vertical (Off-Vertical Axis Rotation) Has the Illusion of Describing Either a Conical or a Cylindrical Motion When Rotation Is at Low or High Velocity, Respectively. *Right*. In the z-Axis Aligned Gravitoinertial Force (ZAG) Paradigm, the Subject Is Sinusoidally Translated While Simultaneous Tilted Such as the Gravito-Inertial Force (GIF) Remains Aligned with the Longitudinal Body Axis.** Both OVAR and ZAG Allow the Investigation of the Ambiguity Between tilt and Translation Motion Perception During Stimulation of the Otoliths on Earth [Clément and Reschke, 2008]. (Credit Philippe Tauzin).

sense of translation during OVAR than preflight [Clément et al., 2007]. A follow-up experiment is currently being conducted to evaluate perceived tilt and translation in astronauts returning from spaceflight when they are exposed to ambiguous inertial motion cues. During this z-axis aligned gravito-inertial force (ZAG) paradigm, the astronauts sit in a chair that tilts within an enclosure that simultaneously translates so that the resultant linear acceleration vector remains aligned with the subject's longitudinal body axis (Figure 3.18, right). This condition provides a spaceflight analog in that tilt signals from the semi-circular canals conflict with the otolith signals that do not indicate tilt. The crewmembers generally perceive larger translational motion during this passive stimulation immediately postflight compared to preflight, which is in agreement with the OTTR hypothesis [Clément et al., 2008a].

Another experiment is being performed on crewmembers of the last shuttle missions, in preparation for the Mars landing. Subjects in complete darkness ride a motion-base simulator that moves in pitch, roll or translate, and they use a joystick to null-out these motion disturbances [Clément, 2011]. A tactile display countermeasure is being evaluated as an aid to piloting performance. The tactile display consists of a matrix of electromechanical tactile stimulators applied on the subjects' torso. These tactors convey orientation cues to the skin, such as the individual's amplitude of body tilt relative to gravity. Preliminary results indicate that such aid is a promising tool for reducing spatial disorientation mishaps by overcoming the limitations of multi-sensory integration when sensorimotor function is compromised [Rupert, 2000].

Another otolith test is achieved using a centrifuge where sitting subjects are displaced minimally from the rotation axis, so that one labyrinth becomes aligned on-axis, while the second labyrinth alone is exposed to the centripetal acceleration. This technique allows investigating subjective vertical and otolith-ocular responses during stimulation of the otolith on one side at a time.

It is interesting to note that the motion perception of astronauts when exposed to linear translation, centrifugation, or OVAR is fundamentally different postflight compared to preflight, whereas the eye movements, in particular torsion, are not. This dissociation between otolith-driven eye movement and perception during passive vestibular stimulation after spaceflight suggests that eye movements and orientation perception are governed by qualitatively different neural mechanisms. Ocular torsion is primarily a response of otolith activation by low-frequency linear acceleration along the interaural axis, whereas perception of tilt is primarily governed by the integration of graviceptive cues, including somesthetic, presumably centrally processed through neural models of the physical laws of motion. The peripheral vestibular organs would experience little or no changes after spaceflight (at least after short-duration flights), but the central processing of graviceptors inputs and the outputs of internal models for spatial orientation are likely to be affected. This dissociation would explain why otolith-driven eye movements appear relatively unaffected by microgravity, while perceptual and oculomotor responses depending on central vestibular processing can be greatly disrupted. Whether such dissociation is still present after longer stay in microgravity remains unknown.

Very recently, scientists have discovered that, on Earth, the eye movements also reflect an orientation to the resultant linear accelerations during turning. During either passive rotation, as in a centrifuge, or while walking or running around a curved path, the axis of eye rotation tends to align with the resultant axis of the summed linear accelerations. The same phenomenon occurs when viewing a visual scene that moves in the horizontal plane, but with the head tilted to the side. The eye movements (also called optokinetic nystagmus) are then oblique relative to the visual scene, as if they tried to align with the resultant of visual motion and gravity. Space experiments have shown that this gravity-oriented response was absent in microgravity, and that a return to the normal preflight response was observed 2 days after return to Earth.

Our eyes can rotate around three axes whereas normally only two are used in normal gravity. The plane where these axes are positioned is named "Listing's plane". This plane normally holds an upright position, but there are indications that its orientation changes in some conditions, such as in patients with vestibular disorders. A recent experiment performed onboard the ISS indicated that the orientation of the Listing's plane was consistently altered in some crewmembers in 0 g. Its elevation was tilted backwards by approximately 10°, and the azimuth angles of the left and right eyes also diverged in 0 g, with a statistically significant in the vergence angle and torsional eye position [Clarke, 2008]. It appears that given the lack of voluntary control of ocular torsion, the tonic otolith afferences are instrumental in the stabilization of torsional eye position and consequently of Listing's plane. The torsional divergence is the largest in those astronauts who also exhibit space motion sickness, which supports the otolith asymmetry hypothesis in generating space motion sickness (see Section 3.5.2).

On Earth, the eye movement responses tend to be asymmetric for upward and downward stimulation. For example, it is generally easier to follow a visual scene moving upward than downward. The interpretation generally proposed for this phenomenon was the following: when we walk, there is an apparent downward motion of the floor. However, this motion would be ignored, and the downward eye movements suppressed to pay more attention to a further distance in case obstacles could occur. Space experiments have shown that the vertical asymmetry tends to be eliminated in spaceflight, suggesting instead a role of gravity (presumably through a role of the otolith signals on the eye position) in this phenomenon [Clément, 1998].

3.4. Spatial orientation

3.4.1. Visual orientation

The visual system is addressed here principally in the context of its relationship to the vestibular system. Vision may compensate in large measure for modified otolith sensitivity. It helps in spatial orientation, and is essential to motor coordination. Astronauts working in microgravity must rely much more on vision to maintain their spatial orientation, as otolith signals no longer signal the direction of "down." It has long been known that moving visual scenes can produce compelling illusions of self-motion ("seeing is believing"). These visually induced illusions become even stronger in space, because visual cues are unhindered by constraints from the otoliths, which in microgravity do not confirm or deny body tilt. This has been confirmed in experiments wherein crewmembers observing a rotating visual field felt a larger sense of body rotation in space than on Earth [Lackner and DiZio, 2000]. It is interesting to note that frogs born in microgravity also showed stronger behavioral response to moving visual scenes when tested after their return to Earth than control animals born on Earth.

Crewmembers who remained seated in the relatively small *Soyuz*, Mercury, Gemini, and Apollo capsules rarely encountered orientation problems. However crews of the larger *Skylab* and shuttle reported occasional disorientation, particularly when they left their seats, and worked in unpracticed, visually unfamiliar orientations. The problem occurred both inside the spacecraft, and also outside, as when performing an EVA (Figure 3.19). For example, Bernard Harris, an astronaut of the *STS-63* shuttle mission reported: "As I was getting ready to step out of the spaceship, it felt like gravity was going to grab hold of me and pull me down toward Earth". Your natural response is to hesitate and grab on harder. I felt myself hanging on to the handrail and saying: "No, you're not going to fall toward the Earth, this is the same thing you've been seeing for the last 5 days."

Although episodes of visual disorientation are observed by many crewmembers, some seem more affected than others. In some individuals, static visual cues become increasingly dominant in establishing spatial orientation in microgravity. Other subjects are more "body oriented" and align their exocentric vertical along their longitudinal body axis. The latter individuals exhibit no problems in spatial orientation aloft even in the absence of visual cues for vertical orientation. Further, these individuals appear able to strengthen their perception of subjective verticality by using localized tactile cues, especially by pressure exerted on the soles of their feet.

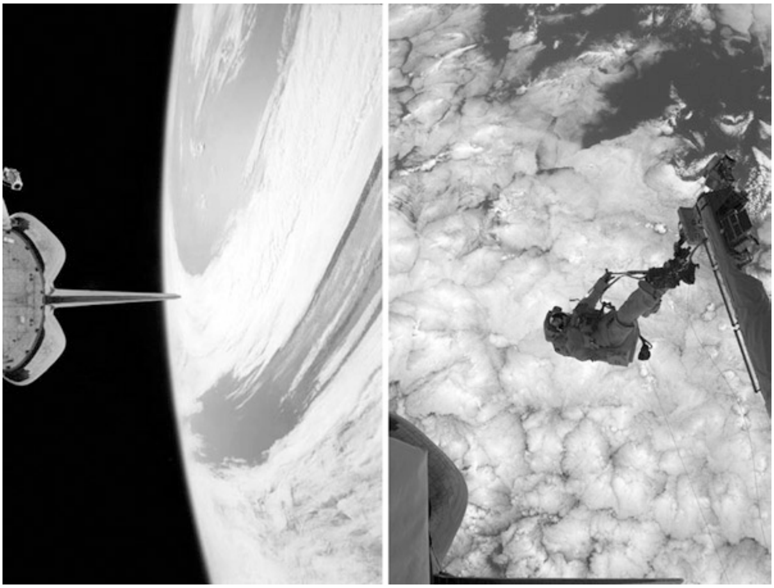


Figure 3.19. ***Left*: Because the Observation Windows of the Shuttle and ISS Face Earth, Astronauts Often Have the Sensation of Looking "Down" to Earth. *Right*: Astronauts During EVA Occasionally Feel Uncomfortable When Working Upside-Down or When Their Feet Point to the Earth "Below".** (Credit NASA).

Part of the difficulty of the people who predominantly rely on visual cues for spatial orientation is a result of the natural tendency to assume that the surface seen beneath our feet is the floor. When working "upside down" in the spacecraft, the walls, ceiling, and floors then frequently exchange subjective identities. Also, when viewing another crewmember floating upside down in the spacecraft, they often suddenly feel upside down themselves, because of the subconscious assumption carried over from life on Earth that people are normally upright. Fluid shift and the absence of otolith cues also contribute, and make some crewmembers feel continuously inverted, regardless of their actual orientation in the spacecraft. The inversion illusion may be understood using a model that includes an internal (idiotropic) orientation vector. This vector may also explain the sensation of the "downs" [Mittelstaedt and Glasauer, 1993].

There is also a natural tendency to perceive Earth as "down." Consequently, when looking at the Earth out of a window "above" their head, some crewmembers may feel that they are just standing on their head. Astronauts often report "if you lose something in weightlessness, you instinctively look down, which of course is not the solution" [Pettit, 2003].

It was once thought that these inversion illusions could trigger attacks of space motion sickness during the first several days in weightlessness. Many crewmembers have reported getting sick when looking out the space shuttle middeck window and find Earth at the top of the window frame instead of the bottom. However, though space sickness susceptibility eventually subsides, crewmembers on long-duration flights say that visual illusion episodes continue to occur. The observation that inversion illusions do not provoke space motion sickness as the flight progresses indicates a resolution of the factors that triggered the motion sickness early on. As a countermeasure for these visual illusions, it is thought that visual experience of working in unfamiliar orientations during preflight neutral buoyancy training (in a water tank) and virtual reality might help maintain spatial orientation while on orbit.

3.4.2. Cognition

The word "cognition" is often used in computer science-related fields to denote the level of activities that require "understanding" of what is going on, rather than merely signal-level reaction. We will review here the few cognitive functions that have been investigated during and after spaceflight.

Brain functions have developed on an evolutionary time scale to deal with the specific constraints that gravity imposes on human behavior. For instance, the world in which we live is primarily two-dimensional, particularly for Earth-bound creatures such as humans. While humans have constructed massive, three-dimensional (3D) structures such as skyscrapers, these edifices can essentially be described as multi-layered two-dimensional (2D) environments. Neural processes that allow us to navigate within this world may thus be specialized for the representation of 2D spatial maps. On Earth, we also expect to see objects disposed in particular fashions within the environment: objects lying on a table will usually be found in a stable upright or horizontal position; objects in free fall accelerate downward; we usually meet people in an upright position. In building these expectations, we are essentially modeling the expected behavior of objects in the world. These models can be used to predict upcoming events and optimize performance on a variety of cognitive tasks [McIntyre et al., 2001].

3.4.2.1. Navigation

Vertebrate brains form and maintain multiple neural maps of the spatial environment that provide distinctive, topographical representations of different sensory and motor systems. For example, visual space is mapped onto the retina in a 2D coordinate plan. This plan is then remapped to several locations in the central nervous system. Likewise, there is a map relating the localization of sounds in space and one that corresponds to oculomotor activity. An analogous multi-sensory space map has been demonstrated in the mammalian hippocampus, which has the important function of providing short-term memory for an animal's location in a specific spatial venue. This neural map is particularly focused on body position and makes use of proprioceptive as well as visual cues. It is used to resume the location at a previous site; a process called navigation.

This system of maps must have appropriate information regarding the location of the head in the gravitational field. So it follows that the vestibular system must play a key role in the organization of these maps. Only recently has this been demonstrated by experiments carried out in space. During an experiment performed on board Neurolab, rats ran a track called the Escher staircase, which guided the rats along a path such that they returned to their starting location after having made only three 90° right turns. On Earth, rats could not run this track. But in space, it provided a unique way to study the "place cells" in the hippocampus that encode a cognitive map of the environment. The rats had multi-electrode recording arrays chronically implanted next to their hippocampal place cells. Recordings in space indicated that the rats did not recognize that they were back where they started, after only three 90° right turns.

Such studies could help to explain the visual inversion illusions and the navigation difficulties experienced by some astronauts when they arrive in space. A weightless environment presents a true 3D setting where Newton's laws of motion prevail over Earth-based intuition. We normally think in terms of two dimensions when we move from place to place. However, in orbit, one might decide the best way is to go across the ceiling and then sit on a wall.

In addition, each module of the ISS provides a local visual frame of reference for those working inside. Inside the ISS, the modules are connected at 90° angles, so not all the local frames of reference are co-aligned. It is sometimes difficult to remain oriented, particularly when changing modules. Even after living aboard for several months, it is difficult to visualize the three-dimensional spatial relationships among the modules, and move though the modules instinctively without using memorized landmarks. Crewmembers not only need to learn routes, but also develop 3D "survey" knowledge of the station. Disorientation and navigation difficulties could be an operational concern in case an emergency evacuation is required in the event of a sudden depressurization or fire. Researchers are working on you-are-here maps that would be displayed in strategic locations on the ISS, so that visitors, first time or experienced astronauts, will be able to quickly identify escape route or emergency equipment.

3.4.2.2. Mental rotation

On Earth, gravity provides a convenient "down" cue. Large body rotations normally occur only in a horizontal plane. In space, the gravitational down cue is absent. When astronauts roll or pitch upside down, they must recognize where things are around them by a process of mental rotation that involves three dimensions, not just one.

It is well known that on Earth, a familiar visual environment, a face or a printed text cannot be recognized or analyzed when it is tilted by more than roughly 60°. In a very simple experiment, I once asked one crewmember to report the tilt angle of his body with respect to the inside of the spacecraft from which he had more difficulty in mentally rotating the visual features. The reported angle was about 60° on the first day in-flight, 90° on the second day, but after 3 days in-flight his perception was independent of the respective orientations. One interpretation is that weightlessness, by providing a release of the gravity-dependent constraint on mental rotation, would facilitate the processing of visual images in any orientation with respect to the body axis.

In a series of subsequent mission, a mental rotation paradigm with pictures of 3D objects was tested on several cosmonauts (Figure 3.20). Responses showed that the average rotation time per degree was shorter in-flight than on the ground. This difference seems to be particularly marked for stimuli calling for mental rotation about a roll or a pitch axis. An actual body rotation around both of these axes would induce different responses from the otolith organs in weightlessness compared to Earth. However, a later study in which the repertoire of objects was different among all experimental sessions to avoid a learning effect, showed no significant differences in rotation time in space versus ground data [Léone, 1998]. So, the results are inconclusive at this point and further studies are needed to investigate whether mental rotation is facilitated or not in microgravity. One concern is that a poorer ability to mentally rotate the visual environment could be a determinant factor for the apparition of space motion sickness. Another concern is the ability for the astronauts to recognize their fellow crewmembers when upside-down. However, preliminary tests suggest that after a few days in space it is less difficult to identify an upside-down face (the so-called "inversion effect") in space than on Earth.[8]

Other experiments have investigated whether it was easier to detect the presence of a symmetry axis in absence of gravity. For example, it is well known that on Earth, the

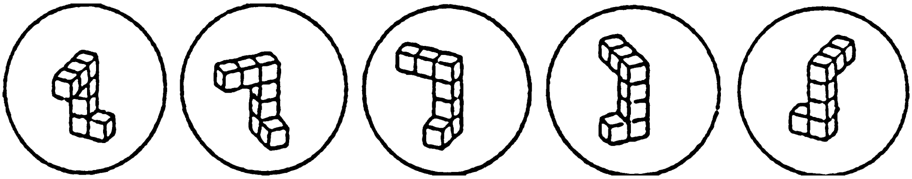


Figure 3.20. Examples of Shapes Used for a Mental Rotation Test. When the Shape on the Extreme Left Is Presented with, Let's Say, the Shape on the Extreme Right (a 180° Rotation), the Time Taken to Decide that Both Shapes Are the Same Is About 5 s. When the Shape on the Extreme Left Is Presented with the Shape in the Middle (a 90° Rotation), the Response Time Is Now Only 2.5 s. Therefore the Speed of Mental Rotation in This Test Is About 33°/s.

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[8] There was one instance on a shuttle mission where a crewmember was "lost". Several of his crewmates looked for this individual but couldn't find him…yet all the while he was right in front of them. The lost crewmember was actually inverted relative to those looking for him [Millard Reschke, 2006].

vertical axis of symmetry is easier to identify than a horizontal or an oblique axis of symmetry. A change in the position of the head relative to the trunk on Earth influences symmetry detection. One experiment performed in space on five astronauts indicated that both vertical and horizontal axes of symmetry were equally easy to identify [Léone, 1998].

Interestingly enough, mental tasks that demand logical reasoning, decision-making, as well as memory retrieval functions, seem unimpaired during spaceflight. This result is in conflict with what is frequently reported by crewmembers. That is, it is difficult to evaluate elapsed time periods while in space.

3.4.2.3. Mental representation

An accurate representation of the visual environment is crucial for the successful interaction with objects in an environment. It is clear that humans have mental representations of their spatial environment and that these representations are useful, if not essential, in a wide variety of cognitive tasks such as identification of objects and landmarks, guiding actions and navigation, and in directing spatial awareness and attention.

In physics, a coordinate system that can be used to define position, orientation, and motion is called a reference frame. It has been argued that the Earth's gravitational field is one of the most fundamental constraints for the choice of reference frames for the development and the use of cognitive representations of space. For example, a subject looking at a diamond-shaped figure (in retinal coordinates) perceives a square-shaped figure when he/she and the figure are both tilted relative to gravity. This result indicates that the perception of the form of an object generally depends more on the orientation of the object in world (spatial) coordinates than on its orientation in retinal coordinates. In other words, gravity is critical for the extraction of an object's reference frame.

One problem with ground-based studies on perception is that tilting the observer relative to gravity on Earth creates a conflict between perceived gravitational (extrinsic) vertical and retinal- or body-defined (intrinsic) vertical, but does not suppress the gravitational information. On the other hand, the loss of the gravitational reference in spaceflight provides a unique opportunity to differentiate the contribution of intrinsic and extrinsic factors to the spatial orientation system.

Measuring the changes in the mental representation of an object throughout a space mission is a simple way to assess how the gravitational reference frame is taken into account for spatial orientation. Results of space studies by our group suggest that the absence of the gravitational reference system, which determines on Earth the vertical direction, influences the mental representation of the vertical dimension of objects and volumes. For example, I once asked a French astronaut to write his name with his eyes closed vertically and then horizontally on a notebook attached by Velcro to his knee. The physical length dimension of these words on the page was compared between in-flight and preflight tests. Results showed that the length of the written words decreased in-flight for both vertical and horizontal directions, but the vertical direction was the most affected [Clément et al., 1987]. In another astronaut, the reduction in the vertical length of words was observed during several days after returning from a 28-day space mission (Figure 3.21). It is interesting to note that in both experiments,

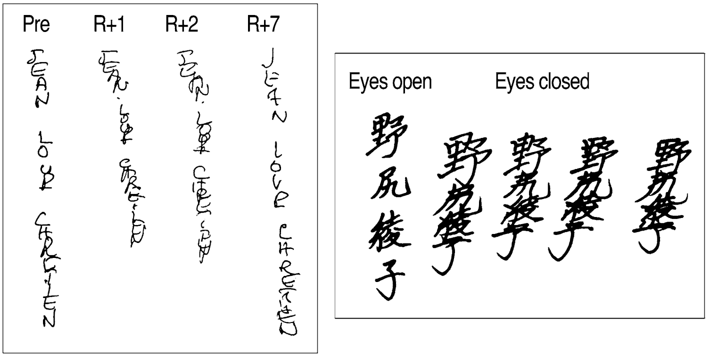

Figure 3.21. ***Left*: Vertical Writing Test with the Eyes Closed in an Astronaut Before (Pre) and After (R+1 to R+7 Days) a Spaceflight. *Right*: Vertical Wri-ting Test in a Vestibular Patient.** (Adapted from Fukuda [1983]).

the size of the letters did not change in-flight or postflight, but the vertical distance between them was decreased. This observation indicates that the changes were not due to an alteration in proprioception or motor control. Interestingly, these tests are variants of tests traditionally used in oriental medicine (the Fukuda Writing test, the Square Drawing test) to diagnose patients with impairment in motor function (when the size of all characters is irregular) from those with vestibular disorders (the writing or drawing is deviated to one side). And the astronauts' responses are close to those of patients with otolithic disorders on Earth. These results suggest that adaptive changes in the mental representation of a vertical layout of letters take place when the gravitational frame of reference is removed either by microgravity or by central disorders [Clément and Reschke, 2008].

During another test, two crewmembers were requested to draw the well-known Necker's cube. This figure is the simplest representation of a three-dimensional object in a two-axis coordinate system. Comparison between the length of the lines between the cubes drawn on the ground and the cubes drawn in space revealed a 9% decrease in length in the vertical dimension (i.e., the height) of the cubes drawn in weightlessness (Figure 3.22). Similar results have been found in another study involving two astronauts. The trajectory of hand-drawn ellipses in the frontal plane in the air with their eyes closed revealed a 10–13% decrease in the vertical length of the ellipses, whereas the horizontal length of the ellipses was basically unchanged. This result supports our hypothesis that the mental representation of the vertical dimension of objects or volumes is altered during exposure to weightlessness.

3.4.2.4. Depth perception

Depth perception is based on accommodation, binocular disparity, motion parallax, as well as aerial and geometrical perspectives (Figure 3.23, left). In the absence of atmosphere and with different lighting conditions affecting color and contrast, as in spaceflight, aerial perspective is presumably the most reliable of cues for depth perception. Space experiments have begun to investigate the role of depth cues in absence of a gravitational frame of reference. Howard et al. [1990] had shown that the perception of concavity or convexity of a shape depends on a "light comes from above" assumption,

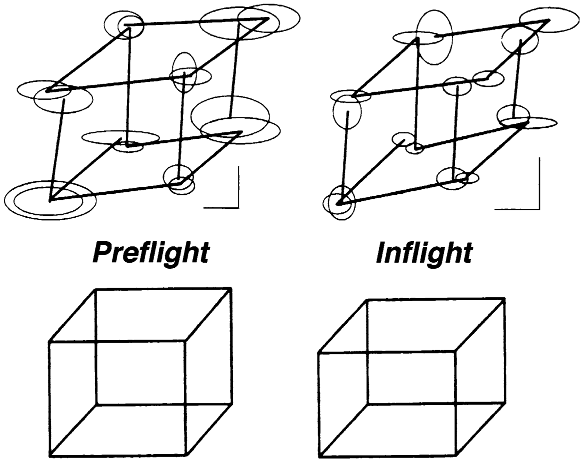

Figure 3.22. *Top*: Mean ± SD of Each Point of Cubes Drawn by an Astronaut Preflight and In-Flight. *Bottom*: Averaged Mean Preflight and In-Flight Cubes. Horizontal and Oblique Lines Were Unchanged, but the Vertical Lines Were Shorter in Microgravity. (Adapted from Lathan et al. [2000]).

Figure 3.23. Monocular Cues for Depth Include Aerial Perspective, Which Entails the Loss of Contrast, Color, and Shading with Increasing Distance Due to Scattering of Light in the Atmosphere (*left*) and Geometrical Perspective, in Which Objects Appear Smaller When They Are Farther Away (*right*). Aerial and Geometrical Perspectives Are Both Affected by the Spaceflight Environment, Either Directly or Indirectly.

where "above" depends on the head orientation relative to the object and gravity. During the Neurolab mission, crewmembers were presented with convex or concave shaded figures. After several days in space, they could not use so reliably that light information for depth, because they had been exposed to situations where the light source could come from any direction while they were free-floating in the cabin [Oman, 2003].

Our ISS experiment called 3D-SPACE (see Figure 3.10) is using classic geometrical illusions of size, which on Earth generate inaccurate judgments because they provide misleading depth cues. Those illusions based on perspective depth cues are particularly relevant to the space environment. Indeed, geometrical perspective uses converging lines and vanishing points to determine how much an object's apparent size changes with distance (Figure 3.23, right). It is based on the principle that there is a theoretical horizon line representing the point of view of the observer, and that the angle of converging lines toward a vanishing point, generally in the straight-ahead direction, provides depth information. In the absence of a gravitational reference, such as in microgravity, it is more difficult to define a horizontal line. Also, previous studies have shown significant deviations in the vertical position of the eye in microgravity due to the stimulation of the otolith organs by changes in the amplitude of the gravito-inertial forces, which could alter the direction of the "straight ahead." Consequently, because the rules of geometrical perspective are less accurately defined in microgravity, the subjects should rely less on the perspective cues for depth perception. The preliminary data from this experiment tend to support this hypothesis.

The results of these studies may have important consequences for human performance during spaceflight. For example, if an astronaut cannot accurately visualize the volume of the station, its surroundings, or a planetary surface, navigation may cause delays and frustration. There may also be consequences for space habitat design if squared volumes do not look square to people in space. Virtual reality training might be a way to train the astronauts to compensate for such altered spatial representation.

Recent research studies have used electroencephalogram (EEG) recordings to monitor and measure working memory and other indicators of cognitive ability. A recent experiment conducted over the course of three spaceflights quantified the EEG oscillations at 10 Hz, which are the most prominent rhythms observed in subjects who are awake with their eyes closed. This activity increased in five cosmonauts in-flight compared to preflight. The authors of this study attribute this increase to a reduction in graviceptive inputs to cortical networks participating in the mental representation of space [Chéron et al., 2006]. Further investigations carried out in space will perhaps reveal that other higher cortical functions are impaired in weightless conditions. The combination of virtual reality with EEG recordings (for the measurement of evoked-related potentials and brain mapping) should soon provide insightful results on the adaptive mechanisms of cerebral functions in absence of gravity.

How will the cognitive processes of spatial orientation differ from the terrestrial norm after a long absence of a gravitational reference? We speculate that the way of processing three dimensions will be more developed. Creativity will certainly be more three-dimensional and definitely thinking will be out of the gravitational box. Like the way culture and language influences our ability to think creatively, being free from gravity will elicit thoughts never before possible for the human mind, and thus give opportunities for new art and scientific discoveries [Pettit, 2003].

3.5. What do we know?

3.5.1. Space motion sickness experience

The severity of SMS is categorized depending on its impact upon crew performance (Table 3.1). For example, "Mild" SMS has no operational impact, because the crewmember can still perform all the required activities. "Moderate" or "Severe" SMS are

Table 3.1. NASA Categorization of Space Motion Sickness According to the Severity of Symptoms.

None	No signs or symptoms reported
Mild	One to several transient symptoms No operational impact All symptoms resolved in 36–48 h.
Moderate	Several symptoms of a persistent nature Minimal operational impact All symptoms resolved in 72 h.
Severe	Several symptoms of a persistent nature Significant performance decrement Symptoms may persist beyond 72 h

operational concerns since the workload must be redistributed among the remaining, unaffected crew.[9]

In the space shuttle missions between 1981 and 2000, about 69% of the 471 crewmembers making their first flight reported symptoms of SMS. About 35% reported mild symptoms, 23% moderate symptoms, and 11% severe symptoms. Most recovered by the end of the third day in space. In a few cases in the Russian and U.S. missions, however, crewmembers were ill for 7–14 days.

The severity of SMS among those making a second flight remained unchanged in 56% of crewmembers, whereas a slight improvement was observed in 35%, but even more symptoms were noted in 9%. This indicates that symptoms are not significantly reduced on a following flight.

In addition to feelings of vertigo and nausea, SMS can cause sopite syndrome, which includes lack of motivation to work or interact with others, drowsiness, fatigue, and the inability to concentrate. Sopite syndrome is often a byproduct of dizziness experienced by astronauts during space travel.

SMS is self-limited. Complete recovery from major symptoms (i.e., adaptation to the spaceflight environment) occurs within 2–4 days. After complete adaptation occurs, crewmembers appear to be immune to the development of further symptoms. This development of immunity to further SMS symptoms was demonstrated by rotating chair tests, designed to provoke an SMS response, that were conducted in-flight during *Skylab* missions.

3.5.2. Theories for space motion sickness

Two major theories advanced to account for SMS are the fluid shift theory and the sensory conflict, also known as the neural mismatch, sensory mismatch, or sensory rearrangement theory [Crampton, 1990]. Although both theoretical positions have some merit and neither is ideal, the fluid shift theory does not explain the development

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[9] In the jargon of the flight surgeons, “Mild” symptoms are sometimes referred to “one bag”, “Moderate” to “two bags”, and “Severe” to “three bags”.

of motion sickness during spaceflight (we don't get sick when lying in a bed). While the fluid shift theory of SMS could be associated with sensory conflict, there are mechanisms whereby the headward fluid shift accompanying microgravity could bypass the classic vestibular inputs to induce vomiting.

Briefly, the sensory conflict theory of motion sickness assumes that human orientation in 3D space, under normal gravitational conditions, is based on at least four sensory inputs to the central nervous system. The otolith organs provide information about linear accelerations and tilt relative to the gravity vector; angular acceleration information is provided by the semicircular canals; the visual system provides information concerning body orientation with respect to the visual scene or surround; and touch, pressure, and somato-sensory (or kinesthetic) systems supply information about limb and body position. In normal environments, information from these systems is compatible and complementary, and matches that expected on the basis of previous experience. When the environment is altered in such a way that information from the sensory systems is not compatible and does not match previously stored neural patterns, motion sickness may result.

The sensory conflict theory postulates that motion sickness occurs when patterns of sensory inputs to the brain are markedly re-arranged, at variance with each other, or differ substantially from expectations of the stimulus relationships in a given environment. In microgravity, sensory conflict can occur in several ways. First, there can be conflicting information (i.e., regarding tilt) transmitted by the otoliths and the semicircular canals. Sensory conflict may also exist between the visual and vestibular systems during motion in space; the eyes transmit information to the brain indicating body movement, but no corroborating impulses are received from the otoliths (such as during car sickness). A third type of conflict may exist in space because of differences in perceptual habits and expectations. On Earth, we develop a neural store of information regarding the appearance of the environment and certain expectations about functional relationships (e.g., the concepts of "up" and "down"). In space, these perceptual expectations are at variance, especially during the inversion illusions described above.

It is important to note that no single course of sensory conflict appears to entirely account for the symptoms of space sickness. Rather, it is the combination of these conflicts that somehow produces sickness, although the exact physiological mechanisms remain unknown. Thus, sensory conflict explains everything in general, but little in the specific. Shortcomings of the sensory conflict theory include: (a) its lack of predictive power; (b) the inability to explain those situations where there is conflict but no sickness; (c) the inability to explain specific mechanisms by which conflict actually gives rise to vomiting[10]; and (d) the failure to address the observation that without conflict, there can be no adaptation. The hypotheses outlined below may be helpful in overcoming some of the weaknesses associated with the construct of this theory.

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[10] It has been proposed that motion sickness results from the activation of a vestibular mechanism whose physiological function is the removal of poisons from the stomach. Nausea and vomiting would also tend to keep a disoriented or dizzy individual from moving about the environment in search of food when he would be at risk doing so [Money, 1990].

Some investigators have proposed a mechanism complementary to the sensory conflict theory to explain individual differences in SMS susceptibility. They suggest that some individuals possess slight functional imbalances, for example weight differences, between the right and left otolith receptors that are compensated by the CNS in 1 g. A weight imbalance between the left and right otoconia is reasonable since there is a continual turnover of otoconia, and it is unlikely that the two otoliths would ever weigh exactly the same. This compensation is inappropriate in 0 g, however, because the weight differential is nullified and the compensatory response (either central or peripheral) is no longer correct for the new inertial environment. The result would be a temporary asymmetry producing rotary vertigo, inappropriate eye movements, and postural changes until the imbalance is compensated or adjusted to the new situation. A similar imbalance would be produced upon return to 1 g, resulting in postflight vestibular disturbances. Individuals with a greater degree of asymmetry in otolith morphology would thus be more susceptible to SMS.

A sensory compensation hypothesis has also been proposed. Sensory compensation occurs when the input from one sensory system is attenuated and signals from others are augmented. In the absence of an appropriate graviceptor signal (or perhaps the presence of atypical signals) in microgravity, information from other spatial orientation receptors such as the eyes, the semicircular canals, and the neck position receptors would be used to maintain spatial orientation and movement control. The increase in reliance on visual cues for spatial orientation could be explained by this mechanism. Closely related to this sensory compensation hypothesis is the OTTR hypothesis already discussed (see Figure 3.7).

3.5.3. Countermeasures

The disruptive nature of SMS, occurring as it does during the early, critical stages of a mission, has led to a variety of approaches for the prevention or control of this medical problem.

Prediction of susceptibility has been a major objective of the SMS research. Various approaches ranging from the use of questionnaires, history, experience or personality traits, vestibular function tests, physiological correlates, and tests in specific nauseogenic environments have been directed toward the question of SMS susceptibility. However, striking differences were found in the pattern of symptoms generated during flight compared to the pattern generated during the ground-based tests. Further, the specific nature and time course of in-flight symptomatology were highly variable. The preflight questionnaire results did not correlate with the reported incidence of SMS. Differences in the results between susceptible and non-susceptible crewmembers for each of the preflight tests were not significant, nor was the correlation between susceptibility to motion sickness in the ground-based tests and susceptibility to SMS. Individual variations in preflight experience, medications, in-flight tasks (i.e., mobility), and personal strategies for symptom management have further compounded the problem. Consequently, the use of a single ground-based parameter or test procedure is inadequate for predicting SMS susceptibility. Despite the inability to identify ground-based predictors of SMS susceptibility, one reasonably accurate predictor was identified, and that is spaceflight itself. Of 16 crewmembers who had flown two or more space missions, the response pattern of only three changed from one flight to the next.

While research on predictors of SMS has been inconclusive, some progress has been made in the development of countermeasures. Current areas of investigation include preventive training techniques, in-flight techniques for minimizing head and body movement, and use of anti-motion sickness drugs [Lackner and DiZio, 2006].

Attempts by the Russian program to prevent SMS by pre-selection of individuals with a high tolerance to motion sickness during complex vestibular stimulation have not met with success. Vestibular testing was once used in the U.S. space program for the early selection of astronauts, but it is no longer used for shuttle and ISS crewmembers. Vestibular training prior to spaceflight in the Russian space program has primarily involved Coriolis and cross-coupled angular accelerations. However, this training is rather demanding for the crewmembers and its efficacy against SMS has never been proven.

One preventive technique, developed at the NASA Ames Research Center, is a combined application of biofeedback and autogenic therapy (a learned self-regulation technique). This technique proved quite successful in controlling some symptoms of SMS associated with the autonomic nervous system, such as nausea and vomiting. In some individuals, autogenic feedback has produced improvement in motion tolerance with as little as 6 h of training. However, it does not work with all individuals.

Training procedures that pre-adapt astronauts to the sensory stimulus rearrangements of microgravity gave promising results. The NASA Preflight Adaptation Trainer (PAT) provides astronauts with demonstrations of and experience with altered sensory stimulus rearrangements that produce perceptual illusions of various combinations of linear and angular self- or surround-motion (Figure 3.24). Crewmembers who were exposed to this training before flight had a significant reduction (19–54% depending on the symptoms) in the severity of SMS symptoms by comparison with those who were not exposed to it.

Because crewmembers have reported that rapid head movements worsen the nausea and spatial disorientation associated with SMS, head and neck restraints that restrict such movements have been used, but with limited success.

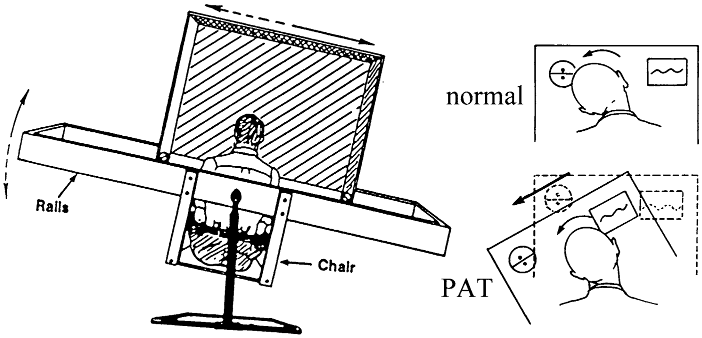

Figure 3.24. Preflight Adaptation Training. Before the Flight, Crewmembers Are Passively Tilted in Roll or in Pitch While Exposed to a Lateral Translation of the Visual Scene (Such as on the *left panel*) or to a Fore/Backward Translation, Respectively, in Order to Induce a Reinterpretation of Their Otolith Signals by the Visual System. (Credit NASA).

Drugs that diminish the SMS symptoms are being used and studied. During the Apollo, *Skylab*, and the first shuttle missions, scopolamine and a combination of scopolamine and dextroamphetamine, given orally, were used to treat SMS, with limited success. Since STS-36 (1990), shuttle and ISS crewmembers experiencing severe SMS have been treated primarily via intramuscular injection (25 or 50 mg) or suppository (25 mg) of promethazine. Oral promethazine or a combination of promethazine and dexedrine are also used. While promethazine is effective as therapy, clearly there remains room for improvement: 25% of crew treated become sick the next day, the injections are painful, and are usually only administered prior to sleep due to sedating effects. Mild cases of SMS – involving "sopite" symptoms such as drowsiness, lethargy, and short-term memory deficits – typically go untreated. Recent research indicates, however, that promethazine can cause deleterious side effects that further degrade human performance, including reaction time, grammatical reasoning ability, and pattern recognition, and negatively impact mood and sleep. No SMS drug, including promethazine, has yet been identified that is clinically acceptable for prophylactic use during an EVA or by pilots during landing. Promethazine cannot be used with the anti-orthostatic drug midodrine on landing day. The lack of effective SMS prophylactic drugs has a dramatic impact on crewmember efficiency: timeline developers deliberately reduce scheduled activities by 25% during the first 2 days, hoping crewmembers will limit their head movements [Oman, 1998].

Russian crews employ different drug formulations and procedures to prevent and treat SMS, and report a somewhat lower overall incidence. Progress has been made since 1990 on the physiology of nausea and vomiting, receptor targeted anti-emetics, as well as phenotypic and genotypic biomarkers of motion sickness susceptibility. New intranasal formulations of traditional drugs are in development. Unfortunately SMS has received relatively little clinical research attention recently. The level of SMS risk control actually being achieved and the effects of SMS drug use on sensorimotor adaptation remain poorly understood. Vomiting in 0 g is not dangerous, except during EVA. NASA currently manages the risk by prohibiting EVAs during the first three mission days. Nonetheless, there has been at least one episode. On planetary missions, a limited number of suits are planned for all mission phases. A vomiting episode renders a suit non-reusable, due to biological contamination. In the absence of a proven effective SMS prophylactic drug, suit containment is essential, and should be designed into the new suit from the start. Physiological issues are involved in design and test, and should not be entirely relegated to engineers [Oman, 2007].

Although past research has yielded a great deal of information applicable to SMS, a definitive solution to this vexing problem is urgent. Among the objectives of current SMS research is the development of: (a) more precise predictive indices; (b) more effective drug treatments; (c) more efficient preflight adaptation procedures; (d) methods to evaluate performance impairment induced by SMS and anti-motion sickness drugs; and (e) the early detection of incipient symptoms.

Over the past 50 years, efforts in space neuroscience have been directed at understanding the acute changes that occur in the neurovestibular and sensorimotor systems, mostly during short-duration space missions. Very few experiments have been performed during the first minutes or hours of adaptation to microgravity and re-adaptation to Earth's gravity. This is a shortcoming of all the research that has been performed during the space shuttle program. Major research emphasis should be placed on obtaining an understanding of the acute changes that occur during the first few minutes and hours of spaceflight, and immediately after landing. These periods are characterized by transitions in gravitational levels, which have an impact on sensorimotor functions. The suborbital flights might be an opportunity to investigate these acute changes. The results of this research will be useful for exploration missions that will include several transitions between gravitational levels, and for commercial suborbital missions as well.

Based on our previous experience in orbital and parabolic flight, space motion sickness, mal de débarquement, sensorimotor disruptions in eye movements, postural stability, and motor coordination are likely to occur in the participants of commercial suborbital missions McDonald et al. [2007]. Some strategies have been proposed to overcome these problems, such as sensorimotor adaptation during periods of reduced and enhanced gravity on board parabolic flight and centrifuges [Karmali and Shelhamer, 2010]. Further research into the required quantity and timing of these pre-adaptation flights and the tasks conducted during these flights are required to improve safety and comfort of the participants during suborbital flights.

Before a mission to Mars can safely be undertaken, the adaptive processes of the sensory, motor, and cognitive systems to microgravity need to be better understood, and countermeasures must be devised for a faster re-adaptation of the CNS functions that are expected to occur following the transitions between various gravitational environments. In particular, future investigations should address the following issues:

(a) Motion sickness upon return to a gravitational environment, including postflight motion sickness, needs to be better understood and mitigation strategies developed.

(b) The dynamic range of the adaptation of sensorimotor responses in various gravitational environments needs to be identified. This may be accomplished by using a centrifuge on board the ISS or in a Moon habitat. Accurate predictions of the effects Mars gravity may be accomplished via modeling.

(c) It is not known if permanent functional deficits result from the decrease in afferent input to the vestibular, proprioceptive and somatosensory systems as a function of the adaptation associated with long exposure to 0 or 0.38 g.

(d) Morphological or structural changes in CNS and neuromuscular functions that may account for these deficits need to be identified (Figure 3.25).

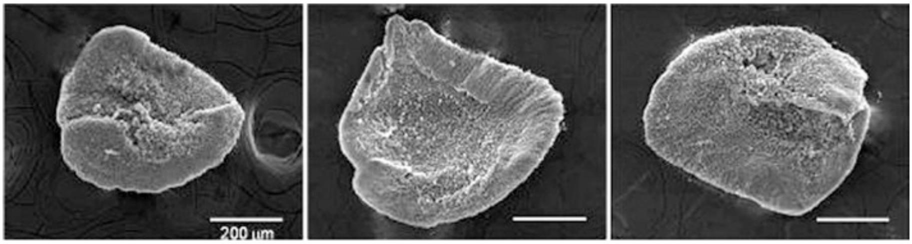

Figure 3.25. Scanning Electron Micrographs of Otoliths from Quail Embryos That Were Raised from Fertilization in Microgravity (*left*), in an Onboard 1-g Centrifuge (*center*), and in a 2-g Centrifuge on Earth. (Adapted from Evans et al. [2009]).

(e) The procedures that produce rapid and complete adaptation to Martian gravity and Earth's gravity after exposure to microgravity must be validated. This may be accomplished using Martian gravity simulation by executing parabolic flight maneuvers on Earth, or using a centrifuge on board the ISS or in a Mars habitat.

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Chapter 4

The Cardio-Vascular System in Space

One of the major concerns for both short- and long-duration spaceflight is the phenomenon of cardio-vascular deconditioning. Exercise deconditioning during spaceflight may significantly affect a crewmember's ability to perform strenuous or prolonged tasks during and after a spaceflight mission, respond to an emergency situation, or assist a crewmate who might be incapacitated. This chapter introduces the principles of cardio-vascular fluid and electrolyte control to shed light on the symptoms typically reported by astronauts during and after spaceflight. Data from flight experiments are discussed, as well as the value of ground-based models such as bed rest studies. The value of exercise, inflatable suits, saline loading, and artificial gravity is also discussed (Figure 4.1).

4.1. The problem: postflight orthostatic intolerance

The primary function of the cardio-vascular system is to circulate blood through the body. It is composed of the heart, the circulatory system, the lungs and the kidneys. Blood supplies nutrients to and collects waste from cells, and maintains the body's internal environment by regulating the acid-base balance, fluid content, and body temperature, a process called homeostasis. Clearly, this process is crucial to maintaining health. Although the responses of the cardio-vascular system to microgravity seem to have been relatively free of major threats to well being and performance during flight, problems such as orthostatic hypotension and diminished exercise capacity are commonly observed after return to Earth.

Orthostatic intolerance is characterized by a variety of symptoms that follow standing: lightheadedness, increase in heart rate (tachycardia), decrease in blood pressure, and pre-syncope or syncope (fainting). Diminished exercise capacity is the observed decrement in ability to perform given amounts of work and is usually measured by duration of treadmill or stationary bicycle exercise up to a maximum level of oxygen consumption (VO_2 max). Both orthostatic intolerance and diminished exercise capacity become more severe with longer exposure to microgravity and require more lengthy recovery times after returning to Earth.

Orthostatic hypotension has been noticed since the earliest human spaceflights. A modest increase in heart rate was observed after the *Mercury-8* mission, which lasted only 9 h. More significant increase in heart rate (132 beats/min supine; 188 standing) was measured after the *Mercury-9* mission, which lasted 34 h. Fainting episodes were later observed during Gemini missions and heart rhythm disturbances were noted during Apollo missions.

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Figure 4.1. Astronauts Onboard the ISS Are Using an Ultrasound Machine to Perform Exam of the Heart and Other Internal Organs. Ultrasound Probes Send High-Frequency (Megahertz) Sound Waves into the Body. Because Sound Waves Travel Through Each Organ, or Tissue, at a Different Speed, the Probe Is Able To "See" What the Reflected Sound Waves Have Found. (Credit NASA).

Orthostatic intolerance affects about two-thirds of the astronauts returning from spaceflight, even after missions of relatively short duration [Buckey et al., 1996a]. This is an even greater problem for space shuttle pilots, who must perform complex re-entry maneuvers in an upright, seated position. Operational concerns have increased since astronauts began using the heavy, bulky partial-pressurized launch and re-entry suit, required for all post-*Challenger* flights. However, essentially no testing of cardio-vascular function has been performed on space shuttle pilots during re-entry. This may pose a problem for "space tourists" during suborbital flight. They will be exposed to re-entry forces even higher that those experienced in the space shuttle or *Soyuz* capsules (by well cardio-vascular fit professional astronauts). Another threat is whether a debilitated crew can respond to an emergency upon landing.

It is estimated that approximately 83% of crews on long-duration missions experience some degree of orthostatic intolerance after return to Earth. The extent of orthostatic intolerance postflight is variable and depends on the duration of the flight, individual differences in cardio-vascular function among the astronauts, and the elapsed time after landing and method of postflight testing. Recovery to the preflight level of orthostatic tolerance occurs within a day or so following flights of less than a 1-month duration, but longer recovery is associated with longer duration flights [Watenpaugh and Hargens, 1995].

Recovery of exercise capacity is also relatively rapid but takes about 1 week following a short duration spaceflight. Following long duration spaceflights on board the Russian space stations *Salyut* and *Mir*, many returning cosmonauts were incapacitated and were unable to egress the capsule without assistance from ground personnel (Figure 4.2). As a standard routine, crews returning from a 6-month spaceflight undergo many weeks of rehabilitation, with graduated exercises, guided movements in a warm swimming pool, and massage. Even with this rehabilitation program, after a few months some reported that they couldn't jog without becoming short of breath [Payne et al., 2007].

The ISS crewmembers are encouraged to exercise during the early phases of a mission as a countermeasure to mitigate the effects of microgravity, just like the *Skylab* and *Mir* crewmembers who went before them. The *Skylab* and *Mir* crewmembers did not manifest any differences between their heart rate responses during flight as compared to preflight values. The exercise program begins with 1 h of scheduled exercise time on flight day 5 and increases to 2.5 h of exercise after space shuttle or *Soyuz* undocking. A detailed analysis of ISS crew exercise capability was not possible prior to *Expedition-13* because of payload constraints, payload priorities, and budgetary issues. Recent data has revealed a decrease in functional capacity both in orbit and upon landing in nine U.S. astronauts and four Russian cosmonauts, unlike what was observed in the *Skylab* astronauts [Moore et al., 2010].

The effects of exposure to microgravity on the cardio-vascular system beyond 9 months are largely unknown. This is of great concern, because such effects may involve not only amplification of reversible changes already known, but also the

Figure 4.2. After a Long-Duration Stay in Orbit, Cosmonauts Are So Severely Debilitated That They Cannot Egress the Soyuz Capsule Without Assistance from Ground Personnel. (Credit Roscosmos).

emergence of unrecognized and irreversible alterations in cardio-pulmonary function. For example, some observers have speculated that there is a loss of cardiac mass during prolonged microgravity exposure. Will lengthy missions render space travelers unfit for return to a 1-g environment?

Jet pilots often fly upside down at −1 g with no problem (Figure 4.3). Why then would flying in 0 g pose a problem? How can these space travelers perform nominally on orbit and then be so debilitated when they land? Symptoms of orthostatic hypotension are seen on Earth with patients who have certain types of cardio-vascular disease. Did the space agencies somehow pick individuals who were susceptible to these problems? In fact, the astronauts selected by NASA are initially screened for significant cardio-vascular diseases (see Chapter 7, Section 7.2.2). They are in excellent physical shape and many have increased heart muscle mass compared to the terrestrial "normal" population.

So, what is the risk? The risk of cardio-vascular medical events happening during or after a mission can be divided into two categories: (a) those medical events which occur as a consequence of pre-existing cardio-vascular disease which must not be detected during the selection medical examination and are aggravated by spaceflight; and (b) those medical events that occur as a consequence of the expected cardio-vascular physiological changes induced by spaceflight. A recent study based on experience with aircraft pilots has determined that the risk of a "mission loss" due to serious cardio-vascular event, like a heart attack or a sustained rhythm disturbance, during a 16-day spaceflight with a six-person crew is 0.3% per flight. The worst-case cardio-vascular risk of an incapacitating event for ISS crews over a 1-year period is 1% per person per year if all other space-related factors are ignored [Barratt and Pool, 2008].

Figure 4.3. During Acrobatic Flying, Pilots Often Fly Upside-Down and Are Exposed to –1 g with No Problems. (Source Unknown).

4.2. Cardio-vascular system physiology

4.2.1. Basics

The major functions of the cardio-vascular system include: (a) delivery of O_2 and nutrients to all areas of the body; and (b) removal of CO_2 and cell metabolic wastes to specific organs, such as the lungs or kidneys. Other functions of the cardio-vascular system as it circulates blood include the transport of hormones, transport of immune system components such as white blood cells or antibodies, and heat regulation.

These functions were originally localized within the unique cell of early, unicellular organisms. However, as organisms increased in size and in number of cells, isolated individual cells also needed to ingest nutrients and excrete waste (Figure 4.4). The development of a vascular tree, able to reach all individual cells, was therefore required. Such a system includes both the heart and the blood vessels that pass to and from the heart to the tissues of the body. These vessels include the large arteries that receive blood from the heart, branching into smaller arterioles that branch further into capillaries. From the capillaries, blood flows into small collecting venules, then into larger and larger veins for return to the heart.

The overall organization of the cardio-vascular system consists of a driving pump, the heart, and the two key circulatory systems that it powers: the pulmonary circulation (the lungs) and the systemic circulation (the rest of the body). In the systemic circulation, the arteries transport oxygenated blood under relatively high pressures to the body at approximately 80–90 mmHg pressure, and the veins return deoxygenated blood to the heart at lower pressures of 5–15 mmHg. The capacity of the venous system is large and at least 70% of the blood volume in humans is found in the veins. The mean arterial pressure represents the average pressure that pushes blood through the capillaries and other vessels of the systemic circulation. This pressure level provides insight into the average blood flow to the tissues. On Earth, there is a large pressure gradient from the head to the feet, with the mean arterial blood pressure being about

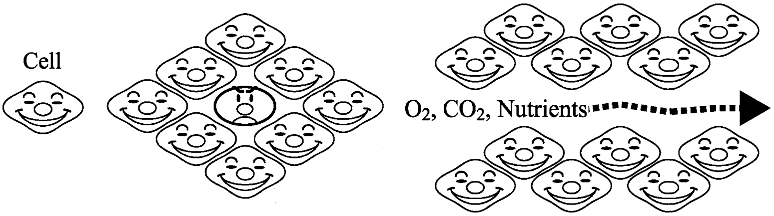

Figure 4.4. Why Do We Have a Cardio-Vascular System? When Single-Celled Organisms, Living in an Aqueous Environment, Evolved to Larger and Larger Multi-cellular Organisms, the Metabolic Needs of the Cells in the Interior of the Enlarging Structure Could No Longer Be Satisfied by Simple Diffusion with the Surrounding Liquid Environment. A Vascular Tree Was Eventually Required to Bring in the Necessary Materials to the Individual Cells and to Carry Out the Undesired By-Products of Their Metabolism. Thus, the Primary Function of the Cardio-Vascular System Is to Deliver a Flow of Blood to Local Tissues So That Individual Cells in Those Tissues Can Be Maintained in Optimal Condition [Churchill, 1999]. (Credit Philippe Tauzin).

70 mmHg at the head level, 100 mmHg at the heart level, and 200 mmHg at the feet level. This is because the vascular system is essentially a set of vertical "columns" of blood, and pressure in these columns increases with depth, just as pressure increases with depth in the ocean (Figure 4.5).

In the pulmonary circulation, the deoxygenated blood is carried by perfusion from the right ventricle of the heart to the lungs via the pulmonary artery. This is a low-pressure system, typically 10–20 mmHg, with low resistance to blood flow. In an individual standing upright, this pressure may be insufficient to overcome hydrostatic gradients, and so very little flow reaches the upper regions of the lungs, but a relatively large portion of pulmonary blood flow perfuses the lower portions of the lungs. Air in the alveoli flows somewhat preferentially into the middle and upper regions of the lungs. These regional differences create a mismatch of air ventilation and blood perfusion and are the basis for the system of classification of lung zones [West, 1968]. As the blood flows through the capillaries in the lungs, waste gases (i.e., CO_2) are released and oxygen is absorbed by simple diffusion. Blood then passes to the left atrium of the heart via the pulmonary veins. From there, the oxygenated blood passes to the left ventricle to be pumped out of the heart again.

The contraction of the heart, first atria and then ventricles is termed systole. Between beats, the heart pauses briefly for the atria to refill with blood for the next contraction. This period is termed diastole. Blood pressure in the arteries fluctuates during these phases of the full cardiac cycle. Arterial pressure rises sharply during ventricular systole and drops during ventricular diastole. Flow through a blood vessel is determined by both the force that pushes the blood through that vessel and the resistance of the vessel.

It is also important to note that the flow of blood in the body is directly influenced by gravity. When a person is standing, gravity causes blood to pool in the relatively compliant leg veins. The force of gravity also makes it more difficult for the blood to flow upward to return to the heart and lungs for more oxygen. Because the veins

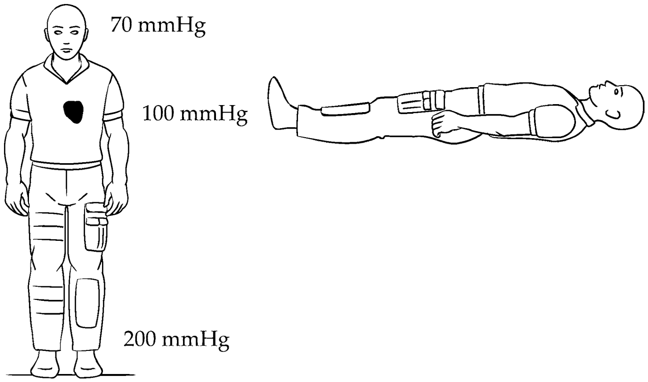

Figure 4.5. On Earth, When We Are Standing, There Is a Hydrostatic Pressure Gradient from Head-to-Foot. The Veins of Our Lower Legs Sustain a Pressure of Approximately 200 mmHg. An Immediate Effect of Transition to Micro-Gravity Is loss of Hydrostatic Gradient in the Venous Vascular System, Similar to Being Supine on Earth.

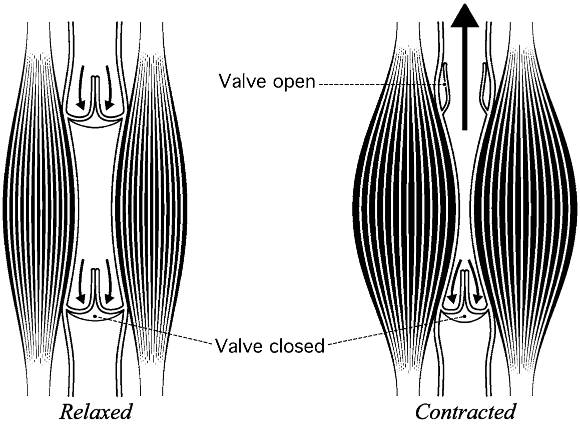

Figure 4.6. The Contraction of Skeletal Muscles in the Legs Helps to Pump Blood Toward the Heart, but Is Prevented from Pushing Blood Away from the Heart by Closure of the Venous Valves. (Adapted from Lujan and White [1994]. Credit Philippe Tauzin).

comprise a low-pressure system with very distensible walls, in many cases, blood would tend to pool in them unless something aids the flow. Most veins have valves in them, which prevent any "back-flow." In addition, a periodic pushing of blood forward every time skeletal muscles in the legs contract assists venous return (Figure 4.6). This mechanism effectively counteracts the force of gravity.

4.2.2. Control mechanisms

4.2.2.1. Control of blood pressure

The cardio-vascular system is well known as the major fluid transportation system of the human body. Its regulated transport to and from the capillaries is central to life from the cellular to whole-person level. Yet the plasma of the cardio-vascular system contains only about 3 L of the total body water content of 42 L (about 7%) for a 70-kg "average" male. Another 11 L of water are located in the extracellular interstitial spaces, the spaces in between the cells, and in the lymphatic vessels that drain those spaces. The remaining 28 L of water is the intracellular fluid inside cells of the body.

Except in the case of bleeding, changes in blood volume usually occur because of changes in the water content of the blood plasma. Increasing total blood volume ultimately increases the "filling pressure" of the vascular system and the amount of blood to be ejected by the heart with each stroke.

The volume of blood discharged from the left ventricle of the heart with each contraction is called the stroke volume (about 70 mL at rest). With a heart rate of 72 beats/min, blood flow in the entire human circulation is about 5,000 mL/min at rest, but may be 5–6 times greater during exercise. The amount of blood pumped by the heart in 1 min is called the cardiac output:

$$\text{Cardiac Output} = \text{Stroke Volume} \times \text{Heart Rate}$$
$$(\text{mL of blood / min})(\text{mL of blood / beat})(\text{beats / min})$$

Both heart rate and stroke volume can change, thus varying cardiac output and the supply of blood to the entire circulation. Controlling blood vessel radius, which is done by the sympathetic nervous system, is also a very powerful way for the body to vary the resistance of the vessel to the blood flow, divert flow from one area to another, and vary blood pressure overall. Blood pressure will also vary as a function of the viscosity of the blood, such as the quantity of blood cells within the plasma (Table 4.1).

Both heart rate and blood pressure are controlled by the autonomic, unconscious, nervous system, which consists of two parts: the para-sympathetic and the sympathetic nervous systems. These two systems have opposing roles and are activated according to the different needs of the individual. The parasympathetic nervous system is activated during rest and assists in energy restoration by means of the digestion and absorption of food. This system also acts to decrease heart rate. The sympathetic nervous system, on the other hand, prepares the body for an emergency and counteracts the parasympathetic nervous system to maintain the required energy supply. During any emotional or physical stress, adrenaline is released by the sympathetic nervous system, which acts to increase heart rate and blood pressure.

Accordingly, a balance between the parasympathetic and sympathetic nervous systems activity controls heart rate. On a beat-to-beat basis, however, it has been observed that heart rate is not constant and there are periodical fluctuations indicative of the relative contributions of each of these two components of the autonomic nervous system. There have been various methods employed in an attempt to quantify the relative contributions of each of these systems. One of the most commonly used methods is the frequency domain analysis of heart rate variability. This method uses highly sophisticated techniques to determine different frequencies of heart rate, and from this analysis one can identify which of the two systems is predominantly active during both rest and exercise.

Table 4.1. Some Factors That Influence Arterial Blood Pressure and the Associated Mechanisms.

Factors	Why Blood Pressure Increases
Increase in blood volume	Increased total “filling pressure” in the semi-flexible cardio-vascular system; increased venous return to the heart, leading to higher stroke volume
Increase in heart hate	Increased cardiac output which, without a countering change in peripheral resistance, increases pressure
Increase in stroke volume	Same as increased heart rate
Increase in peripheral resistance	Normally varied by changing vessel diameter, particularly in the arterioles, increased constrictive resistance increase pressure in the vessels leading up to it
Increase in blood viscosity	Increased resistance, as thicker blood does not flow as easily

4.2.2.2. Baroreceptor reflexes

Baroreceptors, or "pressure receptors," are specialized nerve endings located in both the arterial and venous systems, which are stimulated when the blood vessels are stretched by increased pressure. The baroreceptors in the arterial system are located in the neck as the carotid artery ascends to the brain, and in the aortic arch, immediately as blood leaves the heart in the aorta (Figure 4.7). When blood pressure increases, the corrective response via the stimulation of the baroreceptors and sympathetic nervous system includes a decrease in heart rate and stroke volume and vasodilatation of the arterioles to decrease vascular peripheral resistance. In addition, secondary effects act on the kidney to allow increased urine production. The reverse effects take place if blood pressure is decreased.

Baroreceptors in the venous system are rather diffusely located and less understood classically. In general, these receptors are scattered in the major veins entering the heart, the atria, and the pulmonary vessels (also called the vena cava). Because the large veins are very compliant, changing greatly in volume with small pressure changes, the venous baroreceptors are actually monitoring rather significant changes in venous blood volume in the upper body. Although less well characterized than their arterial counterparts, it is possible that these are the first baroreceptors activated by fluid shifts that occur in spaceflight.

It is now believed that spaceflight deconditions the baroreceptor response, resulting in larger changes in the baroreceptor distention needed to induce the same changes

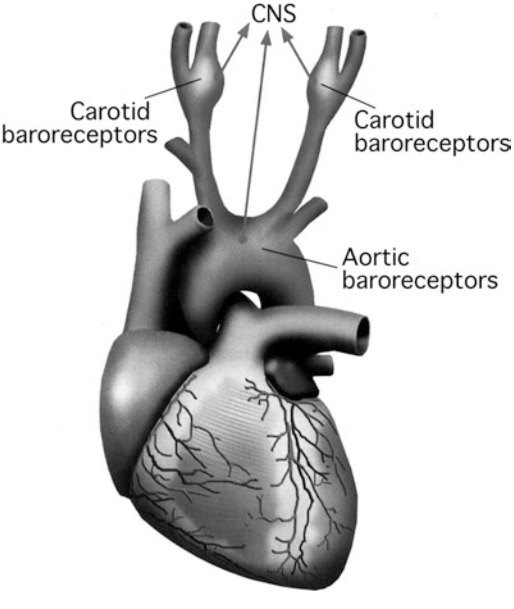

Figure 4.7. Arterial Baroreceptors Are Located in the Aortic Arch and the Carotid Sinuses of the Left and Right Internal Carotid Arteries. Whenever These Sensors Are Stretched or Relaxed, Nervous Signals Are Transmitted to the CNS, Which Communicates with the Heart and Peripheral Arterial Resistance Vessels. (Adapted from Norsk and Karemaker, [2008]).

in heart rate in 0 g compared to 1 g.[1] There is also more and more evidence that the vestibular system plays a significant role in the regulation of blood pressure. During the transition from various postures, the stimulation of the otolith organs by the changes in head orientation relative to gravity could be used as a signal for triggering fast adjustment in blood pressure [Yates, 1996]. This response would, of course, be altered in microgravity.

Overall, although the baroreceptors and vestibular receptors respond rapidly to pressure and acceleration changes, respectively, the response is not immediate. Anyone who has stood up very quickly from a reclining or kneeling position knows that a few seconds of dizziness may result. This dizziness is the period when the brain is receiving too little blood flow while the body's reflexes work to correct blood pressure in the upper body. Jet pilots performing high-g turn experience the same thing. There is a "lag" period before cardio-vascular responses begin to accommodate to the g-induced movement of blood downward from their heads to their feet. During, and even before, this critical time pilots must be especially vigilant to maintain their blood pressure by special straining maneuvers that increase blood pressure (further aided by a rapid-reacting anti-g suit that inflates on their legs and abdomen to push blood back towards the upper body). Such lag times in body reflexes are not so important in microgravity, because the headward fluid shift to which the baroreceptors are responding is a much slower and chronic condition, beginning as the astronauts recline in their seats for launch and continuing on-orbit.

4.2.2.3. Fluid volume regulation

Long-term regulation of blood pressure and related blood volume are primarily controlled by the kidneys. The main parameter controlled is blood plasma volume, the liquid portion of the blood. Ultimately, the cellular components of the blood are also controlled by producing or destroying red and white blood cells, and platelets. However, this is a secondary and longer-term phenomenon.

The kidneys play a large role in the regulation of fluid volume in the body and aid in the control of red blood cell production and blood pressure. The kidneys also help to maintain the normal concentrations of water and electrolytes in the body fluids. This control is dependent upon hormones regulating the salt and water balance. For example, the *anti-diuretic hormone* (ADH) is a polypeptide hormone released through the posterior pituitary gland of the brain when it senses an increase in plasma osmolarity, relative salt concentration. The ADH hormone acts directly on the kidneys to cause them to retain more water. This water then dilutes the blood plasma and increases plasma volume. Alternately, a reduction in ADH levels will cause the elimination of more water from the body.

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[1] Earth's gravity may determine the location and size of internal organs such as the heart. For example, Lillywhite et al. [1997] noticed that the heart of the tree snake, that is crawling up and down trees and therefore must cope with gravity, was closer to the brain than the land or sea snakes, who spend most of their life in a horizontal position or are neutrally buoyant. The tree snake was the most tolerant to centrifugation, suggesting that it would be more gravity tolerant than the other snakes as it did not have to carry blood over as great a distance from the heart to the brain [Morey-Holton, 1999].

Certain kidney cells are also sensitive to arterial pressure in a baroreceptor fashion, sympathetic nervous system activity, or circulating epinephrine from the sympathetic nervous system. In response to low blood pressure or increased sympathetic nervous activity, these cells initiate a rather complex, multi-stage process that serves to retain or eliminate water and electrolytes.

In summary, I cite the analogy proposed by Levine [1999]: "It is helpful to think about the system as made up of "the plumbing", comprised of the "pump" (the heart) and "pipes" (the blood vessels), and the "control system" (the autonomic nervous system, hormones regulating salt and water balance, and local endothelial derived mediators of microvascular flow). For acute demands, such as during exercise or rapid changes in posture, higher order centers in the brain initiate an increase in the heart rate, termed "central command". Sensors located in skeletal muscle respond to changes in both metabolic and mechanical state and send back signals to the brain reflective of the intensity of effort. The heart itself is a sensory organ and detects the adequacy of hydration and cardiac filling through "mechanoreceptors". Pressure sensors or "baroreceptors" in the walls of the large blood vessels detect the pressure within the vasculature. These signals are integrated in special centers in the brain, which respond by regulating both the strength and frequency of the heart's contraction and the resistance of the blood vessels, primarily by neural mechanisms."

4.3. Effects of spaceflight

Rapid transition between upright, sitting, and lying down postures requires that the heart and blood vessels respond very quickly. On Earth, this is achieved by very sophisticated control centers. These control centers are challenged during spaceflight. When hydrostatic gradients are removed, such as changing from the upright to the supine position or exposure to microgravity, blood is shifted from the lower part of the body towards the chest virtually doubling the amount of blood inside of the heart. The heart responds to this volume load by increasing the amount of blood it pumps, and by initiating both a redistribution and elimination of plasma.

Research studies have focused on understanding the effects of spaceflight on the cardio-vascular system by studying cardiac output, heart rate, blood vessel behavior, blood pressure, and blood volume during spaceflight and upon return to Earth. One aim of these studies is to determine precisely when fluid shifts occur, because they are believed to be the precursor of other physiologic changes that occur in microgravity.

4.3.1. Launch position

It is important to realize that the astronauts are oriented in almost a horizontal position while waiting for a launch in the space shuttle or *Soyuz* (Figure 4.8). The crew is placed in this position approximately 2.5 h prior to the expected launch time, and they can stay there for as long as 4 h before Mission Control considers a launch scrub. This supine position with a 90° hip and knee flexion is chosen to direct the launch acceleration in the horizontal direction of the body (+Gx, back-to-chest), for which the tolerance is greater (Table 4.2) (see Figure 1.18).

Figure 4.8. During Launch on Board Soyuz, Astronauts Are Reclined on Their Backs in Molded Couches, with Their Legs Higher Than Their Heads. This Prevents Blood from Pooling in the Legs During Ascent and Assists the Heart in Pumping Blood to the Rest of the Body. (Credit NASA).

Table 4.2. Tolerance to Vertical (Gz) and Horizontal (Gx) Acceleration [Elert, 2002].

Vertical Acceleration (g, Up Is Positive)	**Event or Symptom**
16	Limit of human tolerance, centrifuge[a]
12–14	Ejection seat
11.4	Acrobatic airplane
4.5–6.3	Loss of consciousness
3.9–5.5	Complete loss of vision (black-out)
3.4–4.8	Partial loss of vision (gray-out)
4.5	Roller-coaster, maximum at bottom of first dip
−1	Congestion of blood in head
−2	Severe blood congestion, reddening of vision (red-out)
−5	Limit of sustained human tolerance
Horizontal Acceleration (g, Magnitude Only)	**Event or Symptom**
0.4	“Pedal to the metal” in a typical car
0.8	“Pedal to the metal” in a high performance sports car
2	Extreme Launch™ roller-coaster at start

(Continued)

Table 4.2. (Continued)

Horizontal Acceleration (g, Magnitude Only)	Event or Symptom
3	Space Shuttle, maximum at takeoff[b]
	Jet fighter landing on aircraft carrier
8	Limit of sustained human tolerance
21–35	Limit of human tolerance, centrifuge[a], 5-s duration
40–80	USAF chimpanzee, centrifuge[a], 60-s duration
60	Chest acceleration during car crash at 48 km/h with airbag
70–100	Car crash that killed Diana, Princess of Wales, 1997
83	Human subject, rocket powered impact sled, 0.04-s duration
247	USAF chimpanzee, rocket powered impact sled, 0.001 s
3,400	Impact acceleration limit for crash-survivable flight recorder

[a] The passenger capsule of a human centrifuge pivots so that a test subject in a seat would experience a vertical acceleration while a test subject lying down would experience a horizontal acceleration.
[b] During lift off, the space shuttle, which is pointing more or less upward, is accelerated in the direction of its vertical axis, but the passengers (who are lying on their backs) are accelerated in the direction of their horizontal axes.

The effect of this specific supine position is that significant blood volume is placed above the heart, thereby increasing pre-load to the heart (central venous pressure) and cardiac output. During the early portion of this orientation, a subject's stroke volume increases from about 75 mL/beat to about 90 mL/beat. This is entirely expected, because there is a rush of fluids to the upper part of the body and the heart has then more blood to force out during each beat. The body compensates in part for this situation by reducing blood volume through urination and reduced thirst. Shuttle astronauts wear undergarments with a fluid-absorbent material that permits them to urinate inside the launch suits, if necessary. However, some astronauts sometime prefer to restrict their fluid intake from 12 to 24 h before launch and "fly dry" to prevent using the diaper. This may work in the short term; however, it puts them into orbit in a fluid-depleted state. In addition, such reduction in blood volume on the launch pad may impair their ability to execute an emergency egress and could provoke syncope upon standing up quickly.

Space shuttle emergency egress plans during launch or landing call for the crew to escape through the side hatch or flight deck windows. During these phases, the crew is wearing a 45-kg space suit, which includes a life support system and a parachute. It is pertinent to ask whether, after several hours in the launch supine position, every crewmember would be able to use the escape system, and egress rapidly without any assistance.

4.3.2. Early on-orbit

4.3.2.1. Fluid shift

Once the launch phase is complete, the headward fluid shift continues in microgravity relative to normal Earth's conditions. This shift is thought to occur because the mechanisms that normally act to counter the pooling of blood in the lower extremities

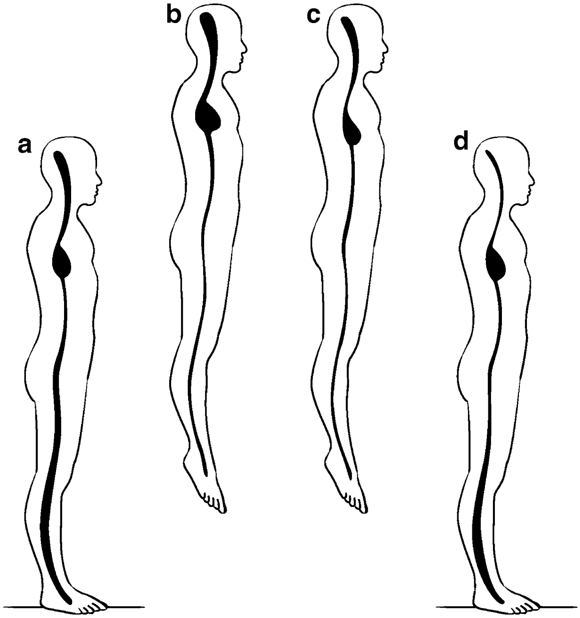

Figure 4.9. Fluid Shift During Space-Flight. (**a**). On Earth, Because of the Down-Ward Pull of Gravity, the Body Easily Supplies Blood to the Lower Limbs. (**b**). Early On-Orbit, Blood Volume Shifts Toward the Chest and Head, Resulting in More Blood Than Usual in the Upper Portion of the Body. (**c**). This Increase Triggers the Receptors, Which Then Cause the Body to Reduce the Volume of Fluid. The Body Functions with Less Fluid and the Heart Becomes Smaller. (**d**). When Astronauts Return to Earth, the Bulk of the Blood Goes Back Down to the Legs, and Because the Total Amount of Blood has Decreased, There Isn't Enough to Fill up the Whole System of Blood Vessels. This Contributes to the Occurrence of Orthostatic Hypotension.

continue to act even in the presence of gravity. This headward fluid shift actually creates a more even distribution of fluids and a more even distribution of blood pressures than is seen on Earth (Figure 4.9b). This initial fluid shift occurs rapidly and is virtually complete within the first 6–10 h of flight. The effects of this headward fluid shift tend to last for the entire duration of the flight. The most obvious effect is a visible distension of veins in the head and neck region, as well as puffiness around the eyes. The astronauts sense this fluid shift and describe it as a "fullness in the head" or a nasal stuffiness similar to chronic sinus congestion. The senses of smell and taste may be altered, as happens on Earth when one has a cold. Some astronauts also report increased pressures inside the eye for a few days and pain in the eyes when they execute large ocular saccades. Occasional headaches have been reported, and intracranial pressure is still being studied to see how and if it changes in microgravity as a possible correlate to this and other effects (such as nausea).

In contrast to the upper body, the legs experience a net loss of fluids as general capillary pressures decrease there. This leads to a so-called "chicken leg syndrome" as leg volume decreases with time in microgravity. Studies have shown that leg circumference may decrease 10–30%, mostly in the fleshier thighs, as up to 2 L of fluid shift headward. Fluid shifts clearly account for the first phase of this decrease [Moore and Thornton, 1987].

Thirst is generally decreased early in-flight, and astronaut fluid intake is reduced. In part, this may be a result of the headward fluid shifts and suppression of normal thirst reflexes. However, there are no indications that urine output is increased in space [Norsk, 2001]. The reduced fluid intake may also be due to the effects of space motion sickness in many crewmembers for the first 1–3 days of spaceflight. Use of anti-motion sickness drugs, mission activities, and many other factors can also affect hydration and urine volume in space.

4.3.2.2. Blood pressure

One measurement of special interest in cardio-vascular physiology is the central venous pressure (CVP). The CVP is the pressure in the vena cava, which are the large veins returning blood from the systemic circulation to the right atrium of the heart. This pressure represents the blood "available" to be picked up by the right atrium before each contraction cycle. This measurement should therefore establish the amount of fluids that redistribute or shift to the upper part of the body and how rapidly that fluids shift occurs. The first direct measurements of CVP in humans occurred during a Spacelab mission in 1993, when one astronaut was launched with a catheter extending into the inferior vena cava near the heart (Figure 4.10). Results were confirmed in later Spacelab missions. Data have indicated an increase in CVP before launch, when the astronauts are in the knees-up seated position, and a further increase during launch and ascent. One minute after reaching microgravity, though, CVP decreased below pre-launch

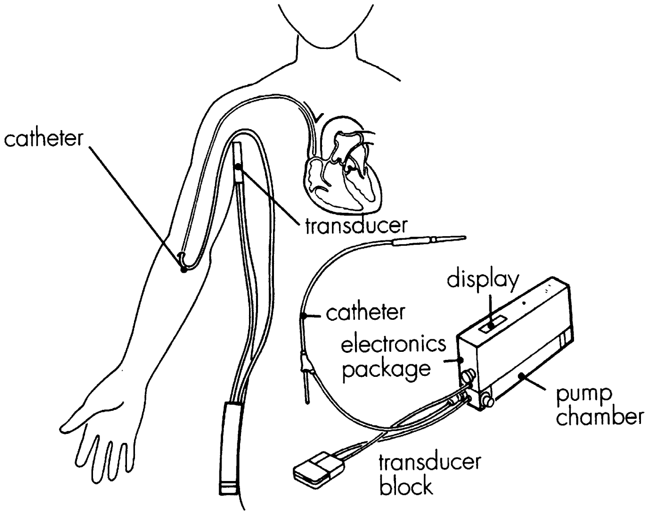

Figure 4.10. One Spacelab Experiment Used a Catheter Inserted Preflight into an Arm Vein of an Astronaut and Later Moved Nearer to the Heart. This Catheter Had a Sensor Attached, Which Measured the Blood Pressure Closest to the Heart. The Experiment Showed That the Astronauts Experience a Much More Rapid Fall in Central Venous Blood Pressure Than What Was Predicted by the Model. (Adapted from Lujan and White [1994]).

levels and stayed lower than normal [Foldager et al., 1996; Buckey et al., 1996b]. The increase in CVP before and during the actual launch phase were expected, because of the rush of fluids to the right atrium due to the supine position and the g forces compressing the chest area, respectively. However, the decrease in CVP once the astronauts arrived in space, even though the body fluids continued to shift upward, and the fact that CVP fell to a level below normal within 1 min upon entering the space environment, was totally unexpected.

In microgravity, the decreased CVP may indicate that venous compliance of thoracic blood vessels increases rapidly to hold the increased fluids at a lower pressure. This increased space for fluid build-up around the heart could be enhanced, for example, by removal of the weight of the lungs on veins that surround the heart. Other short-term changes include an increase in heart rate and an increase in heart size due to excessive fluid volume [Frische-Yelle et al., 1994].

To ascertain whether a change in blood pressure is induced by a change in the amount of blood pumped by the heart or by dilation of the peripheral arteries, cardiac output must be measured. Because the amount of blood that passes through the lungs is equal to the amount of blood that flows out of the heart (cardiac output), measuring gas exchanges can be used to determine cardiac output. Therefore, scientists monitor a gas mixture that the subject inhales and exhales. As it passes through the lungs, the blood absorbs a tracer that is in the gas mixture. The absorptions rate is proportional to the amount of blood flowing through the lungs. This proportionality relationship allows then for a direct calculation of cardiac output. An increase of 18% in the rate of tracer uptake occurs during the first days that an astronaut is in space, as compared to the upright standing position on Earth. Together with the decrease in blood pressure, as described previously, this increase in cardiac output suggests that the arterial resistance vessels are more dilated in 0 g than in 1 g. The values in space are comparable to those obtained in a sitting position on Earth. In other words, the cardio-vascular system relaxes after just 1 week in space [Norsk and Karemaker, 2008].

4.3.3. Later on-orbit

4.3.3.1. Fluid shift

The headward fluid shift triggers the baroreceptors, which inform the control centers, which in turn eliminate the excess of fluid in the upper body (Figure 4.9c). Over several days, the blood volume decreases as a result of decreased thirst and increased water output by the kidneys. Total loss of fluid from the vascular and tissue spaces of the lower extremities has been found to be 1–2 L (about a 10–15% volume change compared to preflight). Within 3–5 days in space, total body water stabilizes at about 2–4% below the normal level and plasma volume decreases by about 22%.

Surprisingly, total body water, as measured using an isotope-dilution technique, is unchanged, although the extracellular fluid and plasma volume are decreased. These results imply that the 2 L lost in the vascular and interstitial compartment of the lower extremities are partially relocated in the intracellular space. After a reduction in blood volume, including loss in plasma volume and red cells count, an astronaut will reach a new state of intravascular hydration that, while adapted for microgravity, is profoundly hypovolemic for 1-g.

Astronauts were given an intravenous saline infusion to investigate the renal output of salt and fluid in space. The rate of salt excretion in space was the same as in a sitting position on Earth. In fact, in space the blood pressure is also same as when sitting on Earth. However, the concentration level in the blood of the sympathetic nervous system hormone transmitter noradrenaline was significantly increased. An increase in cardiac output would normally be accompanied by less sympathetic nervous system activity, which would mean that there is an increased excretion of salt and a decreased release of noradrenaline into the blood stream. The unique lung-heart interaction present in microgravity may be the source of this discrepancy. In microgravity, the thoracic cage expands and leads to an expansion of the central vessels and the heart. This then contributes to an increase in blood flow to the heart. A higher level of activity from the sympathetic nervous system results. Sympathetic activity could also result from the decrease in extracellular fluid volume in the legs. An experiment to investigate the long-term effects of microgravity on sympathetic nervous system activity is now in progress on board the ISS. Blood pressure and cardiac output are being measured over 24-h periods with noradrenaline concentration in the blood platelets also being measured [Norsk and Karemaker, 2008].

It was also discovered that exposure to microgravity impairs the efficiency of the baroreflex loop. A closely fitting neck collar, similar to a whiplash collar, was used on astronauts during the Spacelab *SLS-1* mission to test and record two blood pressure sensing areas located in the neck. By the eighth day of flight, astronauts had significantly faster resting heart rates, less maximum change of heart rate per unit of neck pressure change, and a smaller range of heart rate responses. The changes that developed were large, statistically significant, and occurred in all astronauts studied.

Measurements on humans before, during, and after several spaceflights have also provided echo-cardiographic data taken on cardiac dimensions and function. Ultrasound imaging revealed that heart volume increases dramatically when the astronauts first arrive in space, probably because of the increased volume of blood flowing into the heart (Figure 4.11). The heart volume then slowly decreases as the astronaut's

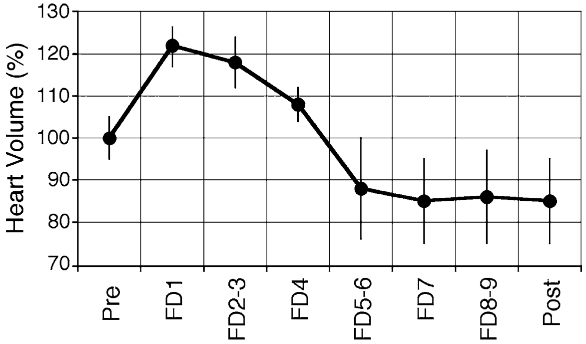

Figure 4.11. Changes in the Volume of the Left Ventricle Just Before Contraction Prior to, During (*FD* Flight Day), and After a Spaceflight. Ventricular Filling Increases Early In-Flight and Decreases After a Few Days Relative to Preflight Levels. (Adapted from Lujan and White [1994]).

body adapts to the space environment, ending up smaller compared with its size on Earth. This decrease in size can be explained by the fact that the excess of blood and fluids has been eliminated, and the heart does not need to pump the blood against gravity. In addition, physical work requirements are generally less in space. The blood vessels also appear to become slightly smaller and stiffer.

4.3.3.2. Maximal exercise capability

When the astronauts were required to exercise at their maximal capability and their consumption of oxygen (VO_2 max) measured in orbit on board the *Space Shuttle*, the measurements were not different from preflight. This indicates that the maximal capacity of the cardio-vascular system, as reflected by maximal exercise capability, was well maintained during short-duration spaceflight. Consequently, the loss of fluid volume and the heart changes seemed to reflect a normal adaptation of the human body to an extreme environment change. This adaptation is a physiological, rather than a pathological response and does not appear to be associated with impaired function.

Exercise has also proven to be the single most effective method for reducing re-adaptation effects, such as the postflight orthostatic intolerance, and for maintaining a healthy cardio-vascular system in space, just like on Earth. For example, only a few exercise sessions were scheduled during the first two *Skylab* missions. In the later missions, more exercise devices were used and the number of sessions increased. During the 84-day *Skylab-4* mission, some astronauts actually improved their cardio-vascular fitness, probably because the rigorous exercise requirements of the mission exceeded their preflight training practices. The space shuttle crewmembers exercise once every second day after being on orbit more than 3 days. More stringent daily physical exercise is scheduled for the ISS crewmembers, which involves exercise periods of 1.5–2.5 h per day for 3 days, with some optional change on the fourth day.

However, recent data reveal a large decline in the maximal exercise capability over the first 30–90 days on board the ISS (Figure 4.12). This loss, which takes place

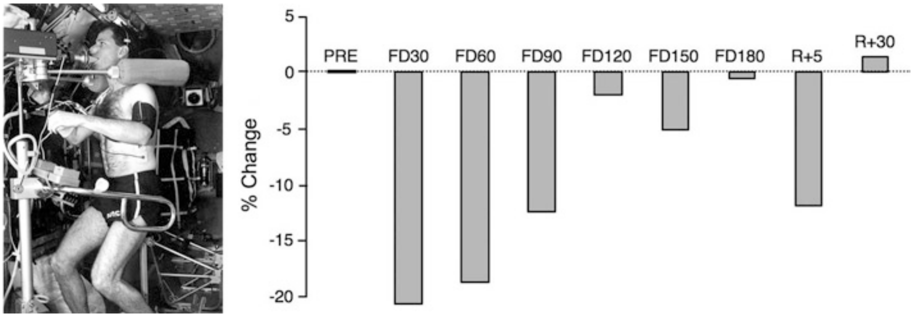

Figure 4.12. ***Left*: The Amount of Gas Absorbed by the Lungs and Heart Rate Is Measured During Exercise on a Cycle Ergometer to Determine Cardiac Output and Maximal Oxygen Consumption.** (Credit NASA). ***Right*: Changes in Maximal Exercise Capability Relative to Preflight (PRE) Baseline Values During (*FD* Flight Day) and After (R + Days) ISS Missions. These Data Are from Nine Crewmembers Through ISS Expedition-18 Who Have Performed Exercise Testing in at Least Four Consecutive 50-Day Intervals During Flight.** (Adapted from Moore et al. [2010]).

despite of the countermeasures,[2] may be related to a phase of adaptation of the control mechanisms of the cardio-vascular system and the changes in body fluid volumes. Subsequent improvement is seen and by the 6-month mark, maximal exercise capability is not different than preflight. On the contrary, VO_2 max is generally reduced immediately postflight. It is interesting to note that fit subjects demonstrate generally larger reduction in VO_2 max and plasma volume than unfit subjects, both in-flight and postflight. Maximal exercise capacity is restored to preflight levels within a week after short-duration spaceflight, and within 1 month after long-duration spaceflight.

4.3.3.3. Extra vehicular activity

During the 15-year life of the Russian *Mir* Space station, 78 two-person EVAs were conducted by 36 crewmembers. Most EVAs were performed between 30 and 180 days of spaceflight, although some occurred as late as 304–350 days of spaceflight. As of ISS *Expedition-18*, there have been 104 EVAs conducted from the ISS, totaling 654 h of EVA time. Of these, 35 were conducted by long-duration crewmembers when the space shuttle was not docked to the ISS. The EVAs were performed during time periods ranging from 32 to 165 days of flight [source: http://www.hq.nasa.gov/osf/EVA/EVA_totals_table.html].

EVAs performed from the space shuttle and *Mir* have elicited an average metabolic cost of about 200 kcal/h, or 0.7 L of oxygen per minute. This represents approximately 30–45% of VO_2 max during upper body exercise over periods of 5–8 h [Moore et al., 2010]. Mean metabolic rates of 800 kcal/h and 5–10 min peaks of over 1,500 kcal/h have been measured in U.S. and Russian EVA suits.

Astronauts lose 0.7–2.2 kg (mostly fluids) during a typical EVA. The space suit is equipped with a liquid cooling garment, which accommodates the heat produced by the high workload requirements. However, overcooling of the extremities is frequently observed, presumably because of the relative decrease in blood flow in microgravity. The astronaut can drink, using a straw, from small containers of liquids within the suit. Failure to do so would result in rapid dehydration. This is a concern because the acute dehydration caused by an EVA might aggravate an already deconditioned state brought on by exposure to microgravity.

The large mass of the suits, which is about 120 kg, is not a significant issue in microgravity. However, the weight of the space suits is expected to have a greater effect on EVA activities when the astronauts are required to ambulate, manipulate tools and scientific equipment, and carry loads of rock samples on the Moon and Mars. During the Apollo missions, with a suit mass of about 100 kg, the average metabolic cost of a lunar EVA was about 15% greater than a microgravity EVA. Heart rates reached 150–160 beats/min during some of the activities.

Apollo astronauts recently stated that they felt that a preflight conditioning program was adequate for short trips to the Moon, which lasted for 14 days or less, stating that exercise countermeasures are not necessary for such missions [Scheuring et al., 2007]. The longest stay on the Moon was 3 days. However, for extended planetary

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[2] The authors of a Russian report [Popov et al., 2004] referred to the initial phase of flight as a "dead period" during which the decrease in physical condition is so severe that none of the countermeasure regimes are sufficiently effective.

stays it is difficult to predict how an astronaut's physical fitness will change. It is not known if Moon or Mars gravity will provide any protection against decreased VO_2 max without additional exercise. Physical fitness maintenance during the transit to Mars will also be a concern [Gernhardt et al., 2008].

A group of NASA investigators have initiated a series of projects to study the physiological, biomechanical, and subjective aspects of work and exercise in the partial gravity of the Moon and Mars. This is part of an effort to determine the levels of cardio-vascular exercise capacity, strength, and countermeasure protection that will be required for EVA activities during missions involving long surface stays. The metabolic cost of ambulation is measured while exercising on a treadmill in normal gravity (Figure 4.13). Then the measurements are repeated during simulated Moon and Mars gravity. These conditions are obtained using a servo-controlled, pneumatic lift system with constant feedback from a strain gauge to provide near constant unloading.

4.3.3.4. Heart rhythm

In the early phase of the U.S. space program, the presence of irregular heart rhythm (dysrhythmia) was taken as presumptive evidence of cardiac pathology. As a matter of fact, the first cardiac grounding of an astronaut occurred because of a heart rhythm disturbance [Johnson and Dietlein, 1977]. The presence of rhythm abnormalities

Figure 4.13. Astronaut Performing Treadmill Walking in the Mark-III Prototype EVA Suit. Ground-Based Estimates Suggest That, Depending on the Terrain, Walking on the Lunar and Martian Terrain May Be Difficult and Will Likely Require an Above-Average Aerobic Capacity to Accomplish Safely [Moore et al., 2010]. (Credit NASA).

during actual spaceflight can only be assessed when a crew is physiologically monitored, e.g., during extra-vehicular activity, exercise, and application of lower body negative pressure. Consequently, these heart rate irregularities seem more prevalent during these activities.

Serious heart rhythm disturbances were noted during the Apollo program, both during EVAs on the Moon and after returning to Earth [Berry, 1974]. Some of these abnormalities have been attributed to electrolyte imbalance or stress. For example, the astronauts were given excessive workloads on the Moon and had low blood potassium levels upon return to Earth.

Significant dysrhythmias were also observed during *Skylab*, *Mir*, and shuttle flights. A crewmember during the *Mir*-2 (1987) mission developed a persistent dysrhythmia during an EVA (Figure 4.14). This resulted in the mission duration being shortened. Earlier on, a Soviet cosmonaut was returned ahead of schedule from the *Salyut-7* space station because of an intermittent cardiac arrhythmia, which originated during the course of a minor mishap during an EVA. The Russian Space Agency (RSA, or Roscosmos) has also reported a cosmonaut suffering from a massive myocardial

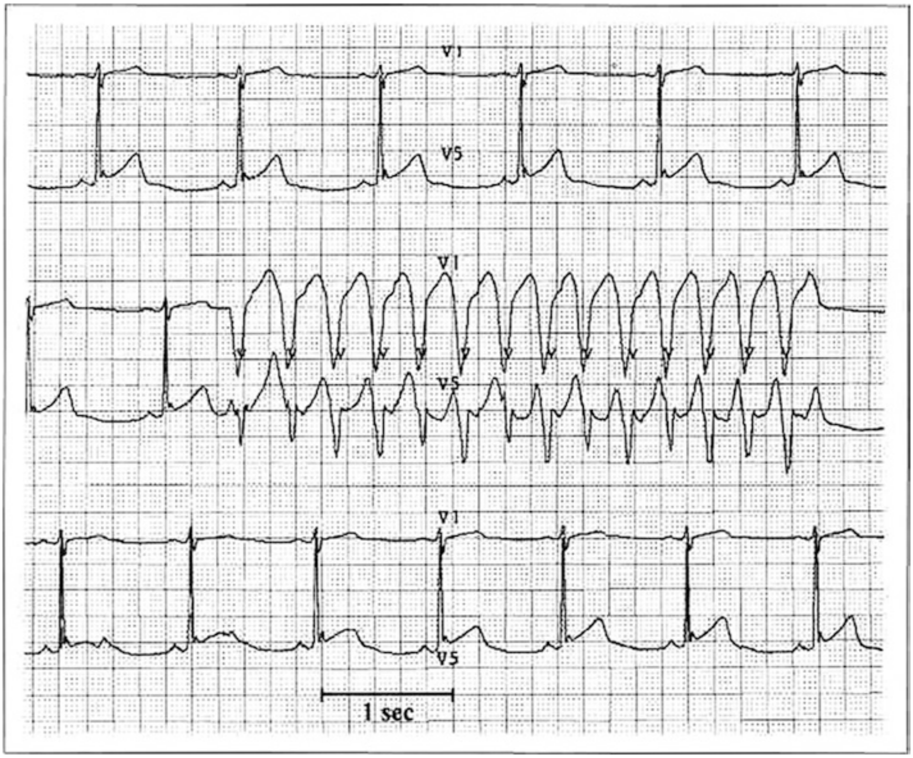

Figure 4.14. During the U.S.-Russian Shuttle-Mir Program, Ambulatory ECG Recordings Were Taken on Several Crews. A Recording in One Cosmonaut Revealed a Non-sustained 14-Beat Run of Ventricular Tachycardia. (Adapted from Fritsch-Yelle et al. [1998]).

infarction at the age of 49 years, just 2 years after his third short-duration flight. Moreover, the Russian medical community has reported to NASA that over the last 10 years of *Mir* operations, they observed approximately 31 abnormal electrocardiograms and 75 dysrhythmias [Hamilton, 2008].

As previously explained, the cardiac atrophy that develops during spaceflight could lead to orthostatic hypotension and abnormal left ventricular function. Such atrophy may also be at the root of the irregular heart rhythms observed in some of the *Mir* crewmembers after long-duration exposure to microgravity. A significant limiting factor for extended duration space exploration missions may be cardiac atrophy, according to the results of recent simulation studies that suggest that this condition may be progressive, and without a clear plateau over at least 12 weeks. The goal of another ongoing ISS experiment is to identify the mechanisms of cardiac atrophy and quantify its extent, time course, and clinical implications during prolonged spaceflight. In addition, the functional consequences of cardiac atrophy, both in space and following return to Earth, will be determined for orthostatic tolerance under Earth, Mars, and Moon gravity conditions; cardiac filling dynamics; exercise tolerance; and arrhythmia susceptibility. In flight, advanced echo-Doppler examinations will be used to determine how heart muscle atrophy influences the way the heart relaxes and fills. On the ground, magnetic resonance imaging (MRI) of the heart, performed both before and after the flight, will pinpoint what kind of atrophy occurs and precisely quantify its extent [Levine and Bungo, 2010].

4.3.4. Postflight

As mentioned in the previous sections, the re-entry forces in the *Soyuz* capsules can go up to 3.8 g[3] exerted along the Gx axis (chest to back). The position the most effective for g-tolerance, lying-on-back with the legs flexed, was chosen because the need for the cosmonaut to “fly” the vehicle is minimal (Figure 4.15). By contrast, the astronauts in the space shuttle are exposed to re-entry forces along the Gz axis (head-to-toe), due to the gliding attitude of the vehicle. These forces do not exceed 1.3–1.5 g for approximately 20 min. However, such small forces during re-entry after 16 days of cardio-vascular deconditioning in microgravity may be as provocative as forces of 5–6 g in a fighter aircraft with a fit pilot. In the worst case, loss of consciousness (syncope) may result from a decrease in blood flow to the brain (cerebral hypoperfusion) (see Table 4.2).

Both the heart rate and arterial pressure increase during re-entry and just after landing (Figure 4.16). After landing, all first-time astronauts are tested for the degree of their intolerance either by laying them on a “tilt table” that moves rapidly from the horizontal to vertical position, or by comparing their heart rates and blood pressures between supine rest and upright standing. After short-duration spaceflight about 27% of crewmembers are unable to complete a 10-min stand test on landing day, and are forced to sit down to prevent syncope. The causes for this orthostatic intolerance are

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[3] During the ISS *Expedition-6* crew return in May 2003, the *Soyuz* headed down at a steeper angle, thus decelerating faster than planned. As a result, the crew was subjected to 8–10 g for several minutes.

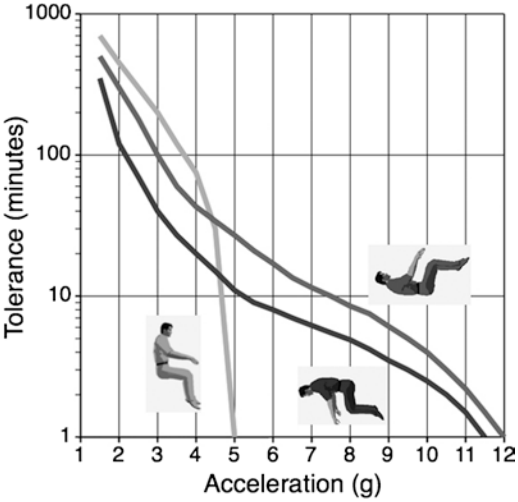

Figure 4.15. Tolerance to Acceleration, Measured as the Time Before Fainting During a Run in a Centrifuge in Various Body Positions. Tolerance Is Stronger in the Supine or Prone Than in the Upright Position Due to the Effect of Acceleration on the Column of Blood.

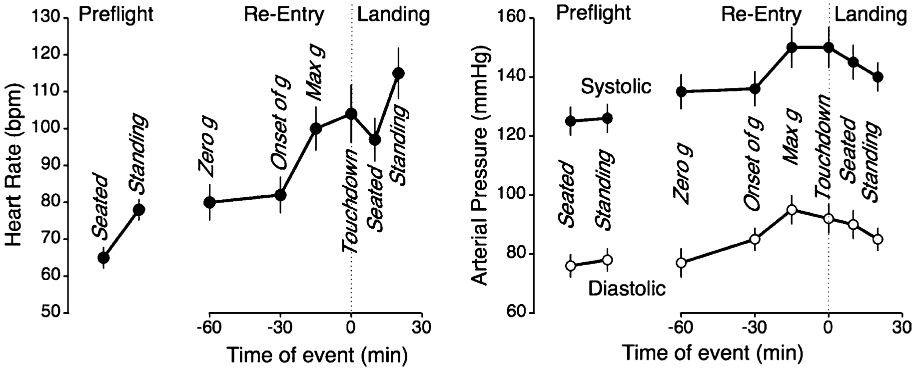

Figure 4.16. Changes in Heart Rate and Arterial Pressure When Going from the Seated to a Standing Position Preflight and Postflight, and During Re-entry and Landing (0-g to Touchdown). When Standing Postflight, Despite an Increase in Heart Rate, There Is a Decrease in Arterial Pressure, Which Can Lead to Pre-syncope or Syncope. (Adapted from Sawin et al. [1998]).

diverse. In some subjects, the syncope is due to a decreased blood flow (less than 30 mL/min per 100 g of brain tissue); in others it is due to a decreased arterial pressure (mean arterial pressure less than 40 mmHg).

A very evident cardiac response postflight is a markedly elevated heart rate (Figure 4.16). This is probably a reflexive action to increase cardiac output and, thus, blood pressure. This increased heart rate seems especially important to cardio-vascular function, as tests have shown that other mechanisms to increase short-term blood pressure, like increasing peripheral resistance or increasing stroke volume through increased heart contractility, via the sympathetic nervous system seem less efficient after spaceflight. Decreased baroreceptor sensitivity acquired in microgravity can also slow the total response.

Recent studies performed on six astronauts before and after long-duration (129–190 days) spaceflights revealed that orthostatic intolerance is even more severe after long-duration than after short-duration flight. Five of the six astronauts studied became pre-syncopal during tilt testing after long-duration flights, whereas only one had become pre-syncopal during stand testing after short-duration flights [Meck et al., 2001].

4.4. What do we know?

4.4.1. Orthostatic intolerance

Postflight orthostatic intolerance is a result of more than just the loss of fluid. Orthostatic intolerance is presumably caused by three factors that are related to each other: the volume of blood in the blood vessels, the ability of blood vessels to expand or constrict to maintain blood pressure, and the functioning of the heart itself. We have already seen that upon return to Earth, when gravity pulls the fluid downward and there is not enough fluid, the system cannot function normally and this contributes to the occurrence of orthostatic hypotension (Figure 4.9d).

Another contributor to this problem is the autonomic nervous system, which helps control blood pressure, among other things. Normally, this system is responsible for making minute and immediate adjustments to the cardio-vascular system to maintain blood flow and pressure during changes in posture. The system does this by releasing a neurotransmitter called norepinephrine that causes the blood vessels to constrict to keep the pressure at the appropriate level to supply an adequate amount of blood to the body's organs. In space, when hydrostatic gradients are removed, such as changing from the upright to the supine position, perhaps those mechanisms "forget" their function.

Research on animals has underlined the importance of the baroreceptors in the regulation of blood pressure. Dogs whose carotid sinus baroreceptors have been excised have a variation of from 40 to 200 in their mean blood pressure. Manual compression of carotid sinuses can cause syncope and bradycardia, or low heart rate in a healthy person. In microgravity, however, the carotid sinus would fire nerve impulses at a more or less constant rate. The extent to which the sensitivity of the baroreceptors may decrease with prolonged spaceflight, and their ability to regain the lost sensitivity, is unknown.

Orthostatic hypotension is also caused by the blood vessels. The vessels themselves have a certain amount of control over the amount of blood flowing to the organ they are serving. For example, when a blood pressure cuff is inflated to the point where there is no blood flow through the vessels of the arm, the arm's vessels dilate to try to increase the flow rate. If the cuff is suddenly released, the dilated vessels allow the blood to rush back into the arm. This increases shear stress, which actually stimulates the lining of the blood vessels to release additional vasodilators, ensuring that the arm will receive increased blood flow. This mechanism is called reactive hyperemia. Similarly, when an astronaut returns to Earth and blood rushes to his/her legs, the vessels might respond not by constricting, to force the blood back up, but by dilating further, which permits more flow downward and less pressure, resulting in less blood in the astronaut's upper body and head. Hence, they faint.

Another trend observed in recent studies is that there is a difference between women and men in the ability of their bodies to maintain blood pressure after spaceflight. Women generally have a higher heart rate and a lower vascular resistance than do men. Thus, when female astronauts return from space, their vascular resistance, already low, is insufficient to combat the lower blood volume. In a recent postflight analysis after a short-duration spaceflight, all female astronauts became syncopal versus only 20% of male astronauts [Harm et al., 2001].

Aging might also be a factor. The differences that aging had made to his body better equipped John Glenn, at age 77, to handle the cardio-vascular adaptations to a microgravity environment (Figure 4.17). When he returned from orbit, far from feeling faint or suffering from cardio-vascular stress, he was calm and stood upright with no problem. An older person has a different strategy than a young person in maintaining blood pressure. Glenn had a high release of norepinephrine, which helped to maintain his blood pressure, both before and after spaceflight. This response is typical of the elderly and for Glenn, this resulted in a normal level of vascular resistance. Glenn also had a higher cardiac output than the other male astronauts, possibly due to a greater venous return. This higher output coupled with a normal vascular resistance,

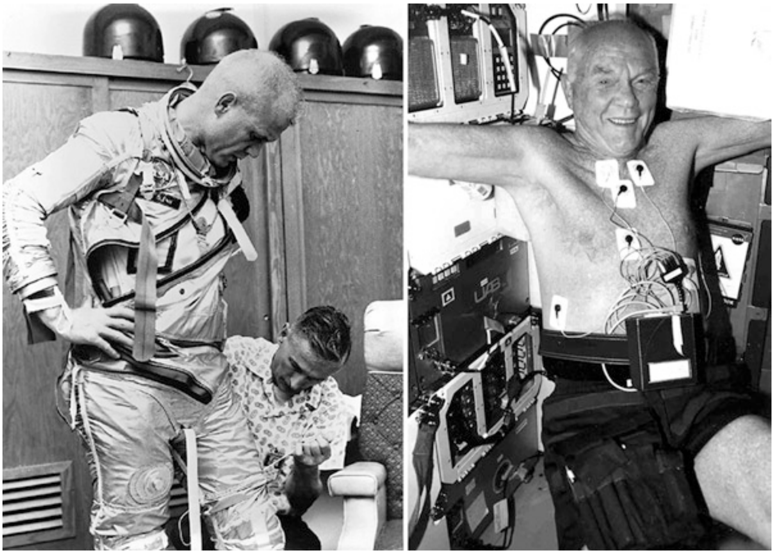

Figure 4.17. John Glenn Returned to Space on Shuttle Mission STS-95 at Age 77, i.e., 37 years After His First Flight on Board Mercury. His Cardio-Vascular Response Was Closely Monitored to Study the Effects of Aging on the Ability of the Cardio-Vascular System to Adapt to Spaceflight. (Credit NASA).

presumably enabled Glenn to maintain an adequate blood pressure on landing day [Rossum et al., 2001].

Finally, although there is evidence that both the autonomic nervous system and hormone secretion are altered, their effects on the kidneys, blood vessels, and heart have yet to be fully understood and must be studied over varying duration of exposure to weightlessness. Elucidation of the mechanisms of these effects promises to shed light on some clinical, non-spaceflight problems such as high blood pressure and heart failure.

In summary, hypovolemia, cardiac atrophy, and autonomic dysfunction have each been hypothesized to contribute to postflight orthostatic intolerance, but their relative importance is unclear. Furthermore, it is unknown whether actual abnormalities in the myocardium itself develop with long-duration spaceflight. Therefore, reliable portable noninvasive methods are needed to detect and quantify these changes. The imaging modalities of radiography, magnetic resonance imaging and computerized tomography would be state-of-the-art techniques. A specially modified commercial ultrasound echocardiograph instrument is being used in the Human Research Facility of the ISS for medical diagnosis and physiology research (Figure 4.1). To date, echocardiography has the most versatile ability to characterize cardio-vascular anatomy and physiology in ground-based models, pre- and postflight, and most importantly during flight [Martin et al., 2003].

4.4.2. Pulmonary function

The pulmonary system works in tandem with the cardio-vascular system to supply the body with the oxygen needed for life. Unlike the cardio-vascular system, no pulmonary system problems have been associated with weightlessness per se, and researchers have devoted less attention to its physiology in microgravity. In fact, an increased lung blood flow and more uniform flow distribution were observed in microgravity, suggesting that overall lung function was actually improved in space [West et al., 1997]. However, in the long term, lung function can be altered by changes in vascular pressure and volume. Also, it is possible that lengthy alterations in the relative flow distribution of blood and air in different lung regions might permanently affect right heart function [Linnarsson, 2001]. Dysbarism, the condition that results from exposure to decreased or changing barometric pressure, is also a problem of increasing magnitude during extra-vehicular activity (see Chapter 7, Section 7.3.4).

Along with alterations resulting from changes in vascular pressures and volumes, inhaled gases, vapors, and aerosols can damage the lungs. Integrity of the pulmonary system cannot be assumed simply because of lack of symptoms or overt clinical signs. The factors affecting the selection of cabin atmospheres and pressures for spaceflight, as well as the problems of cabin atmosphere maintenance and contamination in open or closed environmental systems will be discussed later (see Chapter 8, Section 8.3.1).

The kidneys are central to the above-mentioned physiologic questions. Renal problems may occur in the space environment. As we will see in the next chapter (see Chapter 5, Section 5.1.2), weightlessness causes a monthly 0.4% resorption of bone calcium, which is excreted in the urine. With increased concentration of urinary calcium and some other changes induced by weightlessness, such as urine alkalinity and possible reduction in urine volume, kidney stones may form more easily. In addition to debilitating pain, kidney stones might obstruct the urinary tract and precipitate infection, which is potentially quite dangerous in space. Thus, kidney function must be understood better with regard to calcium metabolism as well as its relation to cardio-vascular phenomena.

We also still need to understand more completely the actions of drugs that affect cardio-pulmonary and renal systems in space. This will be essential for adequate health maintenance. Ordered in descending priority, the following classes of agents must be investigated: anti-arrhythmics, bronchodilators, anti-allergy and anti-anaphylactic drugs, analgesics (including narcotics), hypnotics and psychotropics, diuretics, and anti-coagulants.

4.4.3. Bed rest

Since the beginning of the space program, human bed rest has been commonly used as a ground-based model to test the effects of weightlessness and proposed countermeasures upon the cardio-vascular system. In this model research subjects are required to remain in bed for lengths of time from a few days to several months. The bed is tilted at 6° head-down, so that head is below the heart. This tilt position simulates the same fluid shift as in microgravity. Lunar and Martian gravity may also be simulated with a bed tilt of 9.5° and 22.5° relative to the horizontal, thus simulating a gravitational load of 0.16 and 0.38 g, respectively, along the main column of blood (Figure 4.18).

In fact, studies had been conducted on bed rest patients and on normal, healthy subjects starting as early as 1855. Physicians have used prolonged rest in bed to immobilize and confine patients for rehabilitation and restoration of health even before that time. The rationale is that the horizontal position relieves the strain of the upright posture on the cardio-vascular system, bone fractures, muscle injuries or fatigue. Consequently, there is an almost complete loss of hydrostatic pressure (see Figure 4.5), virtual elimination of longitudinal compression of the spine and long

Figure 4.18. Subjects Are Lying in Bed for Duration Ranging From 5 Days to 3 Months to Simulate the Effects of Microgravity (*left*) or Lunar Gravity (*right*) on the Cardio-Vascular System Responses. (Credit National Space Biomedical Research Institute (NSBRI)).

bones of the lower extremity, and reduced muscular force. Patients on prolonged bed rest experience headward fluid shift, decrease in blood pressure and blood volume, and reduced physical activity similar to those that occur in astronauts in space [Gharib and Custaud, 2002].

Bed rest studies were the first to indicate that baroreceptor reflexes may be impaired with time. In effect, when continuously exposed to increased pressure, the baroreceptors apparently become less sensitive and responsive [Eckberg and Fritsch, 1992]. Similar findings have later been found during spaceflight. These changes in sensitivity and responsiveness may take days to occur and, similarly, may take several days to readjust upon return to Earth. Ongoing studies are being conducted to verify these results.

Following a bed rest, volunteers are monitored while placed supine on a tilt table and suddenly brought upright (Figure 4.19). Getting upright again after 3 months in the horizontal position evidently has its cost! Even after a few days in bed most people experience problems with balance and dizziness. After 3 months in bed the same and more expressed problems, such as orthostatic hypotension are observed. Subjects need considerable time before they can stand and walk without assistance. Rehabilitation activities are then being evaluated. Normally most problems with standing and walking are over within a few days, after which the rebuilding of muscle strength can begin. The full recovery of muscle and in particular bone tissue may take much longer, up to 6 months, although not necessarily being felt by the individual.

The students of the International Space University have proposed an idea of exposing crewmembers returning from a 6-month mission on board the ISS to a bed rest of 3–6 months simulating Mars gravity. Following this bed rest the crewmembers

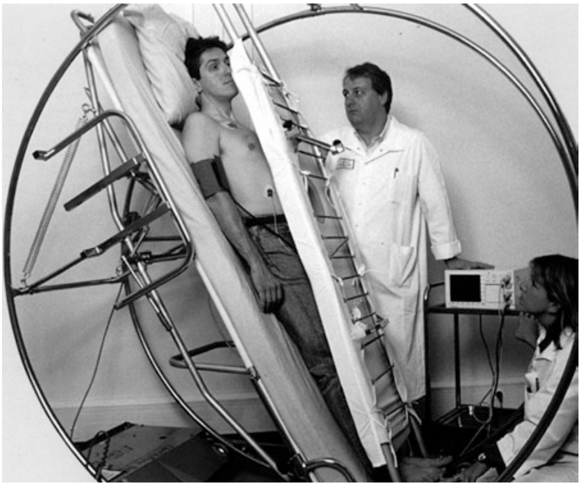

Figure 4.19. At the End of a Bed Rest Study, the Volunteers Are Placed on a Motorized Tilt Table. Their Cardio-Vascular Responses Are Measured When They Are Passively Moved from a Supine to an Upright Posture. (Credit MEDES).

would be sent for another 6-month tour of duty on board the ISS [Smet et al., 2010]. The proposed study, called Martian Feeling, is a dress rehearsal of a mission to Mars aimed at simulating the long-duration effects of 0 and 0.38 g on the cardio-vascular system, evaluating the cardiac tolerance and exercise capability, and validating potential countermeasures and an integrated transit simulation.

4.5. Countermeasures

Researchers remain concerned about devising and refining countermeasures to prevent or avoid cardio-vascular problems associated with the return from microgravity to Earth's gravity. As discussed previously, the cardio-vascular problems associated with spaceflight are multifactorial. Four or five different countermeasures in some combination will probably be needed to solve the problem completely. Current countermeasures include preflight and in-flight exercise, application of lower body negative pressure (LBNP) in-flight, fluid loading prior to re-entry, and rehabilitation after return to Earth.

4.5.1. In-flight

4.5.1.1. Exercise

As a rule, crewmembers are encouraged to drink adequate amounts of fluids and to maintain a regular exercise schedule. Exercise has a protective effect on the increase in heart rate and fall in blood pressure during standing after flight. One way to prevent harmful effects of cardio-vascular deconditioning is to start the spaceflight at a higher level of conditioning by athletic training before the flight. Many of the astronauts run, jog, or participate in aerobic exercise as part of their daily routine training.

An aggressive in-flight aerobic exercise program seems to be partially effective in maintaining postflight aerobic capacity, but its effects on orthostatic tolerance are largely unknown. It is important to note that the discussion of exercise as a countermeasure here is aimed at cardio-vascular conditioning. Other types of exercise (i.e., resistance training) can also be important as countermeasures for skeletal and bone loss seen in microgravity (see Chapter 5, Section 5.6).

Special restraint systems like bungee cords are required to hold the astronauts in place during exercise sessions. Another practical issue regarding exercise in space is that it generates vibrations that are transmitted through the structure of the spacecraft and might impact experiments requiring very low gravity levels. Also, there is no shower!

For ISS crewmembers, the duration of required exercise to balance mission needs and achievable cardio-vascular conditioning remains debated. Exercise sessions typically last 2.5 h per day, including time to change into exercise clothing and clean up following activity, so the effective daily exercise time is approximately 1.5 h. These sessions include training on treadmill, cycle ergometers (Figure 4.20), and resistive exercise devices. To support aerobic training, the U.S. crewmembers typically perform four to six sessions per week for 30–45 min each using the treadmill, and two to three sessions per week for 30–45 min using the cycle ergometer. Aerobic exercise is

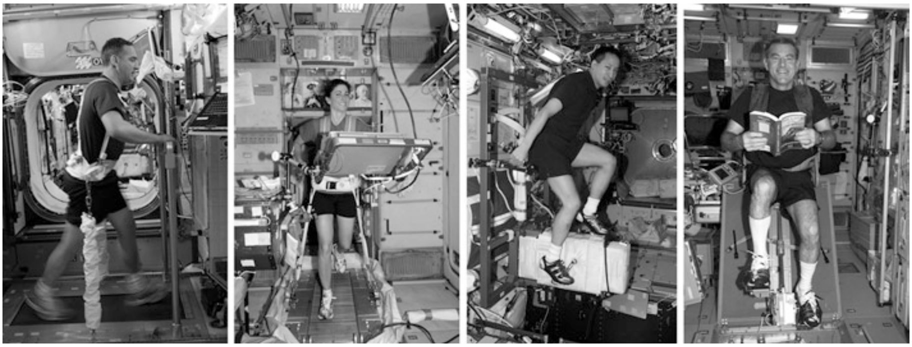

Figure 4.20. These Photographs Show Crewmembers Exercising on the U.S. and Russian Treadmills and Cycle Ergometers, Which Are Located in the Destiny and the Zvezda Modules of the ISS, Respectively. (Credit NASA).

usually at 70–85% of maximal heart rate, with treadmill running at less than one full body weight of resistance[4] [English et al., 2008].

While exercising, the Russian cosmonauts sometimes use thigh constriction cuffs to decrease headward fluid shift. Data on the effectiveness of these cuffs are lacking, but many cosmonauts report significant relief from the head congestion and facial edema otherwise associated with microgravity [Herault et al., 2000].

It is perhaps surprising that, to date, we have very little understanding of the exact physiologic effects (beneficial or harmful) of various types of exercise on the phenomenon of cardio-vascular deconditioning. For example, some evidence suggests that the aerobically trained individual may be more vulnerable to orthostatic intolerance. Protocols for preflight, in-flight, and postflight exercise must be designed and tested in a rigorous manner to determine what, if any, types of exercise may be the best countermeasures to deconditioning. Integrated into the problem of understanding the effects of exercise on cardio-vascular deconditioning is also understanding the responses of blood gases, electrolytes, glucose, insulin, growth hormone, glucagon, and cortisol.

4.5.1.2. Lower body negative pressure

A lower body negative pressure (LBNP, or Chibis) is a device that encloses the lower abdomen and lower extremities to maintain a controlled pressure differential below ambient (Figure 4.21). This device is used in conjunction with heart rate and blood pressure monitoring capabilities. It provides a continuous decompression and maintenance of −60 mmHg. Decompression from ambient pressure to −60 mm Hg can range from 10 s to 10 min (i.e., rapid to slow decompression). However, care is taken in this

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[4] It is interesting to note that research literature overwhelmingly shows the greatest benefits in markers of cardio-respiratory fitness are realized with higher intensity (85–100%), lower duration exercise protocols such as intermittent or interval programs combining short sprints with short to medium rest periods for a wide variety of populations ranging from heart disease patients to endurance athletes [Midgley and McNaughton, 2006].

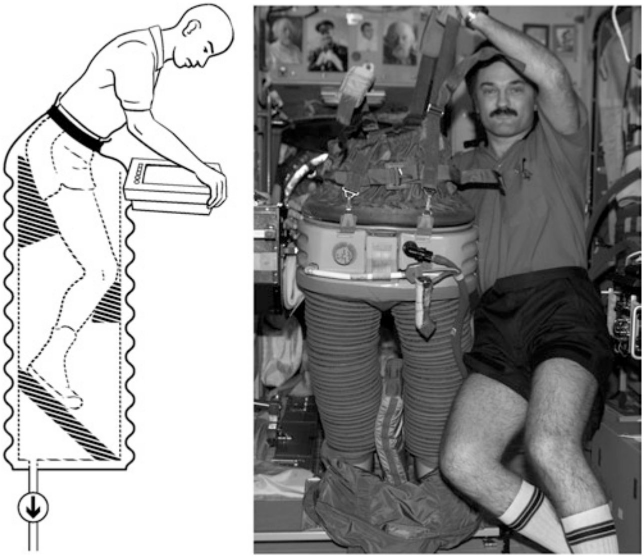

Figure 4.21. ***Left*: A Lower Body Negative Pressure (LBNP) Device Causes the Intravascular Volume to Shift Towards the Lower Extremities in Microgravity, in a Manner Similar to the Orthostatic Load Caused by Assuming an Upright Posture in Earth's Gravity.** (Credit Philippe Tauzin). ***Right*: The Russian Chibis Suit.** (Credit NASA).

approach because, if decompression is too fast, similar effects to postflight orthostatic intolerance can occur. An adjustable foot support, removable saddle, and knee fixation within the device provides skeletal "loaded" and "unloaded" LBNP.

As in standing, the cardio-vascular system responds to LBNP by increasing blood pressure to maintain flow to the upper body and head. LBNP tests performed on-orbit provoke a larger increase in leg volumes, as fluid is shifted rapidly footward, than in control tests on Earth. There is also a much larger increase in heart rate, to maintain upper-body blood pressure, than on Earth. These results may indicate a loss of muscle tone in leg blood vessels and less resistance to expansion by fluids, as well as weakened ability to respond to short-term blood pressure changes in general [Charles et al., 1994]. There is, however, significant inter- and intraindividual differences in the responses to in-flight LBNP tests, which make it difficult to use this test for predicting which astronauts will be more susceptible to orthostatic intolerance after landing.

Further in-flight orthostatic countermeasures and exercise equipment can also include whole-body elastic loading suits, such as the Russian "Penguin" suit (Figure 4.22), pharmacological preparations, and electro-myostimulation.

4.5.1.3. Medication

Orthostatic intolerance is clinically treated using drugs that act by decreasing peripheral venous capacity, preventing blood pooling, increasing vasoconstriction, and increasing total peripheral resistance. Midodrine, a selective alpha-1 adrenergic

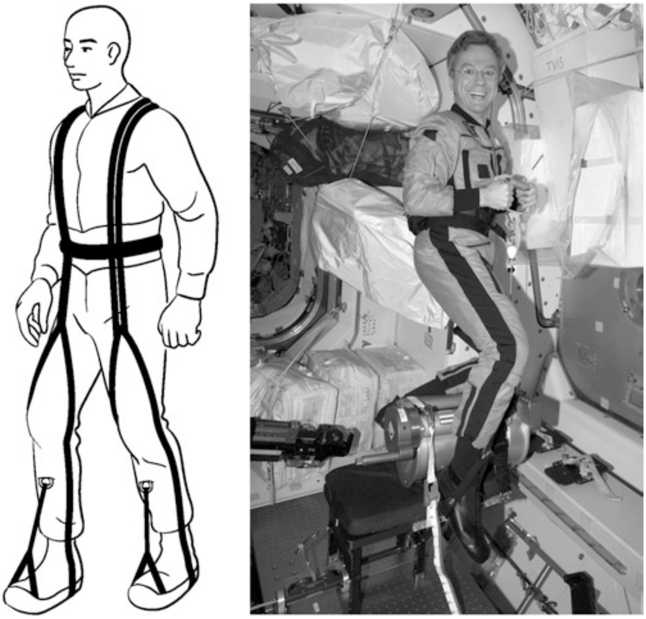

Figure 4.22. ***Left*: The Inside of the "Penguin" Suit Contains a System of Elastic, Straps, and Buckles That Can Be Used to Adjust the Fit and Tension of the Suit. This Suit Forces the Subjects to Use His Extensor Muscles In-Flight to Activate Venous Return.** (Credit Philippe Tauzin). ***Right*: CSA Astronaut Robert Thirsk Exercising with Bungee Cords While Wearing the "Penguin" Suit.** (Credit NASA).

agonist, has been extensively used on Earth to treat low blood pressure. This drug produces arterial and venous constriction resulting in an increase in blood pressure by baroreceptor reflexes. Clinical trials have shown that midodrine is effective in treating orthostatic hypotension secondary to autonomic failure. The ability of this drug to vasoconstrict without increasing heart rate makes it a useful adjunctive treatment to the measures currently being used for postflight orthostatic hypotension. When administered to crewmembers within 2–4 h after landing, midrodine has proven to be a very safe and effective therapy for orthostatic hypotension. Midrodine does not pass the blood-brain barrier when take orally. Therefore this drug has no central stimulant effects. The effects of midodrine are particularly protective of orthostatic tolerance in astronauts who become presyncopal on landing day due to inadequate release of norepinephrine [Fritsch-Yelle et al., 1996].

4.5.1.4. Monitoring

The ISS Human Research Facility (HRF) is outfitted with equipment necessary to make a variety of measurements of the cardio-vascular function. Most of these measurements can be made in conjunction with exercise equipment use. The capabilities available for on-orbit research are summarized in Table 4.3.

Table 4.3. List of Equipment Available on the ISS for Cardio-Vascular Research.

Blood Pressure

Capabilities include noninvasive monitoring and collection of blood pressure data, both extended duration and intermittent, on human subjects. The data can be collected by manual or automated methods during periods of rest or exercise

Electrical Stimulation of Muscle

Local noninvasive muscle stimulation on human subjects using a high current stimulator that provides trains of pulses up to 0.8 amps, according to pre-programmed protocols

ECG/EMG/EEG

Acquisition of human physiological data such as ECG, EMG, EEG, temperature, and skin galvanic responses. Multichannel data (16 differential channels) can be collected by means of portable, crew-worn devices over extended periods of time (24 h), or via rack-mounted devices

Pulse/Blood Oxygen

A pulse oximeter to monitor the percentage of hemoglobin oxygen saturation in the blood

Lung Volume

Respiration of crewmembers can be studied by continuously monitoring lung volume using respiratory impedance plethysmography

Metabolic Activity/Pulmonary Physiology

- Two gas analyzers are available, one based on the use of mass spectrometry and the other on infrared gas analysis techniques
- Combined with ancillary equipment, including gas supplies for supplying special respiratory gas mixtures
- The following measurements are possible: breath-by-breath measurements of VO_2, VCO_2; diffusing capacity of the lung for CO_2; expiratory reserve volume; forced expired spirometry; functional residual capacity; respiratory exchange ratio; residual volume; total lung capacity; tidal volume; alveolar ventilation; vital capacity; volume of pulmonary capillary blood; dead-space ventilation; cardiac output

4.5.2. End of mission

It is well known that drinking about 1 L of a balanced salt solution leads to an increased blood plasma volume loads, by about 400 mL for at least 4 h. Early space shuttle space missions verified that this technique of temporarily increasing plasma volume could be used by astronauts to ease the orthostatic intolerance on landing. The fluid loading protocol consists in ingesting about 1 L of water or juice and eight salt tablets about 1 h before leaving orbit (Figure 1.20). This produces 1 L of isotonic saline solution in the digestive track, which then leads to absorption and subsequent increase in plasma volume. This technique proved effective for short-duration mission. For example, for 26 astronauts, those who had practiced "fluid loading" had lower heart rates, maintained blood pressure better, and reported no faintness (compared to 33% astronauts having faintness in a control group). However, the effectiveness of fluid loading is reduced with longer time in orbit. Maybe factors other than cardio-vascular deconditioning become more important on longer flights with regard to causing orthostatic intolerance [Buckey et al., 1996a].

In the critical period of re-entry and landing, astronauts may routinely wear anti-gravity suits. These suits contain balloon-like pressure bladders in the pants, which can be inflated with air by the astronaut. When the astronaut inflates the bladders in his pants, the bladder presses against his or her legs, forcing body fluid into the upper body. This helps the heart pump the blood more efficiently by pushing the blood out of the lower extremities. The Russians wrap the lower body tightly with elastic strapping (*Karkas*) to achieve the same effect as the anti-gravity suit.

Anyone who has been on orbit for more than 30 days is required to be returned to Earth in the supine position (+Gx acceleration) to reduce the risk of orthostatic intolerance during re-entry and landing. The space shuttle is equipped with recumbent seats for returning long-duration crewmembers from the ISS. The *Soyuz* is equipped with couches that are custom-fit to each astronaut and cosmonaut prior to their flight (see Figure 4.8). The nominal re-entry acceleration levels are 4–5 g. However, the *Soyuz* couches are designed is to endure ballistic loads on the order of 8–10 g. At least six of the approximately 100 human *Soyuz* missions since 1967 have experienced high-g ballistic re-entries, including three from the ISS. The *Soyuz* landing rockets have at times fired prematurely when the system was armed at heat shield jettison, resulting in a “harder-than-normal” landing. So, there is a concern that some long-duration flight crewmembers could probably not egress from the *Soyuz* couches without assistance, especially after ballistic re-entry.

Emergency procedures were implemented four times by the Russian Space Agency during *Mir* missions. The procedures were used twice for medical evacuations, once for contaminated atmosphere, and once for a damaged space station window. NASA flight surgeons performed an evaluation of the *Soyuz-TM* spacecraft along with its launch and re-entry couch for the medical transport role in June of 1993. Because of the *Soyuz* hatch and couch constraints, essentially no medical restraint system was possible so that each patient had to “bend in”. An ill or injured crewmember would need to be secured in the center couch for reach and vision. The study summary concluded that *Soyuz* appears feasible for a medically critical but stable patient [Zak, 2008].

Participants in commercial suborbital flights can expect g forces ranging from 3 to 5 g during ascent, and up to 7 g along the body’s longitudinal axis during re-entry (Figure 4.23). Some companies are touting an “aerodynamic design for a carefree and heat free re-entry followed by a glide runway landing”, while others claim to “feature *Soyuz*-like custom-fit seats for enduring launch and return g-forces.” The custom seats may be kept as a souvenir of the memorable flight. Passengers who suffer from high blood pressure have had a previous heart attack, use an implanted pacemaker or defibrillator, and others with proven heart disease such as cardiomyopathy will be at significant risk as a result of these high g loads.

A person with an unknown, undocumented, pre-existing heart anomaly is the greatest concern for commercial spaceflight enterprises. The spaceflight event could then prove deadly. The high accelerations also put participants with aneurysms in an increased risk situation. The aneurysm may rupture as a result of to the high

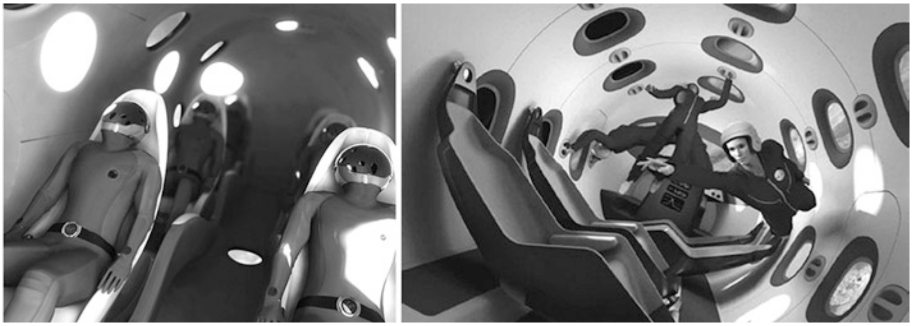

Figure 4.23. Interiors of the Rocket-Powered Space Planes that Would Take Space Tourists in Suborbital Flight. The Cabin Would Feature Hammock-Like Seats That, According to the Astrium Designer, “Balance Themselves to Minimize the Effects of Acceleration and Deceleration. (Credit Virgin Galactic (*left*) and Astrium (*right*)).

accelerations because of the pathologically weak arterial wall failing. For many commercial spaceflight passengers, the accelerations coupled to the emotional stress of the suborbital flight are likely to cause a dramatic increase in heart rate, blood pressure, body temperature, and muscle tension. The after effects of the “adrenaline rush” can also lead to syncope or fainting due to a sudden drop in blood pressure during the recovery phase, as well as orthostatic intolerance and sinus arrhythmia. It is highly recommended that the biomedical parameters of commercial spaceflight participant responses to suborbital flight be monitored during all phases of the flight [McDonald et al., 2007].

In conclusion, despite the use of in-flight countermeasures, orthostatic intolerance remains a major, unresolved, clinical and operational problem [Churchill and Bungo, 1997]. Research on the effects of spaceflight on the cardio-vascular system currently includes three types of approach: (a) mechanistic studies structured to control for many parameters and develop a generic model; (b) descriptive studies of cardio-vascular anomalies that may have operational implications, as well as prospective and retrospective studies on a large number of astronauts that could indicate the risk or incidence of an observed cardio-vascular anomaly caused by space travel; and (c) studies on the validations of countermeasures that are conducted after the mechanisms responsible for cardio-vascular deconditioning or pathology are well understood.

Nevertheless, the problem of long-duration exposure to microgravity looms large; currently observed space effects may intensify or new ones may appear. At present, all cardio-vascular changes are entirely reversible upon return to normal gravity, and there appears to be no deleterious effect of spaceflight directly upon the heart. Might orthostatic intolerance become irreversible after long-duration exposure? How will longer missions affect the time course of cardio-vascular re-adaptation to Earth or Mars gravity? Will long-duration spaceflight bring irreversible myocardial degeneration or “hypotrophy”? These are just some of the questions that remain to be addressed.

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Chapter 5

The Musculo-Skeletal System in Space

Muscle and bone form as a result of life in a 1-g environment and the mechanical forces exerted on the body. In microgravity, support muscles such as those in the calf and thigh decline in volume, strength, and mass. Similarly, bones lose calcium, the mineral from which they derive their structure and strength, through the process of demineralization. Is the reported loss of muscle and bone mass that occurs during spaceflight self-limiting or does it continue? Is it permanent or is it reversible? Could the parallel loss of muscular strength and coordination jeopardize the return of piloted spacecraft or limit work capability and performance for surface operations on Mars? This chapter examines the effects of spaceflight on structure and function of the musculo-skeletal system, what the implications of such changes might be for long-duration exploratory missions, and what countermeasures might be employed to prevent undesirable changes (Figure 5.1).

5.1. The problem: muscle atrophy and bone loss

5.1.1. Muscle atrophy

After a few days of exposure to microgravity, muscle atrophy begins and the urinary excretion of nitrogen compounds increases. This atrophy is characterized by structural and functional alterations in the muscle tissue. There is a decrease in muscle fiber size, with no apparent change in fiber number. Atrophy is considerably greater for postural muscles, i.e., those muscles that support activities such as walking, lifting objects, and standing on Earth, as compared to the non-postural muscles, which undergo only marginal changes. Astronauts lose 10–20% of their muscle mass on short missions. On long-duration flights, the muscle mass loss might rise to 50% in the absence of countermeasures. The visible reduction in the leg circumference has been used as an indicator of muscle atrophy (Figure 5.2). However, as seen in the preceding chapter (see Chapter 4, Section 4.3.2), this reduction is also influenced by the shift of fluids from the lower to the upper body in microgravity.

The muscle loss is presumably caused by changes in the muscle metabolism, i.e., the process of building and breaking down muscle proteins. Experiments performed during long-duration missions on board *Mir* have revealed a decrease of about 15% in the rate of protein synthesis in humans [Di Prampero et al., 2001].

In addition to pure muscle loss, the fibers involved in muscle contractions change their contractile properties and are weakened. Significant decreases in strength of the trunk, knee and shoulder muscles have been found in as few as 6 days in microgravity.

G. Clément, *Fundamentals of Space Medicine*, Space Technology Library 23,
DOI 10.1007/978-1-4419-9905-4_5,

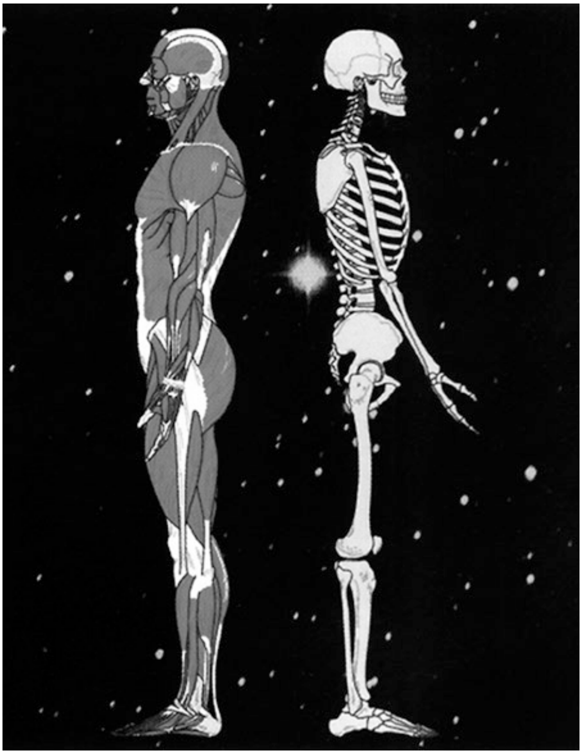

Figure 5.1. Muscle Atrophy and Bone Demineralization Are Serious Concerns for Long-Duration Spaceflights. (Credit NASA).

Extensor muscles are more affected than flexor muscles. Animal studies also revealed that muscle fiber regeneration is less successful in space. The associated continued excretion of nitrogen may also have deleterious hormonal and nutritional effects.

Spaceflight also results in increased susceptibility of skeletal muscle to contraction damage, which occurs in muscular atrophies on Earth-bound patients. These effects may compromise the ability of astronauts to perform some of their activities in orbit. Likewise, they may not be able to withstand the stress of 1-g upon return to Earth. In fact, the muscle weakness, fatigue, faulty coordination, and delayed-onset muscle soreness that astronauts experience after spaceflight mimics the changes seen in bed rest patients and the elderly. Finally, it is important to bear in mind that muscle atrophy caused by weightlessness also participates in the postural instability and locomotion difficulties seen after spaceflight (see Chapter 3, Section 3.3.3).

5.1.2. Bone loss

Bone loss during spaceflight is about 1–2% per month. The effect is especially marked in the weight-bearing bones of the legs and spine (Figure 5.3). Certain individuals spending 6 months in orbit have lost as much as 20% of bone mass throughout their lower extremities. There is no indication that this bone loss abates with longer flights. In addition, after return to Earth, bone loss continues for several months.

Figure 5.2. A "Cast" Placed on the Leg of an Astronaut Is Used To Measure Changes in Leg Circumference, as an Indicator of Changes in Muscle Mass During Spaceflight. Several Times Over the Course of the Mission, an Astronaut Will Put on the Cast, Pull the Tapes Tight, and Mark Them. By Comparing the Marks, Changes in Muscle Volume Can Be Measured. (Credit NASA).

Bone loss of this magnitude leads to a significant increase in fracture risk, which may be as much as five-fold over that expected with normal bone mass on Earth. Bones could fracture under the extreme stress of heavy work during extra-vehicular activity, for example, or even upon return to 1 g.

Bones lose calcium, the mineral from which they derive their structure and strength, through the process of demineralization. This increased excretion of calcium may in turn affect various organs, especially the kidneys. For example, the risk of renal stone formation is increased and could have serious consequences during a mission. In addition to demineralization, changes in bone marrow, which is the site of blood-forming cells, have also been linked to bone loss.

Animal studies have indicated that the structure or "architecture" of the bone formed in space is different from that of animals on Earth. Thus, for laboratory rats that have flown in space, strength does not increase proportionally to the increase in bone size as it does on Earth. If the same changes occur in humans, it is reasonable to ask what will be the new state for bone in microgravity after very long duration missions. The major health hazards associated with skeletal bone loss during these

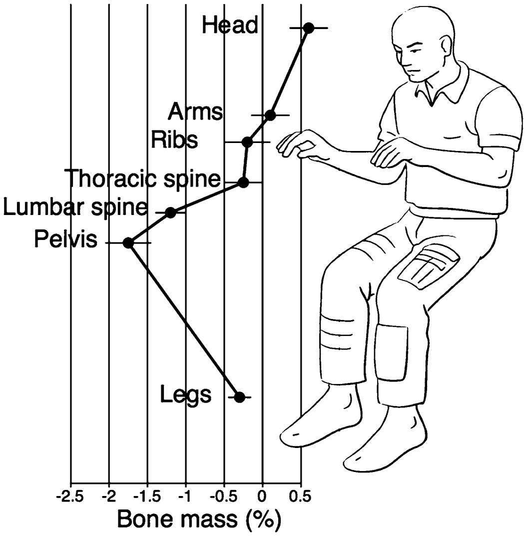

Figure 5.3. Changes in Bone Mass Relative to Preflight Level in Cosmonauts During Long-Duration Missions on Board Mir. Bone Loss Seems to be a Regional Phenomenon in Which the Bone Areas with the Greatest Decrease in Load, i.e., the Hip, Lose the Most Bone. Interestingly Enough, Bone Mass Increases at the Head Level, Presumably Because of the Increase in Pressure Due To the Headward Fluid Shift in Microgravity [Clément et al., 2010].

missions are accumulations of excess mineral in tissues such as the kidney, increased risk of fracture, and potentially irreversible damage to the skeleton.

Bone loss is a concern right here on our own planet as well. Millions worldwide suffer from bone loss, known as osteoporosis. Researchers hope that solving the issue of bone loss in space will reveal important clues about what causes osteoporosis on Earth.

Astronauts regularly perform weight-loading exercises that simulate the gravity of Earth. However, exercise alone has not prevented muscle and bone loss during spaceflight. Different types of exercise are required to build muscle strength and resistance to fatigue and injury, as well as maintain bone integrity. Studies are being conducted to address how muscles and bones should be loaded in microgravity to prevent these changes. A balance among healthy nutrition, therapeutic measures, drugs, and exercise is likely to be the most effective countermeasure.

5.2. Muscle and bone physiology

5.2.1. Muscle physiology

There are several types of muscle tissue in the human body. The muscles that are the most affected by spaceflight are the skeletal muscles, which are those directly attached to the skeleton. Skeletal muscles are the largest tissues in the body, accounting for

40–45% of the total body weight. These muscles are attached to the bones by tendons. Their contraction allows for the movement of joints in everyday activities, like walking, lifting objects and standing. The anti-gravity muscles, also known as postural muscles, owe their importance and strength to the presence of gravity (Figure 5.4).

Skeletal muscle cells, called fibers, are cylindrical cells, about 50 μm in diameter. Each muscle fiber contains several hundred myofibrils, about 1 μm in diameter as well as many mitochondria for adenosine triphosphate (ATP) production and a complex system of internal membranes called the sarcoplasmic reticulum, which regulates calcium ion levels in the fiber. A myofibril consists of many filaments of myosin and actin, the structural unit of contraction (Figure 5.5).

ATP is the basic source of chemical energy for muscle contraction. However, the amount of ATP present in the muscle cells is only sufficient to sustain maximal muscle power for 5–6 s. Consequently, new ATP must be formed continuously. Three processes can be used: (a) the phosphagen system can sustain 10–15 more s of muscle activity; (b) the glycogen-lactic acid system (anaerobic step of glucose breakdown) allows another 30–40 s "bursts" of energy; and (c) the aerobic system provides muscle activity that is only limited by the oxygen and nutrients supplies.

Each muscle fiber is supplied by a motor nerve (axon), and contracts when that axon "fires" an action potential. Muscle action potentials are fast (1–2 ms in duration) and are all-or-nothing, i.e., not graded. When a single stimulus is applied to the muscle fiber, it responds by a twitch. The twitch force is a weak force and is very slow compared to the duration of the action potential. There is a latent period between the start of the action potential and the time when the fiber begins to develop contractile force,

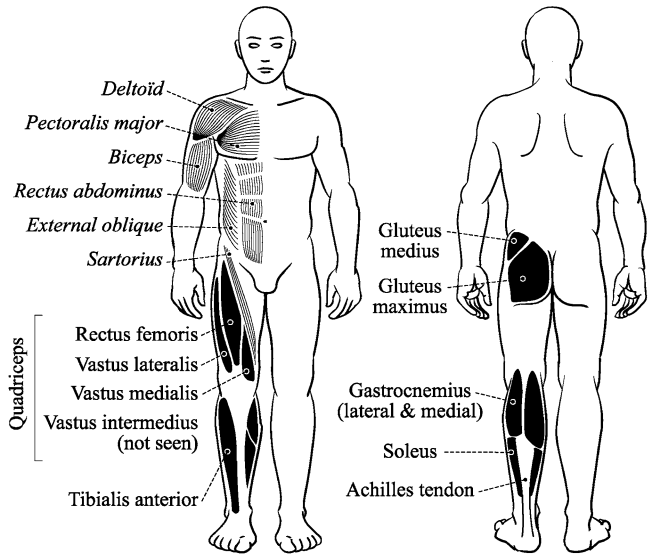

Figure 5.4. Major Skeletal Muscles in the Body. The Postural Muscles (in *Black*) Are Used to Counteract the Acceleration of Gravity During Standing on Earth. (Adapted from Lujan and White [1994]. Credit Philippe Tauzin).

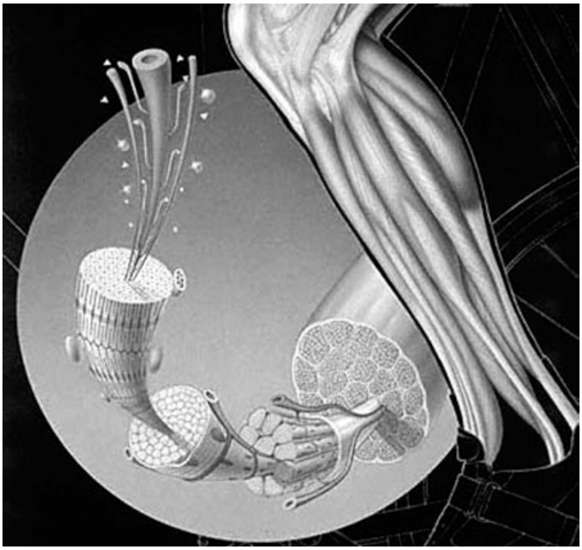

Figure 5.5. Muscles Are Composed of Fibers, Made Up of Smaller Units, the Myofibrils, Which Contain Filaments That Slide for Contraction. (Source Unknown).

during which the muscle fiber cannot be stimulated again. The duration of the twitch for any one muscle fiber is constant but it can be shorter (e.g., 10 ms in large, fast fibers) or longer (e.g., 50 ms in small, slow fibers). The latent period is about the same for both slow and fast types of muscle fibers.

Slow (oxidative) fibers, also called Type I, are characterized by a relatively slow development of force but are able to maintain this force relatively long. Marathon runners typically develop those in the Soleus muscle in the calf for prolonged lower leg muscle activity. Fast (glycolytic) fibers, also called Type II, are able to develop force faster. Sprinters and weight lifters typically develop those in the Gastocnemius muscle in the calf and in the biceps muscle for quick, powerful "bursts" of movement. The downside of fast fibers is that they fatigue rapidly.

Contraction refers to the active process of generating a force in a muscle. The force exerted by a contracting muscle on an object is the muscle tension (Figure 5.6). The force exerted on a muscle by the weight of an object is the load. When a muscle shortens and lifts a load, the muscle contraction is isotonic (constant tension). When shortening is prevented by a load that is greater than muscle tension, the muscle contraction is isometric (constant length).

Another classification of muscle contraction is into concentric or eccentric contractions. Concentric contraction means that the muscle fibers decrease in length. Under the influence of external forces, muscle fibers can increase in length while contracting. This is called an eccentric contraction. An example of an eccentric contraction is walking downstairs, when the force of gravity causes the muscle to lengthen while contracting. During eccentric contraction, the force that is produced by the muscle is even greater than during isometric contraction. This greater production of force is still

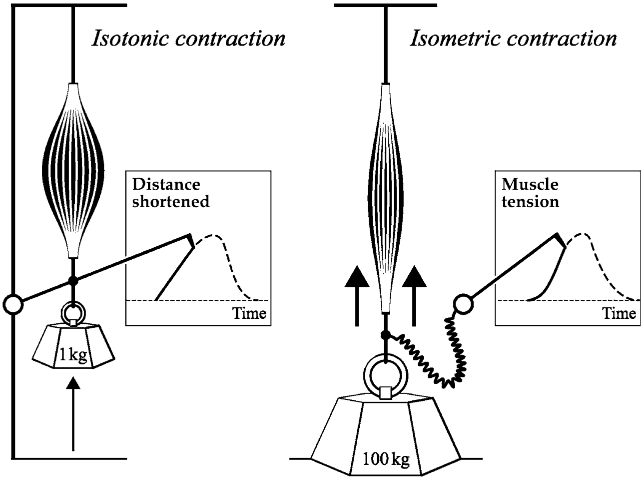

Figure 5.6. Isotonic Contraction (*Left*) Is Associated with Constant Tension, Whereas Isometric Contraction (*Right*) Is Associated with Constant Fiber Length. (Adapted from Lujan and White [1994]. Credit Philippe Tauzin).

unexplained, but is surprisingly at the cost of hardly any ATP. When gravity is absent, eccentric contractions rarely occur, which has been suggested to be an important reason why muscles atrophy in microgravity [Convertino, 1991].

During muscle contraction, there is a strict relationship between force and length. Because of this relationship it is important to standardize the angles of the relevant joints (i.e., standardization of the length of the muscle) when comparing muscle strength production before and after a certain period of time. In addition, the highest forces are developed at slower velocities of contraction. Consequently, it is also important to compare muscle strength production at identical angular velocities (i.e., standardization of the velocity of contraction).

The power a muscle can generate is largely dependent on the amount of actin-myosin filaments that can be used. More filaments mean more potential to generate muscular pull. The length and size of a muscle fiber can vary considerably between various muscles in the body and between individuals of different gender, fitness, and age. The length of a muscle fiber can vary between several millimeters and approximately 15 cm, and is mainly responsible for the maximum velocity of contraction. The strength of a muscle is mainly determined by the size of myofilaments, which is often indicated by the surface area of a perpendicular slice of the muscle, the cross-sectional area. There is generally a high correlation between maximal strength and the cross-sectional area of a specific muscle.

“Eating alone will not keep a man well,” said Hippocrates in 400 B.C. “He must also take exercise.” Training increases the size of muscle fibers and even the number of muscle fibers, thereby increasing the maximal strength of a muscle. During exercise, the capacity of a muscle for activity can be altered by: (a) transformation of one type of fiber to another, e.g., the muscles required to perform endurance-type activity will develop more Type-I fibers and their number of blood capillaries will increase;

or (b) the growth in size (hypertrophy) of the muscles fibers, e.g., weightlifting will induce hypertrophy in Type-II fibers, with an increase in synthesis of actin and myosin filaments.

5.2.2. Bone physiology

We tend to think of bones as something inert, but that's not the case. Bone is a living tissue. Bone tissue is constantly being broken down by certain cells, and built up by other cells to maintain its functional rigidity. Much of the activity from these specialized cells comes in response to the stress put on the bones during walking or exercising. Even when in bed, there are still some muscular forces acting on the bone, providing the stimulus for the remodeling of the bone.

The weight-bearing bones provide a rigid support for the body in Earth's gravity (Figure 5.7). The porous structure of the bone is adapted to resist to mechanical constraints with a minimum mass. An estimated 80% of bone strength is determined by pure bone mass. The remaining 20% are determined by the labyrinth-like structure of bone. In addition, the bones act as a mineral reservoir of calcium. An adult contains approximately 1,000 g of calcium, out of which 99% stays in the skeleton and only 1% in the extracellular space and soft tissues.

The major compartments of a long bone, such as the arm and leg bones, include: (a) the periosteum or outer fibrous envelope of cortical bone, which contains the genes for locally acting growth factors; (b) the compact bone, the outer bony layer, very

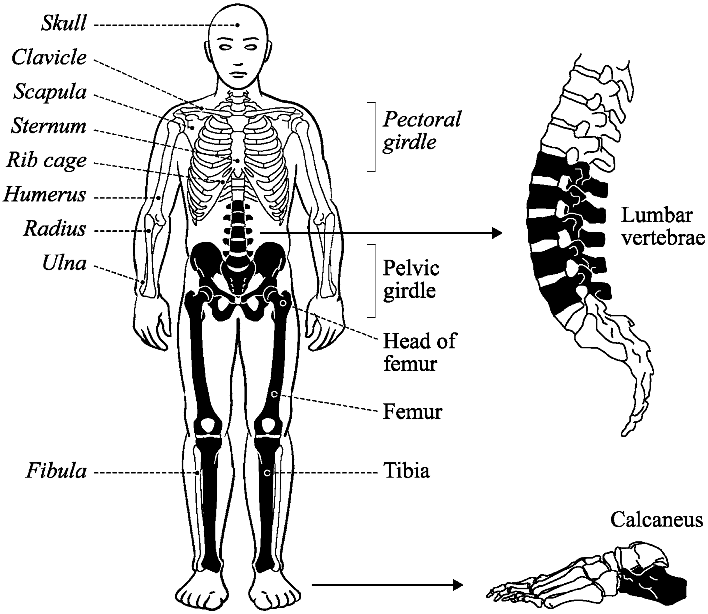

Figure 5.7. Major Bones of the Body with, in *Black*, Those Primarily Involved in Counteracting the Acceleration of Gravity. (Adapted from Lujan and White [1994]. Credit Philippe Tauzin).

strong and dense, which is the site of cortical bone remodeling; and (c) the inner compartment or marrow space which contains both bone- and blood-forming cells (Figure 5.8). The cellular elements are contained within an interconnecting system of spongy bone also termed lamellar or trabecular bone.

Bone contains a matrix of collagen fibers, which gives the bone a certain degree of elasticity. The matrix provides a medium for the deposition of calcium crystals (hydroxyapatite). These crystals provide strength to the bones. A layer of cartilage called the growth plate is where the bone grows longer by increasing its thickness. The cartilage is later calcified with hydroxyapatite. Bone is continually being remodeled under the influence of three types of highly specialized cells. Firstly, osteoblasts, or bone forming cells, synthesize the collagen matrix and control the mineralization of the bone. Secondly, osteoclasts, or bone resorption cells, secrete acids, which dissolve the minerals and act against the formation of bone-components (Figure 5.8).[1] Finally, osteocytes preserve the homeostasis of bone formation and resorption. Osteocytes are differentiated osteoblasts, which have become active to form bone, and are capable of both synthesis and resorption. Osteocytes are extremely sensitive to mechanical stress.

Bone remodeling is a continuous process throughout life: in adults, 20–30% of the bone is replaced each year. An as yet unknown trigger activates the osteoclasts to form holes and tunnels. These holes and tunnels are filled with a new matrix by the

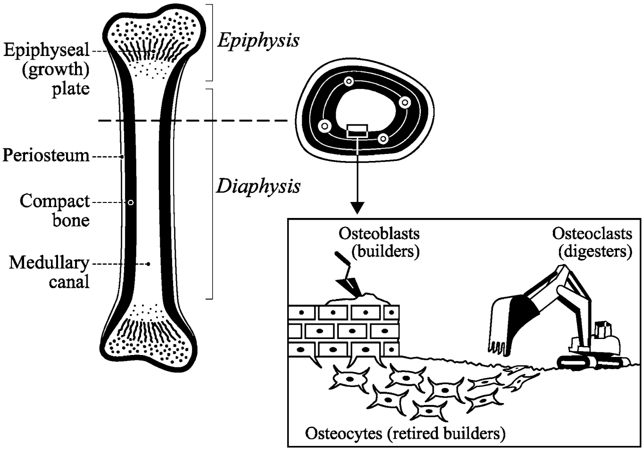

Figure 5.8. Structure of a Long Bone, Showing the Epiphysis, Which Forms a Joint with Another Bone, the Epiphyseal Plate Where Elongation Is Achieved in the Growth Plate, and the Three Main Compartments of Cortical Bone Within the Diaphysis. A Cross-Section of the Compact Bone Shows the Blood-Forming Cells on the Outer Surfaces, Which Continually Build New Bone to Maintain Its Thickness and Strength. (Adapted from Lujan and White [1994]. Credit Philippe Tauzin).

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[1] An easy way to memorize the function of osteoblasts and osteoclasts is the following: osteo<u>b</u>lasts are bone-<u>b</u>uilding cells, whereas osteo<u>c</u>lasts are bone-<u>c</u>rushing cells.

osteoblasts. Calcium compounds must be present for ossification to take place. Twelve to fifteen days after this, the mineralization of the newly formed bone starts. Complete mineralization has taken place after 6–12 months.

The balance of the osteoclast and osteoblast activity is not even. Until approximately the age of 30, more bone is being formed than there is being dissolved, with an extra strong positive balance during puberty. Thereafter, the balance becomes negative and the total amount of bone decreases (Figure 5.9). The decrease is about 1–2% of bone mass per *decade*. For women this rate increases to 1–2% per *year* somewhere between 3 and 8 years after menopause.

When humans lose bone density, some of this loss comes from cortical bone, but the main part comes from trabecular bone. Trabecular bone is mostly located next to joints at the ends of the long bones, such as the femur ball that fits into the hip socket, and in vertebral bones. Any loss of density at such locations, where the skeleton experiences the most stress, significantly increases the risk of fractures, hence the larger number of hip replacements among elderly people.

Osteoporosis is a bone disease in which the bone mass is reduced by 0.5–2.0% per year. It is a silent disease, which often leads to a fracture without any precursor symptoms (Figure 5.10). In Europe, this disease affects about 30% of the women and 6% of the men over 50 years of age, and costs approximately 9 billion Euros per year. With the overall aging of population, osteoporosis is an increasing public health issue. The main risk factors are genetic, hormonal, and related to sedentary life with lack of physical activity.

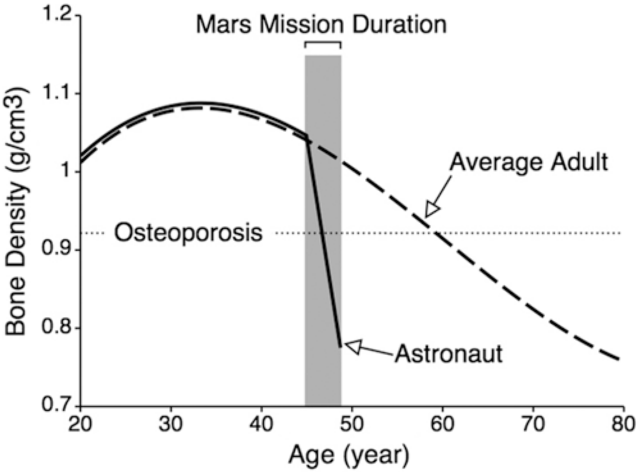

Figure 5.9. Under Terrestrial Conditions, a Loss in Bone Mineral Density of 0.5% Per Year Would Be Considered Normal Past the Age of 40, So Bone Loss During Spaceflight Cannot Solely Be Attributed to That Environment. During a Mission to Mars, a 45-Year-Old Astronaut Could See Bone Deterioration Reach the Weakened State of Severe Osteoporosis. (Adapted from National Geographic [2001]).

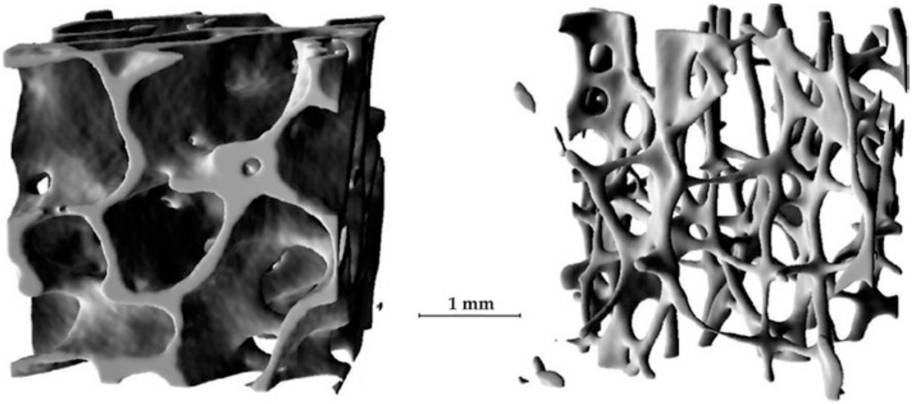

Figure 5.10. Scans of Normal (*Left*) and Osteoporosed (*Right*) Bone. (Credit MEDES).

5.3. Effects of spaceflight on muscle

5.3.1. Decrease in body mass

Because the muscles represent more than 30% of the body mass, changes in body weight during and after spaceflight is an indicator of muscle atrophy. In microgravity, body weight is measured using a special scale: the subject is seated in a device placed between two springs of known constant. When the seat is unlocked, the period of oscillation is proportional to the subject's mass. The mass of the crewmembers is calculated by measuring the oscillation period of their unknown mass and comparing it to the period of a known mass (Figure 5.11). As a rule, body mass decreases by approximately 5–10% relative to preflight during the first 2 weeks of spaceflight. Part of this reduction is due to the fluid loss, as discussed previously (see Chapter 4, Section 4.3.3). Interestingly enough, body weight tends to increase during bed rest or isolation studies. For example, when confined to a terrestrial *Mir* simulator for 135 days under conditions simulating a long-duration spaceflight, three subjects gained between 5.1 and 9.3 kg. This increase in weight is thought to be due to an accumulation of sodium in extracellular space, leading to water retention and weight gain [Titze et al., 2002].

5.3.2. Decrease in muscle volume and strength

A decrease in leg volume, also known as the "chicken leg syndrome", is also observed in microgravity. By the end of a 3-month mission, leg circumference may decrease by 10–20%, mostly in the fleshier thighs. Part of this decrease is due to the headward fluid shift. However, although the fluid shift is virtually complete after 1 week, leg volume continues to decrease throughout the flight, suggesting that muscle loss significantly contributes to this decrease. During the postflight measurements, the leg volume does not immediately return to the preflight level, despite the quick re-hydration of the organism. This difference also indicates that leg volume is reduced in space partly because of muscle atrophy.

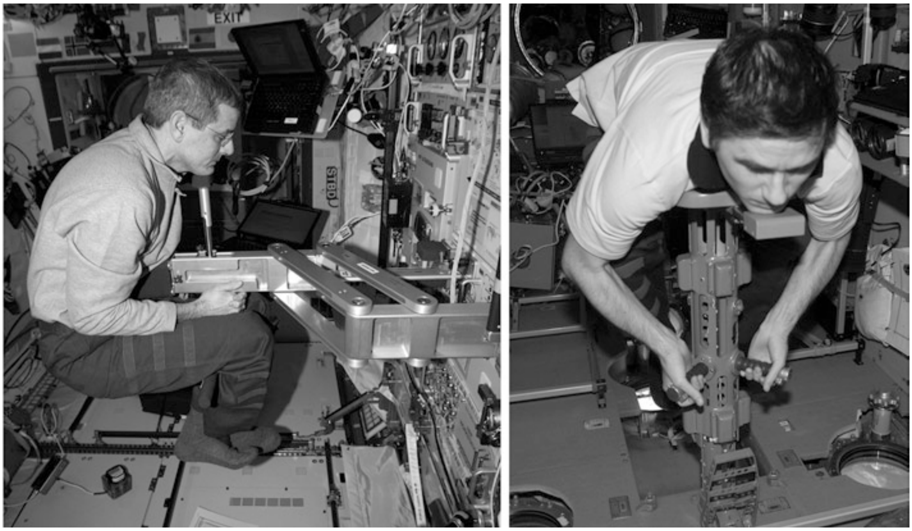

Figure 5.11. Instruments for Measuring the Body Mass of Astronauts and Cosmonauts on Board the ISS. *Left*: NASA SLAMMD Device. *Right*: Russian IM System. Both Devices Use a Rigid Frame That Oscillates Whole Human Body, Equivalent to a Spring-Mass System. (Credit NASA).

Another possible indicator of the reduction in muscle mass is the loss of nitrogen during spaceflight. Nitrogen is an essential element of every protein. Skeletal muscle is the largest active protein pool in the body, thereby being the major site of protein loss. Thus, the determination of nitrogen excretion in urine is an indicator of muscle tissue breakdown. The finding of increased excretion of the proteins 3-methylhistidine, creatinine, and sarcosine during spaceflight, which indicates muscle breakdown, confirmed this concept.

Significant atrophy was evident in human muscles after only 5 days in space (Figure 5.12). It has not been determined whether muscle deterioration reaches a plateau during long-duration spaceflight. The degree of atrophy is different for various muscles [Edgerton et al., 1995]. The muscles of the arms and shoulders show smaller losses than the muscles of the lower back, abdomen, thighs and lower legs. These lower body muscles are critical to the maintenance of posture and balance on Earth, and suffer the most from the disappearance of gravity. The smaller losses in the upper limb may also be caused by an increased use of the arms during spaceflight. Indeed, under weightlessness, predominantly the arms are used to move within the spacecraft and during extra-vehicular activities.

The decrements in muscle strength resemble the decrements in muscle mass. Larger losses in the postural muscles and larger losses with increased flight duration are generally observed. Also, the decrease in muscle strength is commonly more profound in the extensor than in the flexor muscle groups in the legs. This may be due to the rest posture in microgravity (see Figure 3.13), which stretches the dorsal flexor muscles thereby maintaining size and strength of these muscles.

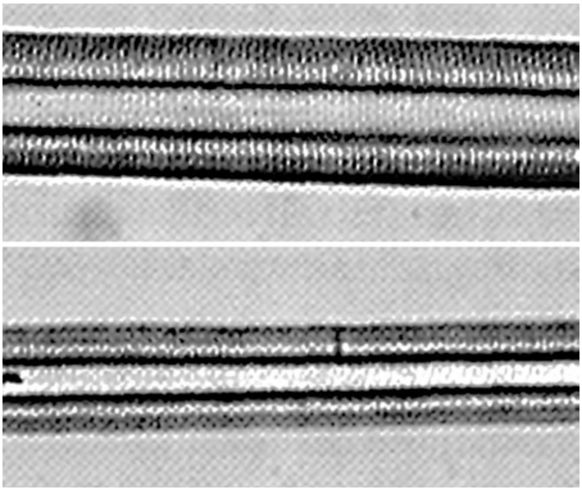

Figure 5.12. This Photomicrograph Shows Normal Skeletal Muscle Fibers (*Top*) and Atrophied Skeletal Muscle Fibers (*Bottom*). Note the Marked Decrease in Size of the Atrophied Skeletal Muscle Below. (Credit NASA).

Besides losses in muscle mass and muscle strength, losses have also been found in muscular stamina and contractile endurance, both in humans and in rats [Baldwin et al., 1996]. Again, these findings were made in the legs, but not in the arms. Although the underlying mechanism may be different, the reasons for these losses are thought to be identical to the reasons for maximal strength losses: disuse due to unloading and confinement in a small space.

5.3.3. Changes in muscle structure

It is well known that, on Earth, if the nerve fibers connected to a muscle are severed or the motor neurons destroyed, the denervated muscle fibers become progressively smaller, their content of actin and myosin decreases, and connective tissue proliferates around the muscle fibers (denervation atrophy). A muscle can also atrophy with its nerve supply intact if it is not used for a long period of time. This phenomenon is known as disuse atrophy.

Muscle weakness following spaceflight is consistent with the reported 20–50% decrease in muscle fiber cross-sectional area and the loss of contractile proteins is space-flown rats [Riley et al., 1996]. Biochemical and structural changes at the cellular and molecular levels have been seen in muscle biopsies collected on astronauts. However, these studies are very limited due to the painful character of such investigation.

Another, indirect method to evaluate structural changes is measuring oxygen consumption. Oxygen uptake and energy expenditure are closely related. When slow twitch muscles are exercised, they rely primarily on an aerobic, oxygen-requiring process, to extract the energy stored in carbohydrates, fats, and proteins. Fast-twitch fibers are more dependent on energy produced by the anaerobic breakdown of storages of glycogen. If a human's maximal oxygen capacity declines in space, the slow-twitch muscles may not be as efficient because of their increased dependence on anaerobic energy sources.

Another difficulty in interpreting data from human subjects comes from the fact that the test subjects participate in a wide range of in-flight payload activities, including EVA, which require variable and undocumented muscle use. Also, a further aspect that might confound the data is the unknown influence of the unreported nutritional status of the astronauts. It is likely that cosmonauts and astronauts are to some degree in an energy-deficit state during spaceflight, at least during the short-duration missions with a heavy schedule, with the consequence being that muscle protein will be lost. This problem becomes less important with increasing mission length, as in longer missions crewmembers have more time to prepare and consume food and consequently get closer to the recommended daily energy intake.

For these reasons, most spaceflight investigations on muscle have focused on animals, growing or mature. In-flight dissections of rodent skeletal muscle tissues have shown that antigravity slow-twitch fibers generally show the greatest deterioration following spaceflight (Figure 5.13). In fact slow muscle fibers seems to acquire fast fiber properties. This shift has the downside of rendering the muscle more fatigable (Figure 5.14). The greater reliance on anaerobic glycolysis contributes to the reduced endurance and increased fatigability.

Biopsies from the calf muscles (*Soleus* and *Gastrocnemius*) were recently taken from five ISS crewmembers following spaceflights of 30–180 days. These tissue samples allowed for determination of the cell size and structural properties of individual fast and slow muscle fibers. The subjects were also tested on a specially designed torque velocity dynamometer to measure muscle strength before and after flight. Microgravity produced a 47% decrease in the peak power of postflight muscle fiber samples compared to preflight muscle fiber samples. This decrease was due to the

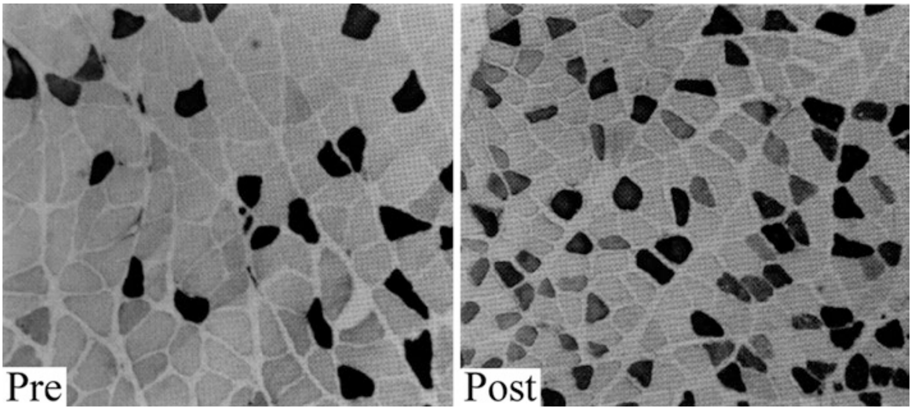

Figure 5.13. These Light Micrographs Show the Effect of Microgravity on the Size and Type of Muscle Fibers in the Leg Muscles of Rats. The Larger Cells (*Left*) Are from the Muscle of a Rat That Remained on Earth and Served as a Control. The Smaller Cells (*Right*) Are from the Identical Muscle of a Spacelab-3 Rodent That Was in Earth Orbit for 8 days. The Dark-Stained Fast-Twitch Muscle Fibers Are More Numerous in the Muscle of the Flight Animal. (Credit NASA).

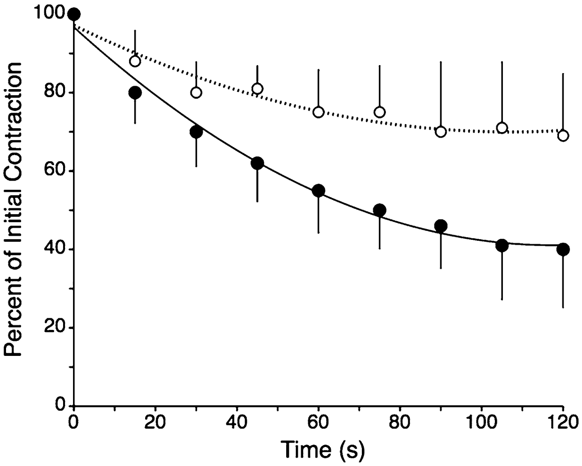

Figure 5.14. Results of a 2 min Isometric Fatigue Test of Control and Flight Soleus Muscles of Rat. The Flight Muscles Were More Fatigable Than the Control Muscles, Presumably Because of Their Smaller Size and Their Changes to Fast-Twitch Properties. (Adapted from Baldwin et al. [1996]).

combined effects of reduced fiber size and a decline in the size of the myofibrils that make up the fiber [Fitts et al., 2004].

Further examination of the data that were collected from the crew indicated that astronauts who performed a higher level of treadmill exercise (greater than 200 min/week) vs. low-level treadmill exercise (less than 100 min/week) exhibited a smaller decrease in peak power. Astronauts who performed high level treadmill exercise showed a 13% decrease compared to a 51% decrease in peak power of astronauts who performed low level treadmill exercise. Sample analysis of the muscle fibers indicated that the ratio of myosin and actin proteins in the muscle fibers was not affected by long-duration spaceflight. Although exercise slowed the onset of atrophy and loss of strength in muscle fibers, a significant amount of muscle volume and strength loss still occurred on long-duration missions [Gallagher et al., 2004].

Although reduced use, such as occurs during spaceflight, decreases muscle size and strength, contractile proteins seem to adjust to maintain power output. Upon return to Earth, terrestrial motor strategies are rapidly restored and executed flawlessly. This occurs well before muscle fiber re-growth in cross-sectional areas and during the period of slow muscle fiber necrosis. It then appears that the central nervous system undergoes significant re-programming (plasticity) and performs compensatory activation of motor units that masks the deteriorated state of the muscular system [Riley et al., 1996].

5.4. Effects of spaceflight on bone

Because of the absence of gravity constraints on the body, astronauts can lose up to 2% of their bone mineral density each month. The bone loss observed after a spaceflight of a few months corresponds to that of several years on the ground. By comparison with osteoporosis on Earth, astronauts could therefore be considered as "hyper-sedentary" persons. It was recognized long ago that understanding the fundamental biochemistry and physics of bone mineralization on Earth is necessary to fully understand the potential effects in microgravity environments [Hattner and McMillan, 1968]. The opposite is also true.

5.4.1. Human studies

The main mineral in bone is calcium, which makes calcium balance an important determinant of the status of bone mineral density (Figure 5.15). An increase in the fecal and urinary calcium excretion was first noticed after the Soviet *Vostok* missions. Calcium in urine and feces increased drastically in *Skylab* astronauts, parallel to a muscle and bone loss [Leach and Rambaut, 1977]. An aggressive exercise program was then implemented, with significant consequences for muscle volume.

During the Gemini missions, bone mineral density was determined by x-ray densitometry, which measures the attenuation of two beams of x-rays by the calcium in the x-ray path. With this technique, which has a precision of 1–2%, a loss of approximately 2–4% of bone mass was detected in the heel bone after 4–11 days of spaceflight. The subsequent Apollo, *Skylab*, and *Salyut* data were obtained by single photon absorptiometry. After the Apollo missions also lasting 10 days, a 3–5% decrease in bone mass was observed. Therefore, 2–3 days spent on the Moon surface at 0.16 g did not prevent bone loss. After *Soyuz* missions, bone density had decreased by 8–10%. *Skylab* measurements revealed a 1–3% per month loss in bone mineral.

Cosmonauts on board *Mir* were examined with quantitative computerized tomography (QCT), which gives a true, volumetric density (in g/cm^3). Results showed a 10% loss of trabecular bone from lumbar spine after a 1-year mission. Other crewmembers were examined both pre- and postflight using dual-energy X-ray absorptiometry (DEXA). DEXA is a specially calibrated X-ray device that provides a

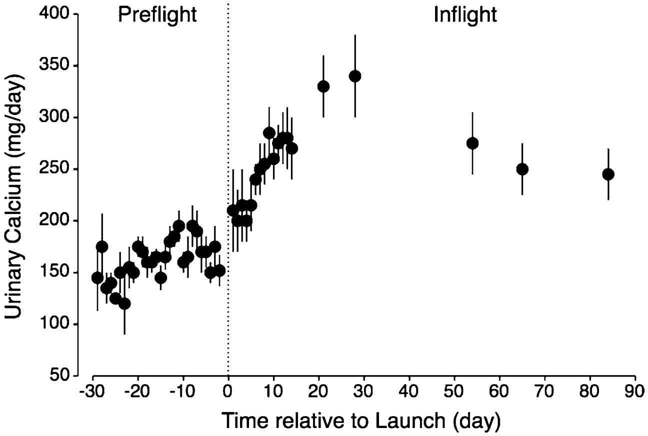

Figure 5.15. Increased Urinary Calcium Excretion Observed in Astronauts in Skylab and Other Flights. Calcium That Is Flushed Out by the Kidneys with the Rest of the Urine Could Form Stones That May Need to Be Removed by Surgery.

two-dimensional measurement of the mass of an entire bone, i.e., the trabecular bone and the cortical bone. These scans revealed that when using onboard exercise countermeasures, there was a 5.4% decrease in bone density in tibia. Bone density did not return to preflight level in some individuals. Without countermeasures, there was approximately 1.3–1.5% per month decrease in bone density. In the worst case, a 15–22% decrease was measured in some bones after a 6-month mission [LeBlanc et al., 1996].

The most compelling data have been compiled from 15 cosmonauts who spent 1, 2, or 6 months on the *Mir* station [Vico et al., 2000]. Bone mineral density was measured at the distal radius and tibia before, just after the spaceflight through 6 months after the mission. Neither trabecular nor cortical bone of the radius was significantly changed at any of the time points. On the contrary, in the weight-bearing tibial site, trabecular bone loss was noted after a 2-month flight, and was greater after a 6-month flight. Tibial bone loss persisted for at least 6 months after flight, suggesting that the time needed to recover is longer than the mission duration (Figure 5.16).

On the ISS, bone mineral density is lost at an average rate of about 0.9% per month in the lumbar spine and 1.4% per month in the femoral neck. Assessed with QCT, losses of mass in the cortical bone (the bone's dense outer layer) of the hip average around 1.6–1.7% per month, whereas losses in the trabecular bone (the bone's inner, spongy-looking layer) averages 2.2–2.5% per month [Lang et al., 2004]. During missions of 6-month duration, astronauts experience an average of 11% decline in femoral bone mass. Bone mass and structure of the astronauts' femurs recover, but not fully, after 1 year back on Earth. While bone mass and volume increase back on Earth, the volumetric bone mass density does not fully recover (proximal femur is larger in size, but less mineralized and more porous than bone lost during spaceflight) [Lang et al., 2006].

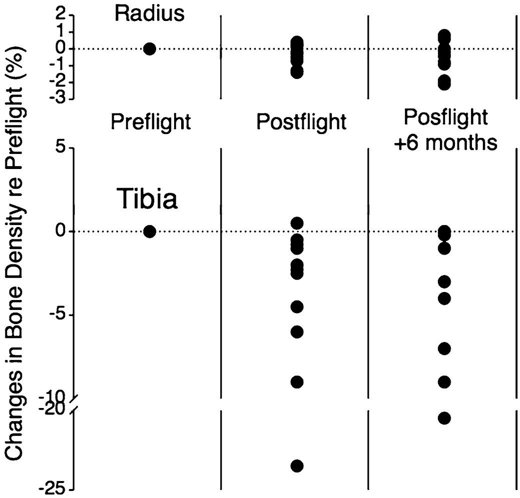

Figure 5.16. Mean Loss of Bone Mineral Density in the Radius and the Tibia Relative to Preflight Values in Cosmonauts Following Spaceflights of 6 Months on Board Mir. In Some Individuals the Bone Loss Continues for About 6 Months After Flight. (Adapted from Vico et al. [2000]).

In a related follow-on study, Sibonga et al. [2007] examined the bone mineral density DEXA measurements in five body sites for 45 crewmembers, both U.S. and Russian, who participated on 56 long-duration flights of at least 4-month duration. The study population showed variable decreases in bone mass density across the five sites. The key result was that they could calculate an estimate for time required to restore 50% of the loss of bone in each site, and that full recovery would take up to 3 years – much longer than the mission duration.

No significant changes in the bone regulating hormones, such as serum calcium, PTH, vitamin D, calcitonin, and growth hormone, have been seen on astronauts after short-duration shuttle flights [Stein et al., 1996]. The duration of stay, calcium intake, and level of exercise performed in-flight all account for the wide range in average percentage losses of bone mineral density, as reported above. Individual values are even more variable, as changes in calcaneal bone density of one particular subject can range from 4% to 30% loss relative to preflight. A method allowing both identification of the recorded site and reproducible measurements are required for more accurate studies. Complementing the DEXA and QCT techniques are magnetic resonance imagery (MRI) examinations being performed pre- and postflight with the ISS crewmembers. These studies will provide the first detailed information on the distribution of spaceflight-related bone loss between the trabecular and cortical compartments of the skeleton, as well as the extent to which lost bone is recovered in the year following return (Figure 5.17).

5.4.2. Animal studies

One problem of using rodents as models is that their bone growth is different from humans. Although bone elongation ceases in humans after puberty, in mice the epiphyses never close and there is continuous longitudinal growth. In rats, the growth

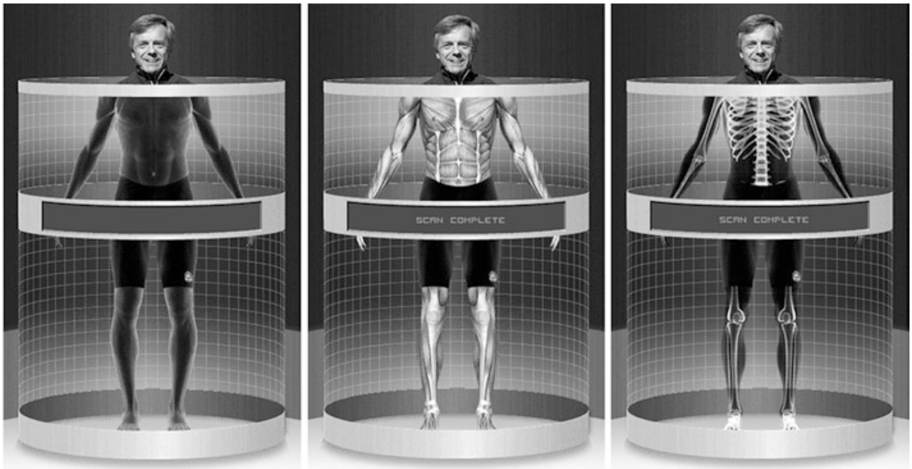

Figure 5.17. Website of the Canadian Space Agency Body Scan Booth Describing the Experiments on Bone and Muscle During ISS Expedition-20–21 with Astronaut Bob Thirsk. (Source: http://www.asc-csa.gc.ca/eng/missions/expedition20-21/body_scan.asp#).

rate is significantly attenuated at about 12–14 months of age (they live to about 3–4 years old), but their cortical bone, which lacks vascular canals, is not similar to that of humans.

In early Soviet *Cosmos* flights, various types of muscle fibers were found in flown rats, together with histologic changes with random deletion of myofibrillar filaments [Ballard and Connolly, 1990]. There was a loss of muscle force and elasticity and some specific changes in enzyme activity. A reduction in the rate of bone formation was observed postflight, with a return to control levels in approximately 4 weeks. It is interesting to note, however, that these changes were largely prevented in the rats that were subjected to centrifugation in-flight [Nicogossian and Parker, 1982].

Studies on young rats flown on board *Spacelab* missions revealed no changes in the length of antigravity bones, such as the tibia, the femur, and the humerus, compared to ground control animals. In other words, the rats grew at the same rate in microgravity as on Earth. However, the bone mass, hence its strength, was reduced.

An animal model used to study muscle atrophy and bone loss is the suspended rat (Figure 5.18). The model incorporates the two features of spaceflight that might affect bone: the unloading of weight-bearing bones and the headward fluid shift. In this preparation, a harness raises the hind limbs off the cage floor and thus "removes" weight from the muscles of the hind limbs. The overhead pulley system has a swivel that allows the animal to move about the cage by only using its fore limbs. After a few days of adaptation, tail-suspended animals are active and eat and drink normally. This relatively benign technique is relatively rapid and represents an accurate simulation of the changes in muscle and bone occurring during spaceflight [Tischler et al., 1993; Picquet and Falempin, 2003].

Neither the communication system between muscle and bone nor the precise mechanism of bone loss is understood. Therefore, the characterization of the response

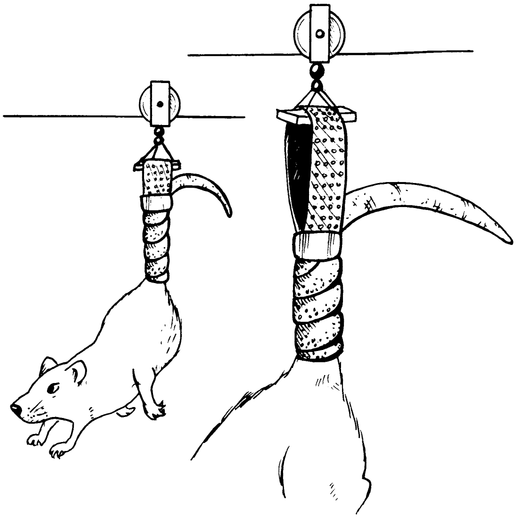

Figure 5.18. The Rat Hind Limb Suspension Technique Is Widely Used to Simulate the Unloading of Muscle and Bone as During Spaceflight [Lujan and White, 1994].

to skeletal unloading at the tissue and cellular level is one of the major contributions of the use of the rat model [Morey-Holton and Globus, 1998]. For example, recording of Soleus muscle activity of suspended rats showed an immediate and persistent 75% reduction in contractile activity. After 7 days, the Soleus muscle showed a decrease in specific tension as slow fibers shifted toward fast fibers and thick, myosin-containing filaments were lost [Riley et al., 1990]. These animals also lose about 25% of trabecular bone in the tibia, and showed a 30% reduction in the mechanical strength of the tibia shaft [Vico et al., 1991].

Unloading studies with immature rats indicate that gravity loading during the third and fourth weeks after birth is essential for normal development of locomotion [Walton, 1998]. Similarly, muscle development was disrupted when gravity-loading exercise was removed from immature rats flown on the Neurolab flight. In the absence of weight-bearing challenge, Soleus muscle fibers failed to grow in size and differentiate normally into slow fibers, and elaboration of the motor nerve terminals was retarded. Once mature, muscle tissue in unloaded animals is more prone to structural failure when reloaded because of fiber atrophy, and the ability to repair internal lesions is compromised [Arnaud et al., 1995]. The role of fiber-type specific factors in regulating gene expression is being studied in transgenic animals [Capetanaki et al., 1997].

5.5. What do we know?

5.5.1. Muscle atrophy

The human body constantly uses amino acids to build muscle protein, which then breaks down and must be replaced. When protein turnover gets out of balance, so that more protein breaks down than the body can replace, the result is muscle loss. But what causes protein turnover to slow down?

One cause is lack of muscular activity. That is why bed rest is a good model because it minimizes activity. In fact, during bed rest there is an increased urinary excretion of nitrogen and muscle loss, just like that observed in space, but these changes are variable and generally greater in degree. Most of the atrophy occurs in antigravity muscles, which are no longer bearing body weight. Of these various possible factors contributing to the excess excretion of nitrogen, muscle atrophy is clearly the main one.

In all long-duration astronauts, the high level of nitrogen excretion continued unabated for the duration of flight. This indicates a serious malfunction not likely to reach a new steady state until an extreme degree of atrophy is reached. This nitrogen loss was accompanied by losses of 15–30% of muscle mass and strength in the lower extremities. This poses a significant handicap to vigorous work in the gravity of Mars or on return to Earth.

Animal studies of muscle atrophy attempt to determine the physiological and biochemical mechanisms underlying muscle atrophy. Although the mechanism of the process of atrophy remains unknown, certain aspects have become evident. Muscle atrophy is accompanied by decreased synthesis of muscle protein and by some degree of increased degradation. As shown in suspended rats with hind limb unloaded, loading and stretching of otherwise inactive leg muscles prevented muscle atrophy and stimulated protein synthesis. The addition of electrical stimulation increased protein synthesis markedly. As shown in muscle cell cultures, stretching stimulates protein synthesis.

The uncertain value of physical exercise for suppressing muscle atrophy in human spaceflight has been noted previously. However, what is the signal and sequence of biochemical steps for initiating increased protein synthesis and deposition in muscle filaments, and what communicates a message to slow down protein synthesis? Answers to these questions would certainly have an impact on muscle research far beyond spaceflight.

The effects of electrical stimulation of muscle have begun to be studied, but the possible combinations of frequency, voltage, and current are almost without limit. Stimulation of the sole cutaneous mechanoreceptors seems to reduce the muscular atrophy after hind limb unloading in rats [De-Doncker et al., 2000].

A variety of techniques are available for muscle research: electron microscopy, electromyography, computerized tomography scanning, and stable isotope metabolic studies. To understand changes of muscle mass and strength, we must first understand their underlying cellular and molecular mechanisms. Therefore, these existing technologies should be coupled with developing techniques in immunochemistry and in recombinant DNA and gene cloning. The genes encoding many major proteins of muscle, as well as their controlling elements, have been sequenced. The current goal is to relate mechanical stress, hormonal levels, and nutrition to the control of expression of these genes.

5.5.2. Bone demineralization

Human bed rest studies correlating inactivity to factors such as diminished bone mass and increased urinary calcium have also proven to be useful models for potential changes during extended spaceflight. Studies of humans during long-duration bed rest have shown that prolonged inactivity results in significant and continuing losses of calcium from the skeleton and nitrogen from muscle, and in considerable atrophy of both body systems. These changes were consistent, but quite different in degree from subject to subject. Genetic factors may account for these differences. However, as of yet, no single gene has been convincingly proven to be a risk factor for osteoporosis. The genetic component has been attributed instead to the cumulative effects of a number of genes, including for example the vitamin D receptor gene, with small individual effects. Identification of such genes is currently under way [Tipton, 1996].

In the severe paralysis of poliomyelitis, calcium losses led to x-ray visible osteoporosis in the bones of the lower extremities as early as 3 months after paralysis. While the overall rate of calcium loss in *Skylab* astronauts was 0.4% of total body calcium per month, the loss was estimated to be ten times greater in the lower extremities than in the rest of the body, based on bed rest studies of calcium losses by metabolic balance compared with decrease in bone calcium density. This could lead in 8 months of flight to a decrease in bone density in the legs similar to that noted in paralytic poliomyelitis.

Studies of immobilized rabbits showed marked decrease in strength of tendons and ligaments after only 1 month. Thus, strains, sprains, and even ligament tears may be more likely to occur, and at an earlier time than bone fractures.

The cellular mechanisms of mineral loss are unknown. Excess excretion of calcium associated with increased hydroxyproline in the urine in humans is indicative of increased bone resorption. On the other hand, histologic examination of the bones of the rats on *Cosmos* showed suppressed bone formation. Many scientists believe that bone mass decreases in microgravity because the lack of stress on the bones slows the formation of osteoblast cells. Fewer bone-building cells, along with a constant level of bone-destroying activity, would translate into a net loss of bone mass. But why should microgravity inhibit the development of osteoblasts? A key chemical in the development of osteoblast cells from precursor cells is an enzyme called "creatine kinase-B." Investigators are trying to figure out which molecules in the body regulate the activity of this enzyme and how those chemicals are affected by reduced gravity, in the hope that this knowledge will point to a way to boost osteoblast formation in space.

In any case, the hypercalciuria associated with loss of mineral from bone in spaceflight might increase the potential for stone formation in the urinary tract. Although 75–80% of renal stones contain calcium, the likelihood of stone formation will depend not only on increased urinary concentration of calcium, but also on other factors such as urinary pH, concentration of the inorganic elements magnesium, potassium, and phosphorus, and concentrations of the organic compounds uric acid, citrate, and oxalate. Bed rest studies have shown a slight rise in urinary pH and a lack of change in urinary citrate, which in ambulatory states rises with increases in urinary calcium. Both of these factors, if also noted in spaceflight, would favor decreased solubility of calcium salts. The likelihood of urinary tract stone formation during spaceflight may be small, especially if care is taken to maintain abundant urine volumes; nevertheless, such stone formation might be catastrophic to health and function for the astronaut involved, and thus to success of the particular flight.

NASA has developed a Human Research Roadmap (HRR) [http://humanresearchroadmap.nasa.gov/] to guide its bioastronautics research in systematically reducing or eliminating the risks to astronaut health, safety, and performance during and after spaceflight. Of the 27 risks identified in this critical path roadmap for human space exploration, at least 6 are associated with altered musculo-skeletal function (see Chapter 7, Table 7.1). Of particular concerns is the acceleration of age-related osteoporosis, the failure to recover bone lost after space missions, and the increased risk of fracture upon return to activity in 1 g. Critical questions to be addressed include:

(a) Will bone mass loss continue unabated for missions greater than 6 months in duration, or will it eventually plateau at some time consistent with absolute bone mineral density?
(b) What are the most important predictors for bone loss during prolonged exposure to hypogravity, especially with reference to ethnicity, gender, age, and bone morphometry?
(c) Is bone loss reversible and within what time frame?
(d) Does prolonged exposure to hypogravity lead to non-union of healing fractures? What evidence supports the alteration in vertebral morphometry during and after extended spaceflight?
(e) What practical diagnostic tools can be utilized during multi-year missions to monitor and quantify X-ray absorptiometry, ultrasound?

(f) Are there other important mechanisms for bone loss with hypogravity that are critical to developing effective countermeasures (e.g., fluid shifts with altered hydrostatic pressure, changes in blood flow, immune system alterations)?
(g) Is there an optimal combination of exercise and a pharmacological countermeasure to minimize decrements in bone mass in hypogravity?

5.6. Countermeasures

The only countermeasure that is used consistently to date to counteract the skeletal muscle atrophy and loss of muscle strength and endurance that is associated with microgravity exposure is physical exercise. For long-duration missions aboard the ISS, U.S. crewmembers are required to complete a 2.5-h bout of combined aerobic and resistance exercise on 6 of 7 days during their assigned mission. This period includes the time that is needed for hardware setup, stowage, and personal hygiene. Typically, through 2008, approximately 1.5 h were devoted to resistive exercise on the *interim* Resistive Exercise Device (iRED) (Figure 5.19) and a further approximately 1 h was devoted to either the Treadmill with Vibration Isolation System (TVIS) or the

Figure 5.19. The Interim Resistive Exercise Device (iRED) on Board the ISS. The Astronauts Can Pull on a Cord to Create Resistance (*Right*), or Use a Shoulder Harness System to Do Deep Knee Bends, Which Stimulate the Anti-Gravity Muscles (*Left*). (Credit NASA).

Cycle Ergometer with Vibration Isolation System (CEVIS), or a combination of the two. Since 2009, an advanced Resistive Exercise Device (aRED) has replaced the iRED. On days when crewmembers are scheduled to conduct EVAs, they are not scheduled for exercise, given that EVAs typically require a significant amount of the duty day and strenuous physical effort. It is interesting to note that Russian crewmembers are required to complete different regimens of exercise, using their own equipment, a treadmill and a cycle ergometer.

5.6.1. Muscle

The considerable and time-consuming exercise activity of the astronauts on *Skylab* and *Mir* resulted in somewhat reduced loss of muscle mass and strength than on the earlier flights, but were obviously not adequate to be fully protective. Flight surgeons recommended only 15 min of exercise daily on short-duration missions, compared to the current 2.5 h on long-duration missions. The current suite of exercise equipment and the associated exercise regimens do not target maintenance of a specific level of skeletal muscle strength or endurance, nor are they particularly optimized to produce beneficial results in the shortest time possible.

The treadmill may be used for walking and running to preserve an aerobic power (see Figure 4.20). There are two treadmills on board the ISS, one in the Harmony Node and one in the Zvezda module. The U.S. treadmill is named Combined Operational Load Bearing External Resistance Treadmill (COLBERT) after comedian Stephen Colbert[2] (Figure 5.20). The device employs various strategies to simulate, as closely as possible, 1-g skeletal loading during exercise. Loads are exerted on the subject by restraint harnesses. The restraint system provides stabilization of the astronaut and load distribution on the body in a weightless environment. The treadmill can be motor-driven or passively operated. So, it is used as an ambulating trainer, endurance exercise of postural musculature, high impact skeletal loading (bone maintenance), and aerobic exercise. Moving air from a nearby duct is used to dry the perspiration produced from exercising.

The cycle ergometer is to preserve aerobic capacity (see Figure 4.20). It provides workload, driven by the hands or feet, which is controlled by manual or computer adjustment. It operates with the subject seated or supine, and provides time-synchronized data compatible with other complementary analyses. The data output consists of work rates (in watts) and pedal speed (in rpm) for use with a data acquisition system. The cycle ergometer is used as both aerobic and anaerobic exercise countermeasure, for the maintenance of lower body musculature endurance, for EVA arm exercise training, and as EVA 2-hour pre-breathe exercise countermeasure.

The iRED that flew onboard the ISS until 2008 was limited in the maximal loads that it could provide, and thus was viewed as an interim solution to the loss of muscular strength. It was replaced by another device, the aRED, as a more long-term solution. The aRED is designed to provide greater exercise capability than the iRED for preserving muscle strength and bone strength and endurance (Figure 5.21). It is a

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[2] Jon Stewart demanded he be honored similarly but turned down NASA's offer to name the ISS Urine Processor "Space Toilet Environmental Waste Accumulator/Recycling Thingy."

Figure 5.20. NASA Selected the Treadmill's Name After Comedian and Host Stephen Colbert of Comedy Central's "The Colbert Report" Took Interest During the Node 3 Naming Poll and Urged His Followers to Post the Name "Colbert," Which Received the Most Entries. "I've Always Wanted To Be an Astronaut. […] I've Already Started at Home Getting Used to Weightlessness; I've Let My Muscles Atrophy for 46 Years," Colbert Said. (Credit NASA).

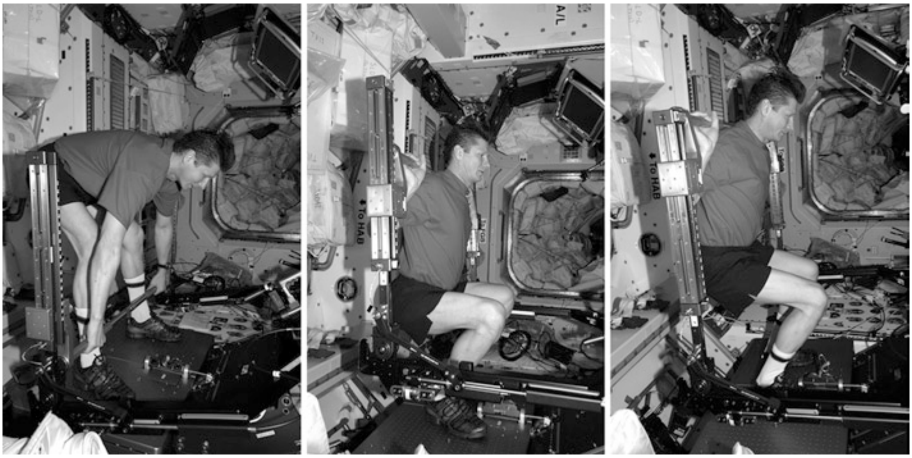

Figure 5.21. The Advanced Resistive Exercise Device (aRED) Used on the ISS Enables Various Weightlifting Exercises. Unlike the Bowflex's Rubber Bands, Which Were Used by the Machine Being Replaced (the iRED), the aRED Uses Piston-Driven Vacuum Cylinders That Provide Adjustable Resistance as the Piston Is Pulled in or out. A Flywheel System Counteracts the Force of the Pistons to Simulate the Response of Free Weights in Normal Gravity. (Credit NASA).

versatile machine that can be used to perform three primary resistive exercises for stimulating bone regeneration and exercising the major muscle groups, as well as 15 other exercises for secondary muscle groups.

The aRED consists of a pair of vacuum cylinders, a frame-and-platform assembly, an arm base assembly, a wishbone arm/lift bar, a cable-and-pulley mechanism, and a flywheel mechanism. The flywheel assembly rotates as the arm base assembly is moved, thus providing an inertial load that simulates the lifting of weights in normal Earth's gravity. The aRED can be configured to provide exercises using the lift bar or the exercise cable. The lever is able to provide loads ranging from 0 to 250+ kg. Using the cable, the loads are limited to a maximum of 68 kg.

A major feature of aRED is the instrumentation system. It includes triaxial force sensors that record force in three dimensions. Load sensors in the main lift arm and the arm base assembly measure unidirectional forces. The arm base assembly also has rotational sensors that record the range of motion of the arm. During exercise, the load and number of repetitions are simultaneously recorded and displayed on a tablet PC, in which the individually customized crewmember profiles are stored. The recorded data can be downlinked to the ground, and exercise prescriptions can be sent from the ground to the aRED tablet PC. The exercise prescription is automatically loaded into an individual crewmember profile. Exercises performed on the aRED are listed in Table 5.1.

Another piece of exercise equipment is the Muscle Atrophy Research and Exercise System (MARES) for research on musculo-skeletal, biomechanical, and neuromuscular human physiology. The MARES hardware is made up of an adjustable chair, a direct drive motor, a linear adapter that translates motor rotation into linear movements, and a vibration isolation frame (Figure 5.22). It works as a dynamometer to measure force or torque on seven different joints. Muscle contraction can be isometric (muscle contraction at a fixed length, i.e., no movement), isotonic concentric (muscle shortens as it contracts at a constant torque), isokinetic concentric (muscle shortens as

Table 5.1. Core and Auxiliary Exercises (Bar and Cable) Performed on the aRED. Typically, a 3-Day Cycle Per Week Is Used as Follows: Day 1: Low Load & High Reps; Day 2: Moderate Load & Moderate Reps; Day 3: High Load & Low Reps.

Core Exercises	Bar Exercises	Cable Exercises
Squat	Bench press	Anterior shoulder raise
Deadlift	Bent over row	Biceps curl
Heel raise	Biceps curl	Rear shoulder raise
Single-leg heel raise	Lunge	Hip abduction
Single-leg squat	Shoulder press	Hip adduction
Straight-leg deadlift	Shrugs	Hip flexion
	Single-arm deadlift	Hip extension
	Upright row	Lateral arm raise
	Wrist curl	One-arm cable row
		Triceps extension
		Triceps pulldown

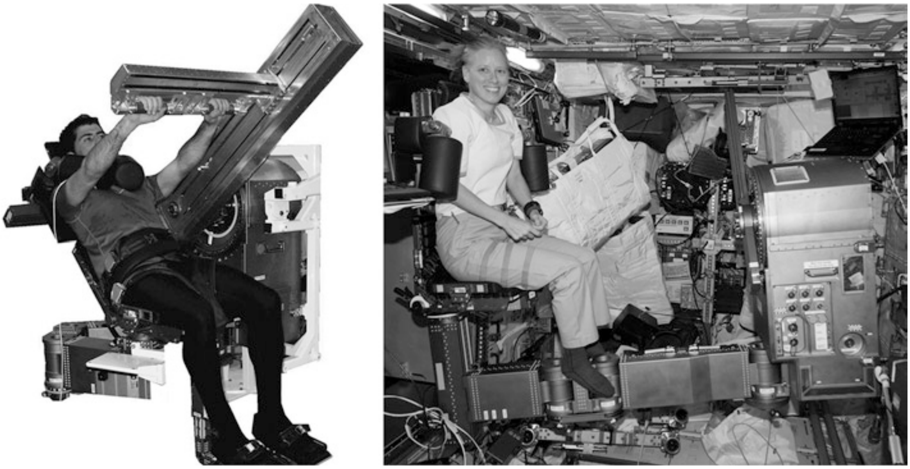

Figure 5.22. Photographs Showing the MARES Hardware Being Tested on the Ground (*Left*) and Recently Deployed in the Columbus Module of the ISS (*Right*). (Credit NASA).

it contracts but at a constant velocity), or isotonic and isokinetic eccentric (muscle extended). MARES may be used together with an associated device called the Percutaneous Electrical Muscle Stimulator (PEMS).

A hand-held grip dynamometer has also been developed to measure isometric force and sustained static exercise of the thumb and opposing finger or groupings of fingers on each hand (not including opposing hand activity) continuously for up to 300 s. This device is used to test forearm muscle fatigue before an EVA.

As previously discussed, Russian cosmonauts wear the "Penguin" suit during long-duration missions (see Figure 4.22). Beside its effect on the cardio-vascular system, the elastic bands in the suit also simulate some of the gravitational effects on the musculo-skeletal system. Expanders or bungee cords (Figure 5.23) are also used occasionally. However, they do not provide sufficient force during axial loading for bone maintenance, and present a reduced range of motion against resistance compared to the interim resistance exercise device described above.

A more unconventional possibility is that astronauts could stave off muscle atrophy by taking a pill. However, anti-atrophy pills are only speculative right now, but there are reasons to believe that they might be possible. That's because when atrophy sets in, the muscle isn't just withering away passively, it is actively breaking itself down! Astronauts use common painkiller drugs for discomfort due to back pain or sore muscles, and N-Acetyl Cysteine and other supplements/pharmacologics for muscular strength and endurance preservation. It has been suggested that protein synthesis rates be increased with supplements of amino acids, which are the raw materials of protein. Indeed, early results during bed rest studies have suggested that the amino acid supplement was able to maintain synthesis rates and body mass. Also, studies in rats indicated that muscles produce a hormone, called insulin-like growth factor 1 (IGF-1), in response to strenuous exercise, and this hormone in turn activates enzymes in the

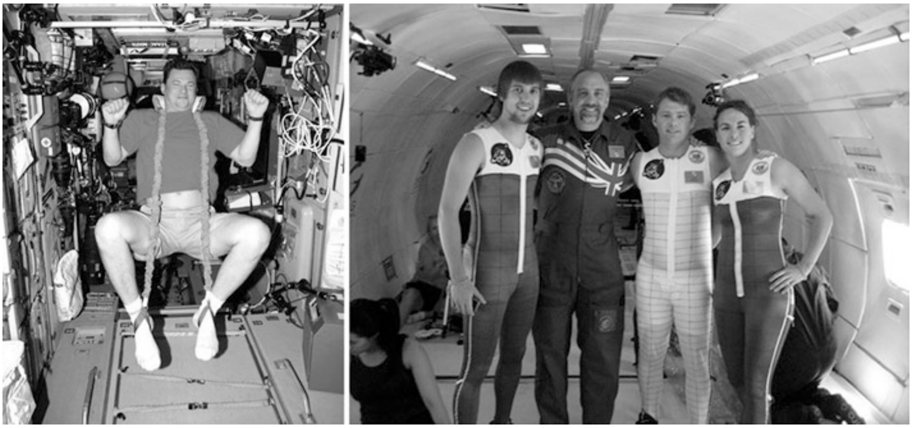

Figure 5.23. ***Left*: Bungee Cords Used for Exercising While Free-Floating on Board the ISS. (Credit NASA). *Right*: The MIT Skinsuit Creates a Loading Regime that Reproduces the Bone and Muscle Weight-Bearing Regime on Earth [Waldie and Newman, 2010].**

muscle cells that cause the cells to grow just after exercising. It is possible that it is the mechanical stress that turns on the gene for IGF-1, but we really don't understand that process yet. Might supplements of IGF-1 be used to ensure that construction of muscle proteins keeps pace with protein destruction in astronauts? Scientists are entertaining the idea and are already discussing ways in which that might be done [NASA, 2010].

5.6.2. Bone

A variety of studies are being conducted on the basic mechanisms of the effects of mechanical forces on bone dynamics and development. Such studies may give insight for countermeasures based on exercise, drugs, or diet.

5.6.2.1. Exercise

Evidence from bed rest studies and spaceflight suggests that bone loss is a regional phenomenon in which the bone areas with the greatest decrease in load lose the most bone [Oganov et al., 1992; LeBlanc et al., 1996]. *Skylab* astronauts averaged 0.5% per month total body calcium loss despite exercising a number of hours a day through a series of exercises consisting of bungee cords for resistive exercises, cycle ergometer exercise, and walking on a treadmill [Thornton and Rummel, 1977]. Exercise schedules typically required 2 h of exercise daily. However, cosmonauts continue to lose bone selectively from the spine and lower extremities while maintaining upper body bone mineral density [Oganov et al., 1992].

The human body is designed to bear weight. Without the stimulation that is caused by placing weight on lower extremities, whether due to the microgravity environment or lack of use on Earth, bones lose mass and muscles lose strength. An experiment recently characterized the load that is placed on lower extremities during daily activities on the ISS and examined to what degree mechanical load stimulus, via an in-flight exercise routine, could prevent the muscle atrophy and bone loss that is associated with spaceflight.

The amount of force that is placed on the bottom of the foot, as well as joint angles at the ankle, knee, and hip were measured. Electromyography electrodes recorded leg and arm muscle activity. Knee-joint motion in space was reduced when compared to that on Earth, thus effecting muscle action. Measurements of forces during exercise suggested that much less force was experienced than would be experienced when exercising on Earth. Based on these data, Cavanaugh and Rice [2007] have compiled a set of summary articles that examines bone health, bone loss, efficacy of exercise and mechanical stimulus, and other factors that are relevant to bone health in space.

5.6.2.2. Mechanical countermeasures

All of the mechanical procedures tested thus far during bed rest studies have been ineffective. Correlative observations have indicated that the required procedure for use in-flight should provide the equivalent force on the skeleton of 4 h of walking per day.

Some scientists currently believe that bone mass is not only controlled by the high-magnitude, low-frequency strain resulting from the mechanical loads on bones associated with vigorous exercise, but also by low-magnitude and high-frequency strain that musculature continuously places on bones while sitting or standing. It is well known that mechanical loads (stress) causes slight deformations called strain. The amount of strain is dependent on loading, elasticity, and geometry of the bone. An upper limit strain must be exceeded to provoke remodeling to increase bone mass. Mechanical strain below a lower limit will provoke adaptive remodeling to reduce mass.

Results of ground-based studies suggest that barely perceptible vibrations may generate enough strain to stimulate bone growth. For example, a group of sheep exposed to 20 min per day of vibrations experienced increased trabecular bone formation when compared to a control group that was not exposed to vibrations [Rubin et al., 2001] (Figure 5.24). In addition, when animals that were prevented from

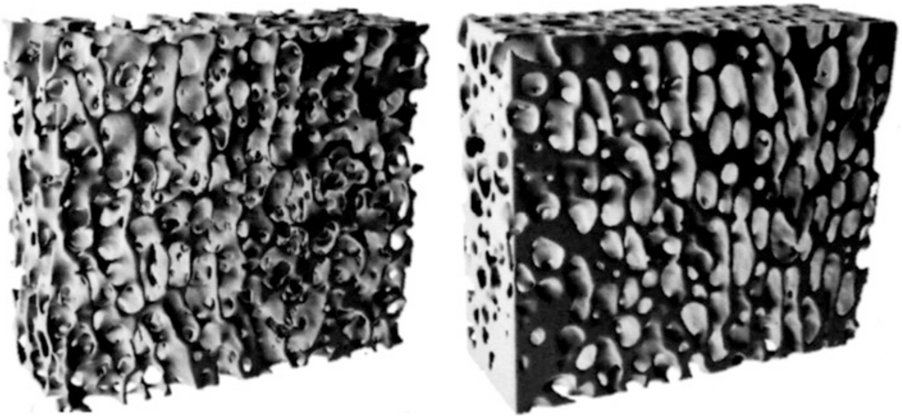

Figure 5.24. After a Year of Daily 20 min Standing on a Vibrating Platform (0.3 g, 30 Hz), Sheep Showed the Robust Striations of Increased Density (*Right*). Control Sheep Showed Normal Bone (*Left*) [Rubin et al., 2002].

regular, weight-bearing activity, were exposed to vibrations daily, bone formation remained at near-normal levels. However, animals not exposed to the treatment, but participating in weight-bearing activity each day, still exhibited signs of significant bone loss. If proven valuable for humans, low-level vibrations during spaceflight may offer an alternative for the current, time-consuming astronaut exercise regimes for long-duration space missions.

5.6.2.3. Nutritional countermeasures

In addition to caloric intake, protein, calcium, and other nutrients that are associated with bone metabolism, including phosphorus, sodium, potassium, and magnesium have no limits or requirements that are specific for the microgravity environment. Nutritional recommendations for spaceflight are no different from the recommendations of the National Research Council for life on Earth [McCormick, 2000].

A reasonable base figure for daily calcium intake in diet formulation for spaceflight is 1,000 mg. The principal purpose of daily calcium supplementation is for "protecting" the skeleton. Among the countermeasures tested have been high calcium and high phosphorus intake in both bed rest subjects and *Skylab* and *Mir* astronauts. The study showed that this procedure maintained calcium intake and excretion level in balance for up to 3 months, following which the gradually rising fecal excretion of calcium caused a negative calcium balance. Hence, there is no basis at this time for recommending a higher intake level than 1,000 mg/day.

Bed rest studies addressing the effects of high phosphorus intake showed some suppression of the tendency of urinary calcium to elevate, but the manipulation was ineffective because of gradually increasing fecal calcium excretion. Furthermore, the calcium to phosphorus ratio should not exceed a ratio of 1:1.8. Indeed, too high an intake of phosphorus will exert some binding effect on calcium in the intestine and tend to inhibit calcium absorption.

The current recommended level for magnesium is 350 mg/day for adult males. While studies of this element in relation to bone are far less numerous than studies of calcium, research to date indicates that deleterious effects apparently do not occur except possibly with low intake, as in an artificial diet, over a very long time. Certain bisphosphonate compounds that bind to bone crystal and tend to inhibit bone resorption show promise. These countermeasure studies continue.

5.6.2.4. Pharmacological countermeasures

Biochemical regimens have been studied during bed rest: (a) synthetic salmon calcitonin, a hormone inhibiting bone resorption; (b) phosphate supplements; (c) oral calcium; and (d) etidronate. All showed no beneficial effect [Fleisch et al., 1969; Hulley et al., 1971]. However, during the last 3 weeks of bed rest, the usual progression of calcaneal mineral loss was no longer observed. Etidronate, however, has been associated with an accumulation of new bone tissue both in animals and man when given at high dose for extended periods of time [Meunier et al., 1987].

New bisphosphonates are being tested for treating global bone loss diseases such as post-menopausal osteoporosis. For example, alendronate was effective in preventing hypercalciuria and maintaining bone mineral density in the femoral neck, femoral trochanter, spine, and pelvis in humans during bed rest studies. Moderate loss of bone mass density occurred in the calcaneus, but the loss was significantly less than in the control group [Ruml et al., 1995]. An experiment using bisphophonates on the crewmembers of ISS has been on going since *Expedition-16*. Bisphosphonates help reduce bone loss by blocking breakdown of bone. This study tests the effectiveness of two bisphosphonates: alendronate, taken as a pill once per week before and during spaceflight, and zoledronic acid, given by intravenous infusion once before flight with an effect lasting for the length of the flight [LeBlanc et al., 2010].

Another possible pharmacological countermeasure is parathyroid hormone (PTH). PTH is the most important endocrine regulator of calcium and phosphorus concentration in extracellular fluid. Secreted from cells of the parathyroid gland, this hormone finds its major target cells in bones and the kidneys. PTH stimulates osteoclasts to reabsorb bone mineral. In addition to stimulating fluxes of calcium into the blood from bones and the intestines, PTH slows the excretion of calcium in urine, thus conserving calcium in blood.

Other studies are looking at the hormone glucose-dependent insulinotropic peptide that is involved in insulin production for which some bone cells have receptors. These studies aim to ascertain whether the loss of bone in space can be prevented by modulating a person's own production of the hormone or by giving it by injection or tablet.

Mice that were exposed to microgravity on board the ISS exhibited a 15–20% decline in femur elastic strength and a 40–60% decrease in bone formation when compared to the controls. The femur elastic strength decline was caused by three mechanisms: reduced bone formation, increased bone resorption, and inhibition of mineralization. Mice that were treated with osteoprotogerin (OPG) before being exposed to microgravity, exhibited no discernable decline in femur elastic strength, and bone resorption was significantly increased [Bateman et al., 2004]. OPG is a bone metabolism regulator that is evaluated by the U.S. Federal Drug Administration as a new treatment for osteoporosis. Mechanical testing data were complimented by serum, mRNA, and histological analyses that indicated a decline in bone formation and an increase in bone resorption in addition to an inhibition of mineralization. OPG mitigated the decline in mechanical strength by preventing increase in resorption and maintaining mineralization [Harrison et al., 2003].

Further studies are also needed to clarify the relationships among the different systems, i.e., musculo-skeletal, nutritional, cardio-vascular, and neuro-vestibular. Indeed, it was recently shown that the sympathetic nervous system regulates bone remodeling. Nerve fibers have been detected in bone in close vicinity to the osteoblasts. Because the sympathetic nervous system controls bone remodeling and the vestibular system influences the sympathetic nervous system, the vestibular system could well be involved in bone remodeling [Denise et al., 2007]. In fact, animal research indicates that the bone loss induced by bilateral vestibular lesion has the same distribution as the bone loss induced by spaceflight. The sympathetic nervous system could possibly modify bone metabolism directly via osteoclastic and osteoblastic β-adrenergic receptors or indirectly via modifications of the vascularisation or both. Consequently, β-blockers such as propranolol are potential countermeasures in preventing bone loss. On Earth, an epidemiologic study demonstrated that the use of β-blockers is associated with reduced risk of fractures [Schlienger et al., 2004]. These new areas of research indicates that a greater effort toward a coordinated, multidimensional approach, with an ultimate goal of prevention and rehabilitation, is required in order to design strategies to counteract the effects or treat as needed, research that will also benefit to osteoporosis patients on Earth.

5.6.3. Aging and Space

There is a need for developing a practical, inexpensive, non-invasive way of making muscle and bone mass and strength measurements, a system sensitive enough to monitor and evaluate small changes. The need for such an instrument goes way beyond spaceflight. Since muscle and bone abnormalities affect a substantial portion of the population, such an instrument would offer broad utility as a tool for clinicians on Earth. For example, the information gained from this instrument may benefit the people here on Earth whose daily activities are affected by metabolic deficiencies, weakened muscles, or loss of bone mass. Some metabolic diseases, for example, result in debilitating muscular weakness, a condition that could be improved by advances in protein turnover research. Likewise, muscle wasting is problematic for senior citizens, patients confined to lengthy bed rest, patients with spinal nerve damage, and even burn victims recovering from traumatic accidents.

Older people also commonly experience a loss of bone mass, a condition often due to the age-related disease osteoporosis. Bone loss in space is not identical to osteoporosis on Earth, because there is a clear hormonal component in osteoporosis. As we age, we also lose muscle mass and strength, a phenomenon called sarcopenia. This continuous reduction of muscle strength is largest in the antigravity muscles. Aging effects differ from spaceflight in that: (a) the entire body is involved; (b) muscle loss in the aging has no plateau; and (c) is characterized by fast twitch (Type II) to slow twitch (Type I) fiber transformation [Rittweger et al., 1999]. There is also a reduction in the number of muscle fibers and cross-sectional area. An imbalance in the natural cycle of protein turnover may be a contributing factor to decreased muscle mass.

Does spaceflight push the astronauts along the irreversible axis of aging? When he flew on the space shuttle at the age of 77, John Glenn was the subject for a muscle loss experiment, whose aim was to investigate whether or how weightlessness can affect the elderly more than younger astronauts (Figure 5.25). Samples of blood and urine were collected during the flight after Glenn swallowed pills containing amino acid N-15 alamine. The study compared the amount of amino acids absorbed into the body to the amount passing out in urine, and calculated how quickly proteins are built up and broken down. The hypothesis was that given the similarities between aging and spaceflight, perhaps an older person might be even better prepared than a younger one for the physical changes brought on by spaceflight. Older individuals might therefore experience fewer changes in space. This did not turn out to be the case for this particular individual. Glenn's muscle loss looked about the same as that of other younger subjects exposed to the same tests. Also, his cardio-vascular and muscle strength data looked like any other healthy middle-aged astronaut. However, his muscle volume and some immune data looked more like he had been in space 2 weeks instead of one. This might merely be a function of his age. The good news is that these results indicate that an older person in good health, as Glenn was, can endure the conditions of spaceflight.

Figure 5.25. U.S. Senator John H. Glenn Works Out on the Ergometer Device Onboard Space Shuttle Discovery During the STS-95 Mission in 1998. (Credit NASA).

But the answer is not so simple, because aging is also associated with changes in hormones, activity levels, nutrition, and often, disease. Nevertheless, by exploring the interaction of aging and spaceflight, research will undoubtedly contribute to our knowledge of the aging process. A better understanding of bone and muscle changes in spaceflight will also lead to treatments for astronauts and Earth-bound patients alike.

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Chapter 6

Psychological Issues of Spaceflight

This chapter emphasizes the importance of mental and social well being in the success of both short and long space missions. What are the psychological and sociological issues, which must be addressed, especially for international missions? This section reviews the factors that may have a critical impact on the success or failure of a space mission, in terms of interactions of the crewmember with his habitat, with the space environment, and with the other crewmembers (Figure 6.1).

6.1. The problem: reaction to stress

According to the media, the Russian Space Agency once launched a rescue mission to the *Mir* space station. Among three men aboard the capsule, one replaced one cosmonaut in the two-person *Mir* space station, and the others escorted him back to Moscow. While cardio-vascular problems were the official reason for the *Mir* cosmonaut early homecoming, some U.S. space experts say there might have been additional difficulties from the stress of prolonged weightlessness, isolation, and confinement [Burrough, 1998].

This example illustrates the problem with psychological issues during space missions: although they presumably exist, most of the reports are anecdotal. In fact, psychiatric problems during space missions, such as anxiety, depression, psychosis, psychosomatic symptoms, and postflight personality changes, have been rare or not methodically documented. Known negative psychological reactions to spaceflight have included sleep problems, reduced energy levels, mood and thought disorders, alteration in time sense, and poor interpersonal relations. Interpersonal issues include interpersonal tension, decreased cohesiveness over time, need for privacy, and task versus emotional leadership [Kanas and Manzey, 2003]. None of these problems, however, seems to have seriously affected a space mission yet, probably due to the extraordinary motivation and commitment of the astronauts. However, Dr. Patricia Santy, a psychiatrist and flight surgeon who worked at NASA, and author of the book *Choosing the Right Stuff* [Santy, 1994], said that even highly motivated people have a limit. She sets that limit at 3 or 4 weeks. “After that, if you have interpersonal conflict in that confined microsociety, things can get out of hand.”

Space travel requires establishing and maintaining effective, stable interactions between individuals in small groups that are under microgravity conditions and are isolated and confined for prolonged periods. Individual behavior adjustment, interpersonal conflict, and group performance effectiveness are typically exacerbated in isolated and confined groups. Such phenomena have been repeatedly documented

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Figure 6.1. Fight Scene of the Movie "Lady Killer" (1933) by Director Roy Del Ruth, Featuring James Cagney, Douglas Dumbrille, Mae Clarke, Raymond Hatton, and Russell Hopton. (Credit Warner Bros).

in operational settings such as remote stations in the Antarctica, undersea habitats, and most pertinently, in spacecraft. However, the fact that observations are made and observed by people who actually share the experience limits the reliability of data.

Crewmen "wintering over" for 8 months in Antarctic stations, which corresponds to the summer season in the Northern hemisphere, have shown an increase of 40% in stress-related symptoms of anxiety, depression, insomnia and hostility [Sandal et al., 1996]. In space, where the stress of isolation is compounded by the stress of prolonged weightlessness, problems can go beyond hostility and anxiety. Astronauts usually complain of various psychosomatic symptoms, including sleep disturbance, time disorientation and headaches. Time compression and heavy work schedules have led to harsh disagreements between astronauts and ground control crews, with the astronauts in space feeling rushed and the controllers on Earth growing impatient.

These problems are amplified by the difficulties of living in microgravity: hygiene routines are time consuming and laborious; food does not taste the same and spices must be added for flavor; privacy is limited; the environment is noisy; the countermeasures may require extra effort and time-consuming activity (Figure 6.2); and motivation to do the required countermeasures becomes increasingly difficult. Related to the question of exercising in space is the problem of limited bathing facilities. The water

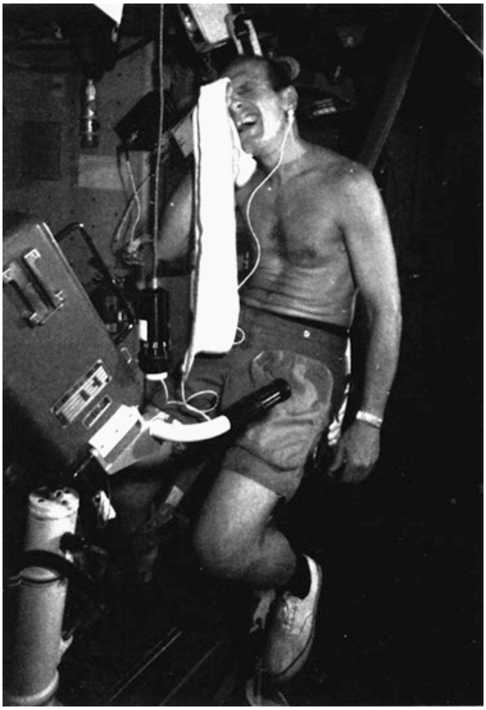

Figure 6.2. Astronaut Pete Conrad Exercises in Skylab. During a Long-Duration Mission, Daily Exercise Sessions Require Extra Effort and Motivation (No Shower!) and Are Very Time-Consuming. (Credit NASA).

dispersed from perspiration during exercise must be collected, and there is no shower, just sponge bath. In addition, the physiological adaptations to microgravity described in previous chapters challenge and stress individuals, and thus impact interpersonal interaction, concentration, and ability to perform group and individual work.

As spaceflights become longer and more routine with the rewards less satisfying, the intense effects of being isolated take their toll. More problems in psychological adjustments are expected. Because of the technical and precarious nature of future, interplanetary long-duration missions, the slightest upset in astronaut performance and behavior could have disastrous effects on the mission.

Typically, when an individual or small group of individuals is removed from a social environment and put into an isolated and confined environment, four groups of symptoms are to be expected [Harrison and Connors, 1984]. The first group includes mental deficiencies, decreased attention and concentration, learning problems, and hallucinations. These problems raise concerns when operating in dangerous environments such as space. In a worse case scenario, a warning light may be missed causing a catastrophe to occur. The second group is a decline in motivation when the individual's or the group's perceptions of the rewards inherent to the situation does not outweigh its costs. By comparison, in the early space missions in which astronauts were treated as heroes, spaceflight becomes more routine, thus creating a situation where reward is perceived as declining [Helmreich et al., 1980]. The third category of problems is somatic complaints, such as sleep disturbances, headaches, upset stomachs, and constipation. All of these complaints have some basis in the physical nature of the environment, but can also easily be exacerbated by or even caused by the unusual levels of stress found in that environment. Changes in mood and morale comprise the fourth category.

It is interesting to note that during the first several weeks of a mission in Antarctica, the interpersonal problems do not play a major role. When crewmembers first arrive, they do not possess enough knowledge about their mission and surroundings to formulate their own ideas. Hence, they are willing to follow whatever the leader says. After the initial shock of the environment wears off, and crewmembers get to know their surroundings somewhat better, they begin to rebel against authority and each other. The increase in mood disturbance after the mid-point of winter isolation found in some studies suggests the existence of a "third quarter phenomenon" that is more psychosocial than environmental in nature. This phenomenon is independent of mission duration. It results from the realization that the mission is only half completed, and that a period of isolation and confinement equal in length to the first half remains [Bechtel and Berning, 1991].

To fully understand group dynamics, individual psychological health, and factors that both hinder and help daily life on the ISS, researchers recorded crew and crew-ground activities during the first nine Expeditions. A computerized questionnaire was the main tool used to collect the data and included questions from three standard mood and interpersonal group climate questionnaires as well as a critical incident log. Input was collected on a weekly basis from the crewmembers in space, ground personnel at NASA Centers in the United States, and the Russian mission control personnel. As the crewmembers adjusted to their new environment onboard the ISS, there was evidence of improved mental health. Results of the study also showed evidence that their mood as well as the social climate onboard improved with time. The conflicts that did occur among the crew as well as between the U.S. and Russian teams did not appear to be related to mood or social climate variables. The study identified communication and geographic separation as the key challenges to leadership and mission management [Kanas et al., 2007].

Psychological monitoring and support for missions to Mars will be restricted as a result of the fact that real-time space-to-ground communications will not be possible for most of the mission. The first astronaut explorers who visit Mars will also be the first human beings to lose a direct visual link with Earth because of the enormous distances involved (Figure 6.3). How individuals will respond to the "Earth out-of-view phenomenon" is not known. Quite a number of reports from astronauts suggest that the psychological importance of looking back to Earth from space is of significant importance. It is possible that not being able to see the Earth might induce feelings of anxiety, sadness, depressive reactions, or even a loss of commitment to the usual (Earth-bound) system of values and behavioral norms. Logically, we can conclude that mission performance might then be adversely affected, as would individual behavior, interpersonal interactions, as well as the acceptance of guidance from mission controllers on Earth [Kanas and Manzey, 2003].

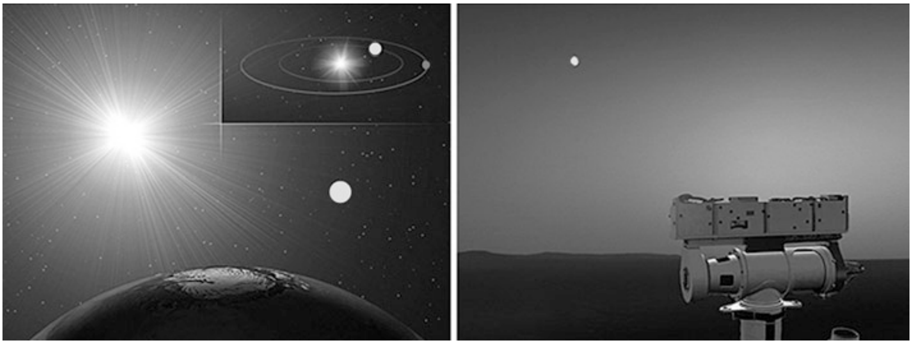

Figure 6.3. ***Left*: Earth and Sun Viewed from Mars. The *Right* Half of This Illustration Shows What the Rovers and Astronauts Would See if They Looked Toward the Earth When the Distance Between Earth and Mars Is the Shortest (50–60 Million km).** (Credit NASA).

6.1.1. Analogs

Much of our understanding of human behavior and performance in space has been obtained from the study of analog environments such as Antarctic research stations, polar expeditions, nuclear submarines, undersea habitats, oil drilling rigs, small rural communities, and space simulator experiments.

Analogs are not perfect simulations of the space environment. None, for instance, have the condition of microgravity. There are also differences with respect to characteristics of crewmembers, procedures for screening and selection, crew size, mission objectives and duration.[1] Despite these differences, analog environments are the only way to study behavioral impacts of isolation, confinement, and stress over long periods of time.

Nuclear submarines have long been the focus of analog studies for long duration spaceflight because of the isolation and danger, as well as the confined close quarters. Whereas diesel submarines only stay below the surface a few days, nuclear submarines spend the better part of 6 months or more under water. The incidence rate of debilitative psychiatric illnesses among the crew is relatively low, with about 20–50 cases per 1,000 men. Psychiatric symptoms generally observed included anxiety, interpersonal problems, sleep problems, performance decrement, and depression, among a host of others [Weybrew and Noddin, 1979]. The low incidence may be due to the fact that submariners are some of the most thoroughly screened, tested, and trained individuals in the world. Also, the presence on board of a nuclear submarine medical officer who has specialized training in psychiatry may explain the low incidence rate for psychiatric symptoms.

Perhaps the closest operational analog of space occupancy is the undersea habitat, where aquanaut divers live and work on the ocean floor with a degree of isolation similar to that in space (Figure 6.4). Under these circumstances, and in Antarctic

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[1] Space simulator experiments allow, however, to control some of these aspects.

Figure 6.4. The NASA Extreme Environment Mission Operations (NEEMO) in the Aquarius Habitat Off Key Largo and 19 m Below the Surface Provides a Convincing Analog to Space Exploration. ISS Crewmembers, as Well as NASA Employees and Contractors, Are Deployed There for up to 3 Weeks at a Time. They Experience Some of the Same Tasks and Challenges Under-Water as They Would in Space. (Credit NASA).

stations and submarine operations as well, observational measurements have focused upon critical individual and group factors that influence performance effectiveness and interpersonal relations.

Palinkas [1986] describes Antarctica as the best analog to the space environment. Because of the extreme nature of the environment, researchers must winter-over for 6–8 months out of the year. During this period, there is little contact with the outside world and groups are confined to their barracks because of the extreme temperatures. Several features of Antarctic research stations are particularly similar to outer space. Antarctic facilities and space facilities have similar scientific and political objectives. They are also similar in: (a) the nature of the work, which is primarily science, exploration, and support; (b) the heterogeneity of the crews that comprise military and civilian men and women, Antarctic veterans and novices; (c) the high level of skills; (d) the organization of the mission, like the division of labor, chain of command; and (e) the rotational structure of tours of duty [Palinkas, 1991]. Outer space and Antarctica are also similar in that their environments are hazardous and stressful to work in and the crews are heterogeneous, confined and isolated from the larger society. Because of these similarities, Antarctica has served as one of the primary means of gathering the psycho-sociological data for the ISS and future interplanetary missions [Harrison et al., 1991].

To some extent, analogs and space missions provide comparable reports of psychological problems (Table 6.1). This is mainly because of the conditions of isolation and

Table 6.1. Reported Psychological Problems During Spaceflight and Analogs.

Reported Problems	ISS/Mir	Shuttle	Submarines	Polar Expeditions
Interpersonal conflicts	Documented	Documented	Documented	Documented
Sleep disturbances	Documented	Documented	Documented	Documented
Boredom, restless	Anecdotal		Documented	Documented
Performance decrement	Anecdotal		Documented	Documented
Decline in group compatibility	Anecdotal	Anecdotal	Anecdotal	Documented
Substance abuse	Anecdotal			Documented

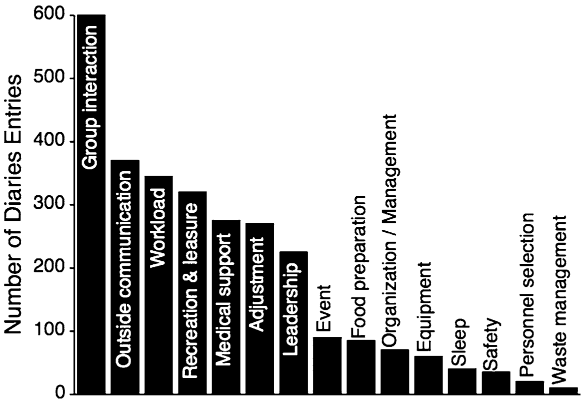

Figure 6.5. Number of Diary Entries Classed by Categories During Expeditions in French Antarctica. (Adapted from Stuster et al. [1999]).

confinement. However, for space missions, most data comes from anecdotal reports like diaries, stories, personal books, and interviews [Bondar, 1994; Burrough, 1998; Chaikin, 1985; Collins, 1990; Lebedev, 1988; Linenger, 2000]. Methodically documented data is lacking.

One method used by psychologists to evaluate the effects of confinement and isolation during a winter-over in Antarctica, for example, is to analyze the diaries of the crewmembers. The assumption is that the frequency that an issue is mentioned in a diary reflects the importance of that issue. Stuster et al. [2000] analyzed nine diaries from several expeditioners in French Antarctica (ranging from 69 to 363 days) written by the station leaders, the medical officers, and the technicians in charge of communications. These reports clearly indicate more negative experiences during the third quarter of isolation and confinement in an Antarctic station, regardless of duration of the expedition. It is also interesting to note that, when grouped into categories, the largest numbers of diary entries, and presumed importance of the issues, concern group interaction, communication, workload, recreation and leisure, and leadership (Figure 6.5).

6.1.2. Space simulators

The Isolation Study for European Manned Space Infrastructure (ISEMSI) was a simulation experiment conducted by ESA in 1990 to provide psychological data on the day-to-day activities of astronauts during a long-duration isolation and confinement inside a ground-based replica of a space station. The crew for ISEMSI consisted of six males, each from a different ESA member state. All subjects were civilians who had backgrounds in science and engineering. They were placed for a 4-week period in hyperbaric chambers and monitored by a "ground" control team. Results from a battery of psychological tests performed showed no evidence of severe social or emotional conflicts during the experiment.

However, observations of social interaction and communication revealed considerable changes in the communication flow among the crewmembers (Figure 6.6). At the beginning of the confinement, all subjects participated in communication in a relatively balanced manner. At the end, subject D, who was the most dominant subject beside the commander, was totally isolated, and the communication of all other crewmembers remained limited to two-way communications with the commander. Despite these problems, the volunteers were seen to coalesce into a tightly knit group, even developing an aggressive attitude towards the "ground" control team [Sandal et al., 1995].

In a more recent experiment, social interactions of a mixed-gender crew from five countries (Russia, Canada, Japan, Austria, and France) were evaluated during a 240-day isolation study in a *Mir* simulator (SFINCSS-99). In this study, the crewmembers sometimes executed different flight programs and were housed in comparatively separate modules. As predicted, several incidents occurred that could be regarded as a conflict situation between crewmembers. For example, a fistfight took place at the New Year's party, and a Canadian female crewmember accused a Russian crewmember of sexual harassment. Later, the commander informed the "ground" control team and insisted on the withdrawal of the two subjects from the study else to close the hatch between the two modules. In accordance with his request, the hatch between the

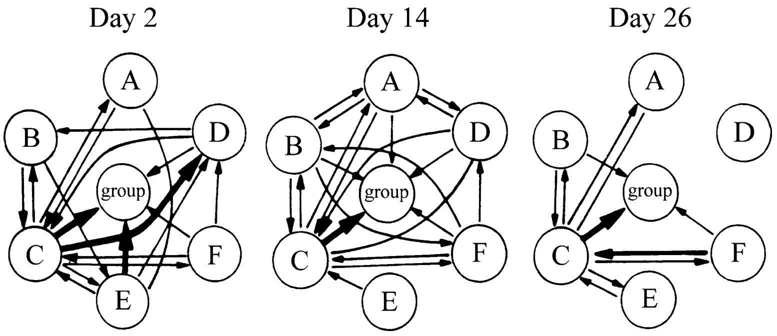

Figure 6.6. Pattern of Communication at Different Days of the ISEMSI Study. The Thickness of the *Arrows* Indicates the Frequency of Occurrence. A, B, C, D, E, F Represents the Different Crewmembers, with C Being the Commander. The Center Island Represents the Overall Group, When, for Example, One Says, "Let's Go Eat!" [Sandal et al., 1995].

chambers was closed. From this point on, frustration grew more intense among the crewmembers and toward the "passive support and insufficient management of crisis" by the ground control team. One volunteer expressed a wish to leave the chamber and did so [NASDA, 2002].

The results of these experiments and others are somewhat consistent with what has been previously observed in actual spaceflights. The "Us vs. Them Syndrome" in particular has appeared at various times on spaceflights and in Antarctic studies.[2] Basically, the teams out in the field see those who stay at base as soft and weak. Their attitude seems to be "They're back there all warm and cozy! What do they know about what's going on out here?" The distance from a central authority seems to force the crew to assume a responsibility for themselves and their environment. As this happens, they begin to see the "outside authority" as unnecessary. Conflicts can occur if the central authority pushes itself on the crew [Nicholas and Foushee, 1990].

At the time of this writing, there are six individuals, including three Russians, two Europeans, and one Chinese, all male, sealed in an isolation chamber at the Institute of Medical Problems in Moscow. They are the crew of the "Mars 500" simulated mission to Mars, which began in June 2010 and is scheduled to last 520 days. The only way that this crew can communicate with the outside world is by e-mail. The only personal contact they have is with each other. Voice contact is maintained with mission controllers in the simulated control center, as well as with family and friends as would normally be the case during a real space mission (Figure 6.7).

The communication transmission latency is simulated with a built-in 20-min delay added to messages sent to/from the Mission Control center. During the "mission asthenia", the crew will simulate all elements of the Mars mission including traveling to Mars, orbiting the planet, landing, and then returning to Earth. They must be self-reliant, organizing most of their daily tasks themselves. They are also responsible for monitoring their own health and psychological states; monitoring, controlling and maintaining all "flight" systems, including life support; controlling resource consumption; executing standard and non-standard cleaning and maintenance; and finally, fulfilling scientific investigations.

A standard 7-day week is maintained that includes 2 days per week off. As work goes on 24/7, a rotating shift scheme has been implemented. To determine the effects of decreased work capacity, illness, or onboard systems failures, both standard and non-standard emergency situations will be simulated. The crew will be divided into two groups of three during the "Mars surface operations" phase of the simulation. When the "landing party" exits for the Martian surface, the hatch between the Martian simulation module and the rest of the facility will be closed. It will only be opened again when the landing party returns from the simulated Mars surface visit.

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[2] The mutiny of the *Skylab-4* astronauts against Mission Control is the perfect example. All the astronauts of the *Skylab-4* mission were first-time flyers (rookies). Before they got adjusted, Mission Control transferred the same busy schedule to them as their predecessors had kept in the space station. After their complaint about a heavy workload did not receive enough attention by the ground controllers, the *Skylab-4* astronauts declared an unscheduled day off to Mission Control and proceeded to turn off the radio while they got some rest. This mutiny led to much-needed workload adjustments [Shayler, 2008]. Perhaps as a result of this event, a rule states that at least one member of an Expedition crew on board the ISS should be a spaceflight veteran.

Figure 6.7. International Space University's Alumnus Diego Urbina Is a Member of the Six-Person Crew in the Mars-500 Isolation Facility. (Credit Diego Urbina).

6.1.3. Space missions

The former Soviet Union has had extensive experience in operating a crewed space station over long periods of time beginning in 1971 with the launch of the first space station, *Salyut-1*. Disagreements between the Russian crew and Mission Control over work overload, or regulations of crew activities imposed by Mission Control, were reported from several missions [Kelly and Kanas, 1993].

Some of the problems that have been observed aboard Soviet stations include a general nervous or mental tiredness called "asthenia." Asthenia symptoms include hypersensitivity, irritability, and hypoactivity in its early stages. These symptoms are sometimes followed by psychosomatic illness and sleep disorders. Asthenia occurs primarily in the monotonous, later portions of the mission. Once recognized, it is treated through a manipulation of work schedules to provide more free time and stimulation, and through increased audiovisual communications with friends and family [Kanas, 1991]. Another problem that manifested itself on board Soviet stations was interpersonal tension. The Soviet proclivity towards the "collective" causes the cosmonauts to suppress their hostile feelings towards one another in the interest of the mission as a whole [Santy, 1994].

The conditions that exist in long-duration space missions increase the potential for adverse effects already reported during relatively short-duration missions (e.g., irritability, depression, sleep disturbances, and poor performance of both group and individual). During the joint NASA-*Mir* missions (March 1995–June 1998), several events caused tension among the crew and between the crew and personnel at Mission Control (Table 6.2). Differences in mood and group perceptions between U.S. and Russian crewmembers, as well as between crewmembers and Mission Control personnel were also identified during ISS missions.

Table 6.2. List of Events Leading to Psychological Disturbances During the NASA-Mir Space Missions. Adapted from Ark and Curtis [1999].

- Crew change at L-8 weeks
- Mission extended by 6 weeks
- Minimal control over in-flight work schedule
- Work overload/underload
- Social withdrawal
- Death of family member
- Dangerous atmosphere (ethylene glycol and contaminant leaks)
- Fire; decompression (loss of module); loss of power (free drift); communication system failures
- Anger with ground control/management ("us vs. them" syndrome)
- Crew friction

Table 6.3. The Countermeasures for Psycho-Sociological Issues of Spaceflight Are Individual and Crew Selection, Training, and In-Flight Support.

Selection
Best psychological profile
Appropriate skills
Team player
Training
Interpersonal communication
Group dynamic and group problem-solving
Multicultural sensitivity
Performance feedback monitoring
Support
In-flight counseling
Communication with family & friends
Scheduled breaks in routine

6.1.4. Rules

Nearly all essential human functions during long-duration space missions will depend critically upon individual and group behavior. Selection, training, and organizational support are the focus of human behavioral initiatives (Table 6.3).

The first priority in considering the effects of individual factors upon personal adjustment to a space mission is the screening and selection of prospective participants. In Antarctica, a good "field person" is one who has a good knowledge of living and working in the new environment, and is committed to science and exploration. This individual is autonomous and can function without direct supervision. He or she also should also have a certain amount of integrity and must accept one leader. Indeed, in a hostile environment, there is room for individuality, but not for "too many chiefs" [Stuster, 1996].

In general, these principles can be applied effectively to space missions. The astronaut should have an intimate knowledge of the environment in which he/she will be spending a lot of time and be committed to the mission of which he/she will be a part. Palinkas et al. [2000a] in his review of the literature found that introverted individuals, those who are "more inner-directed, quiet, retiring types", tend to adapt and perform better in Antarctic situations than do extroverts.

Training should be both didactical and experiential. The goal is to sensitize both the crewmembers and monitoring ground personnel to the influences of socio-cultural factors, such as culture and language differences. Team building and conflict resolution exercises should also be included in preflight activities.

In-flight support is provided by the flight surgeons and psychologists on the ground, as well as family or friends, and includes surprise gifts and events to break the routine. Individuals are also encouraged to talk with one another to resolve interpersonal difficulties.

The countermeasures (selection, training, and support) are further detailed in the following sections.

6.2. Individual selection

At the individual level, selection strategies have two-fold objectives: to eliminate unfit or potentially unfit applicants, and to select from otherwise qualified candidates those who will perform optimally. A distinction is therefore made between "select-out" and "select-in" criteria.

6.2.1. Select-out criteria

The first objective is to "select-out" or disqualify any candidate with a history of a psychiatric disorder, current psychiatric symptoms, or other characteristics that place him or her at risk for a psychiatric disorder during a space mission. "Select-out" criteria are medical criteria specifying those psychiatric disorders, which would be disqualifying. These disorders include schizophrenia, major depression, and all the other psychiatric diseases listed in Table 6.4. To achieve this objective, selection procedures rely upon formal clinical evaluations and use of standardized psychometric tests.

Clinical evaluations generally are in the form of a structured psychiatric interview with at least two independent psychiatrists. Each psychiatrist asks the same question in the same order and generally in the same manner to avoid the problem known as interviewer bias. The interviews are conducted to counteract the tendency of applicants to minimize psychological symptoms ("staying clean"). Patricia Santy gives the following example in her book *Choosing the Right Stuff* [1994]: instead of asking the question, "Have you ever been depressed?" where most healthy subjects would realize it's not a good thing to be depressed and would probably answer "no," the question is formulated in the form of a request – "Tell me about the time when you have been most sad in your life" – which makes it hard for the subject to escape from giving some clinical information on the topic.

To assist the clinician in objectively determining whether or not an applicant is a "risk to flight safety," a series of psychometric tests is generally added to the psychiatric interview. These tests include self-report questionnaires, such as the

Table 6.4. **MMPI Scale.** The First Three Measurements (Validity Scale) Indicate How Well the Candidate Responded to the Test. The Other Measurements Indicate the Scores for Each Disqualifying Psychiatric Disorders. Adapted from Santy [1994].

L – a validity scale; high values indicate evasiveness, e.g., different responses to about the same questions

F – a validity scale; measuring the tendency to present one's self on an overly favorable light (low score = more favorable)

K – a validity scale; measures defensiveness, e.g., underreport, not completely honest in answering personal questions (high score = more defensive)

Hs – Hysteria

D – Depression

Hy – Hypochondriasis

Pd – Psychopathic Deviation

Ma – Mania

Mf – Masculinity/Feminity

Pa – Paranoia

Pt – Psychasthenia

Sc – Schizophrenia

Si – Social Introversion

Note: The Mf score is not considered of any significance in defining sexual orientation: High scoring are described as sensitive, aesthetic, passive; low scoring are described as aggressive, rebellious, and unrealistic.

Minnesota Multiphasic Personality Inventory (MMPI), and the Million Clinical Multiaxial Inventory (MCMI). These tests have been standardized against a normal population, and most of them have built-in scales that detect whether the applicants fake responses to test questions in trying to conceal pathology. Other tests try to create a situation in which the psychological issues of the applicant can be reflected. These projective personality tests include for example the Rorschach Ink Blot test, where the subject's association to ambiguous inkblots are observed and scored. In other projective tests the subject is asked to draw a person or complete a sentence.

Using these methods, Santy [1997] reports the incidence of psychiatric disorders in a study of 223 astronaut candidates to be 8–9%. The prevalence rates for these psychiatric disorders found in the applicant groups are very similar to the rates reported in the general population (0.4–8%) from a number of studies [Robins et al., 1984].

6.2.2. Select-in criteria

The second objective is to "select-in," or identify and select candidates with characteristics that predict for optimum performance in the isolated, confined, and hostile environment of space. This selection does not have specific medical or psychiatric implications. "Select-in" or psychological selection criteria identify those desirable personality traits or characteristics linked to a specific mission ("best person for the job"). Typically, these traits would be those required when applying for a qualified job, i.e., aptitude for the job, intelligence, and "team player". In addition, given the stress and difficulty of the space environment, qualities such as the ability to tolerate stress, trainability and flexibility, and motivation are most important. Finally, sensitivity to self and others, emotional stability, maturity, ability to form stable quality interpersonal relationship, are prerequisites for dealing with sociological issues [Santy, 1994].

"Select-in" criteria were easy to identify for the early space missions, where the astronaut requirements were limited to high piloting skills, good stress tolerance (high acceleration, reduced pressure, high temperature, and other stressors), an ability to make decisions, and a strong motivation for the success of the mission rather than personal objectives. However, when the space program later also required astronauts with engineering, scientific, or medical background, and not necessarily piloting skills, the definition of "select-in" criteria became more complex. In addition, there has been little evaluation of astronaut performance during space missions, which is a requisite for the validation of "select-in" criteria. Psychological tests used in the past have also failed to find significant personality predictors of performance. As a result, "select-in" criteria used by the psychiatrists were reduced from the Gemini to the Apollo program and are basically not used for the selection of shuttle astronauts (Table 6.5).

It is interesting to note that during the psychological evaluations of the candidates for the Mercury space program, two psychiatrists spent over 30 h on each candidate. This included the time for taking the psychometric tests to evaluate motivation and personality, and performance tests to evaluate intellectual functions and special aptitudes. Psychological reactions of the Mercury applicants were also monitored during

Table 6.5. Summaries of Psychiatric and Psychological Selection Procedures in the U.S. Space Program (1959–1985). Adapted from Santy et al. [1991].

Procedure	Mercury	Gemini/Apollo	Shuttle
Number of hours for the psychiatric evaluation	30	10	3
Screening method	2 psych interviews 25 psych tests 5 stress tests	2 psych interviews 10 psych tests 1 stress test	2 psych interviews
"Select-in" criteria used by psychiatrists	1. Intelligence 2. Drive and creativity 3. Independence 4. Adaptive motivation 5. Flexible 6. Motivation 7. Lack of impulsivity	1. General emotional stability 2. High motivation 3. Adequate "self" concept 4. Quality of interpersonal relationships	None documented
Validation of criteria	Data not available	Not done	Not done

Figure 6.8. Astronaut Scott Carpenter During a Stress Test in a Heat Chamber Prior to His Flight on Board a Mercury Capsule. (Credit NASA).

stress experiments simulating some conditions of the mission, such as change in pressure, isolation, noise and vibration, and heat (Figure 6.8).

During the Gemini, Apollo and early shuttle missions, the psychological evaluation of candidates was reduced to 10 h, and the number of psychometric tests decreased from 25 to 10. For shuttle candidates, only "select-out" criteria are used to eliminate possible disruptive behaviors, and the duration of the evaluation does not exceed 3 h. Selection of those individuals evidencing the highest proficiency, a select-in criteria, based on the results of psychological tests is absent after the success of the early space missions.

6.2.3. Psychological profiles of astronauts and cosmonauts

Using data collected over 30 years of candidate psychological evaluations at NASA, Santy [1994] has compared the results of a commonly used psychometric test, the MMPI, among the astronauts and other control groups. This personality test consists of 566 questions for which a subject is asked to respond true or false. This test is used to identify psychiatric disorders. It also includes validity scales to detect if the applicant was honest in answering the questions (Table 6.4). What is remarkable is the similarity of all four groups of applicants (Mercury, Gemini, Apollo, and shuttle) over the 30 years (Figure 6.9).

All groups are extremely defensive and present themselves in the best possible light (LFK scales). The low Si (social introversion) scales in all groups and the

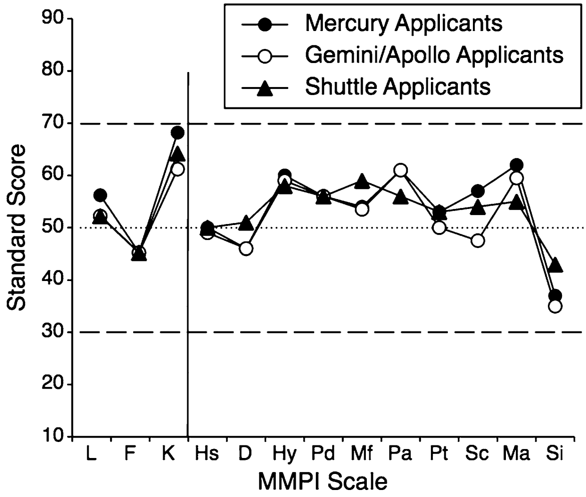

Figure 6.9. MMPI Profiles of Applicants to the Mercury, Gemini, Apollo, and Early Space Shuttle Astronaut Corps. (Adapted from Santy [1994]).

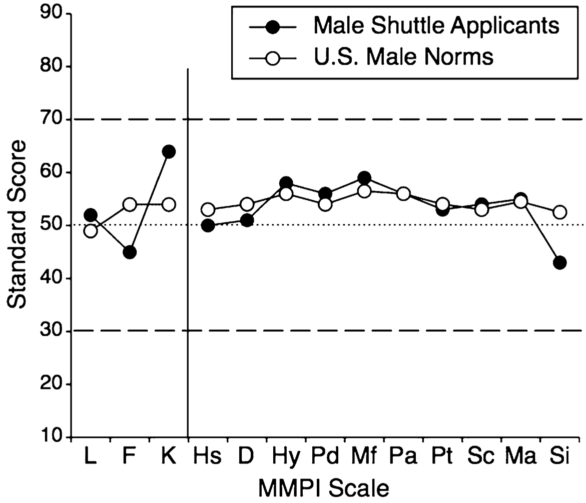

Figure 6.10. MMPI Profiles of U.S. Male Applicants to the Space Shuttle Astronaut Corps Compared with the Normal U.S. Male Population. (Adapted from Santy [1994]).

comparison with the normal population (Figure 6.10) suggest that applicants are much more socially extroverted than the normal population.

Interestingly enough, non-U.S. astronauts show a similar personality profile (Figure 6.11), even though the MMPI scores of the general population in various countries vary due to cultural differences.

Female shuttle applicants are also much more like their male counterparts than like the normal female population (Figure 6.12). On the other hand, the LFK scales of Russian cosmonauts suggest that they are more inclined to express their emotions (Figure 6.13).

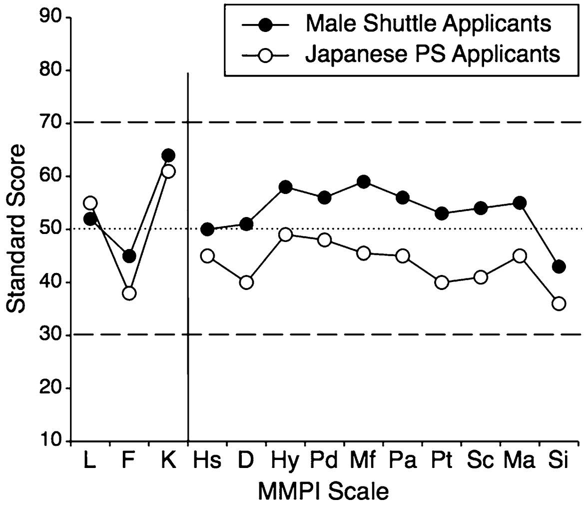

Figure 6.11. MMPI Profiles of U.S. Male Applicants to the Space Shuttle Astronaut Corps Compared with Japanese Male Applicants. (Adapted from Santy [1994]).

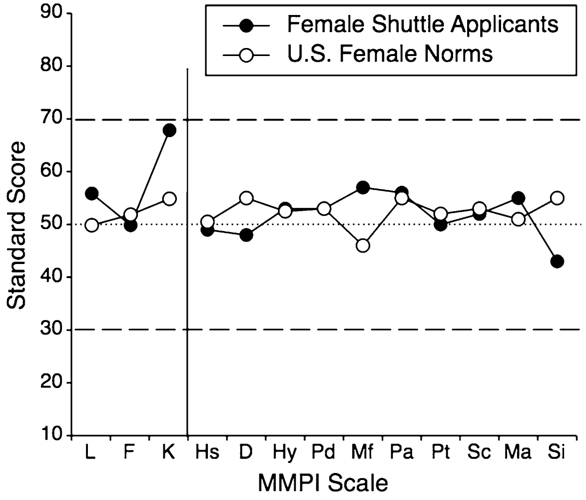

Figure 6.12. MMPI Profiles of U.S. Female Applicants to the Space Shuttle Astronaut Corps Compared with the Normal U.S. Female Population. (Adapted from Santy [1994]).

Although psychometric tests are used to identify psychopathology and select out candidates, they also suggest both commonalties in personality traits and socio-cultural differences. These commonalties and differences will ultimately contribute to the psychological and sociological problems that will develop during a space mission among a group of highly selected individuals.

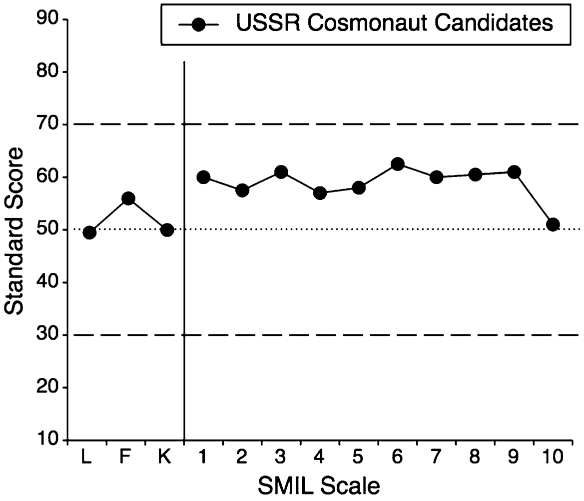

Figure 6.13. SMIL Profiles of USSR Cosmonaut Candidates. The SMIL Test Is Similar to the MMPI Test, Although the Scales Have Been Redefined. The Numbers in the SMIL Scales Roughly Correspond to the Pathology Described in Table 6.3 for the MMPI. (Adapted from Santy [1994]).

A psychiatric examination per se is not particularly helpful in determining which applicants to actually select. This is done though the characterization of those personality traits that are the most adequate for a mission, and through the validation of these criteria by subsequent behavior analysis and performance during training and space missions. This aspect will be developed in the Section 6.4. However, because today's space missions are composed of more than one single individual, let's review the social and cultural issues of group interaction and the process of crew selection.

6.3. Crew selection

6.3.1. Sociological issues

There are many variables that can affect the cohesiveness and performance of a group: culture, leadership, gender, age, personal attractiveness, emotional stability, competence, cooperativeness, and social versatility [Connors et al., 1985]. It is important to note here that these studies were conducted in analog environments with control groups, and that most of subjects are from Western culture.

6.3.1.1. Confinement and personal space

Ground-based studies have determined that psychological impairment started to occur when the available volume was restricted to 1.42 m^3 per person for 1 or 2 days of confinement, 7.36 m^3 per person for 1 or 2 months, and 17.0 m^3 per person for more than 2 months [Fraser, 1968]. Interestingly, except for space stations, the habitable pressurized volume in most spacecraft is less than these values (Table 6.6).

Table 6.6. Habitable Pressurized Volume (in m³) in Past and Present Spacecraft.

Spacecraft	Cabin Volume	Crew	Volume Per Person
Mercury	1.53	1	1.53
Gemini	2.52	2	1.26
Apollo	9.1	3	3.0
Soyuz	10.2	2	5.1
Shuttle	74.3	7	10.6
Salyut	99	3	33.0
Skylab	361	3	120.3
Mir	378	3	126
ISS	1,200	6	200

The number of individuals sharing confinement is believed to be another important variable affecting the amount of space needed per individual. More space per individual is needed as the number of individuals increases [Smith and Haythorn, 1972]. However, confined individuals tend to place heavy emphasis on assigned work and little emphasis on recreational opportunities. When recreation is sought, it tends to be passive in nature. This might account for the fact that astronauts and cosmonauts are not pursuing exercise programs enthusiastically, to say the least.

When two people are talking to each other, they tend to stand a specific distance apart. Each person has an invisible boundary around his/her body into which other people may not enter (Figure 6.14). If someone penetrates this boundary, the "invaded" person will feel uncomfortable and move away to increase his or her distance from the "invader". The major exception is family members and other loved ones. This personal distance is not due to body odor or bad breath. Closeness lends a sense of intimacy, the degree of which varies with the distance between individuals.

The average personal distance varies from culture to culture. Latin Americans, French and Arabs interact at closer distances than U.S., English, Swedish, or German individuals [Hall, 1966]. During two summer sessions of the International Space University, students from the Space Life Sciences Department performed a study attempting to determine the personal space of students from various countries [Bui and Wong, 2002]. During a fake interview, the distance and the angle between the subjects and the interviewer were measured. Results indicated that this distance varied from 150 cm in Asian (e.g., Japanese) students, to 40 cm or less in Latin (e.g., Italian) students. There was also a strong tendency to not directly face the interviewer, but stay at an angle. This angle seemed also strongly correlated with the subject's cultural origin (Figure 6.15).

The use of physical or eye contact also varies by culture. Although in some cultures, eye contact is a way to communicate, in other cultures physical or eye contact may lead to discomfort and may even carry sexual overtones.[3]

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[3] Some astronauts have reported that the swollen face in weightlessness, due to the headward fluid shift, creates a problem in communicating by eye contact.

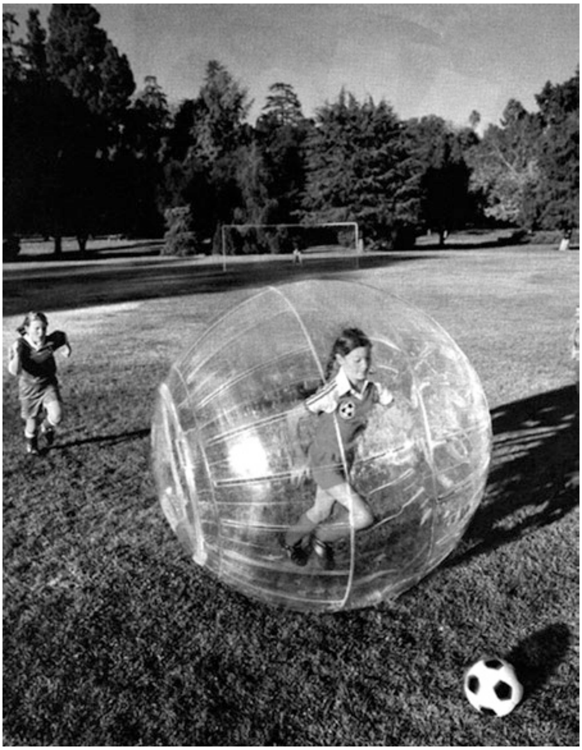

Figure 6.14. Each Person Has an Invisible Boundary Around His/Her Body into Which Other People May Not Come. (Source Unknown).

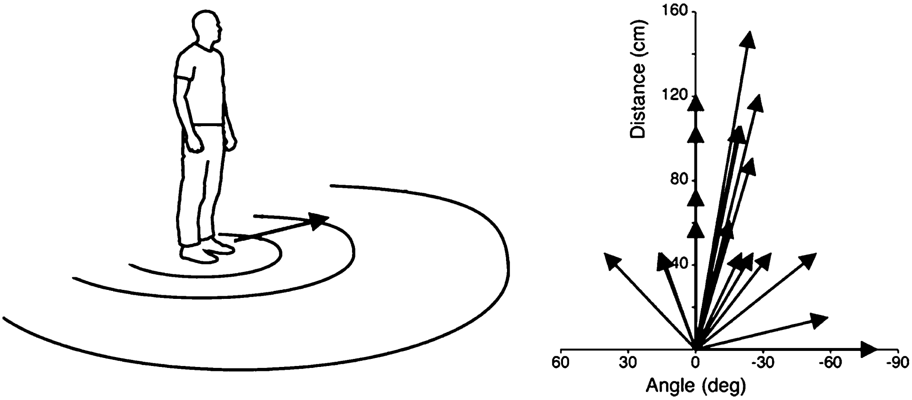

Figure 6.15. Mean Distance and Angle Between Two Individuals During a Seated Interview. Catherine Beaulieu, Julielynn Wong, and Linh Bui Compiled These Results During the ISU 2002 Summer Session Program, on a Population of 23 Students from 13 Different Countries.

When comparing the required personal distance in various environmental conditions, it was found that greater distances are required for personal space: (a) in small rooms versus large rooms; (b) inside locations versus outside locations; (c) in high-anxiety settings versus in low-anxiety settings; and (d) with people with whom you expect to be interacting over a long period of time versus a short interaction [Bishop, 1997]. Interestingly, all these factors (small rooms, inside, high anxiety setting, long interaction) are present during space missions. Consequently, the personal distance of the astronauts should increase in the conditions of a space mission. It would be interesting to actually measure the personal distances of crewmembers on board the ISS and compare for example these distances between astronauts and cosmonauts.

On the other hand, the dimensions of a spacecraft are necessarily small, and there is little to no privacy (Figure 6.16). Ground-based studies indicate that privacy only seems to alleviate anxiety and stress in short-duration missions. In long-duration missions with privacy, it was noted that even with access to another person in the group for conversation and social interaction, stress levels are higher [Taylor et al., 1968]. This also seems to be true for space missions. Indeed, issues of personal hygiene and housekeeping alone account for about 40% of incidents during space missions with U.S. only crews [Santy, 1994] (Figure 6.17).

It is well known that under crowded conditions, men and women react differently. Women tend to perceive small, crowded places as friendly and sociable, while men tend to respond to such environments as irritating and uncomfortable. Men are more likely to feel their personal space violated in crowded places and perceive a continuing challenge to patterns of male dominance. Thus, men respond with greater irritation and hostility to crowded conditions than do women. The interesting note is that mixed-gender groups tend to respond nearly as well to crowded circumstances as do groups of women only [Bishop, 1997].

Figure 6.16. Two Astronauts Looking at Earth from the Observatory Windows of the Space Shuttle. (Credit NASA).

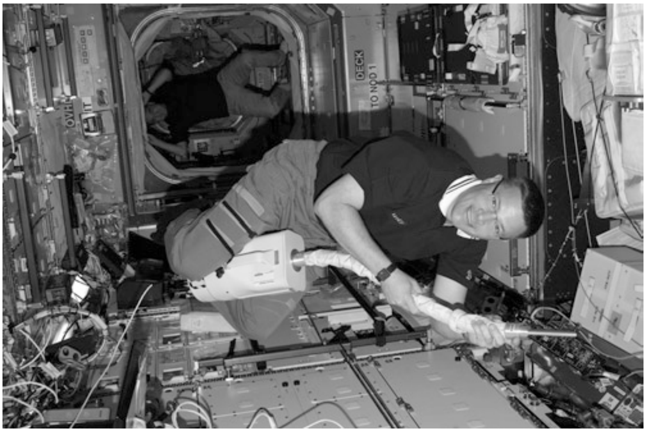

Figure 6.17. NASA Astronaut Douglas H. Wheelock Rides His Vacuum Cleaner Doing Housekeeping Chores in the ISS Destiny Lab. (Credit NASA).

6.3.1.2. Mixed gender issues

Women have performed equally or superior to male counterparts in Antarctic stations and underwater habitat studies [Connors et al., 1985]. Though there is little question about the competence of women to handle space missions, the total number of female astronauts and cosmonauts represents less than 20% that of male astronauts. Hopefully, the increasing number of women astronauts will translate into a large participation in the ISS and interplanetary missions. However, factors associated with long-duration missions may be affected by the presence of women on board.

Antarctic expeditions started including women in 1979, but many stations still refuse to allow women to winter-over. Nevertheless, the results of studies in analogs suggest that the presence of women exerts a positive influence and discourages certain behaviors that could lead to injury or group conflict, like drinking and fighting [Palinkas, 1991]. However, other studies found that the introduction of a female into a male group caused destabilizing effects [Harrison and Connors, 1984].

With the increasing duration of future missions, sexual tensions and prejudices may be forced to the surface creating friction and this could impact both crew cohesiveness and performance. The concern about an affair occurring on board the ISS is probably unwarranted. Even if it were to happen, the question will be what effect, if any, this new level of interaction will have on the performance of the crew. Helmreich et al. [1980] consider that more harm than good can come out of a policy that regulates the moral conduct of the space station crew. Such a policy will not make sexual desire go away, only perhaps frustrate it into another, more dangerous form. He suggests that the space agencies should take a “hands off” approach (no pun intended!) to this issue and see what happens.

Gender stereotyping by members of the crew can also have a destabilizing effect. There is some evidence that male astronauts and cosmonauts [Oberg, 1981] still hold on to outmoded views of women. These stereotypes should be avoided by having crewmembers work together on projects before a space mission to demonstrate each crewmember’s, not just the women’s, competence and technical proficiency.

6.3.1.3. Multi-cultural issues

Today the ISS, and tomorrow the exploratory missions, present the opportunity to have greater representation of different nationalities in space. This will bring problems that were not present in the more homogenous missions, which have occurred up to now. The space shuttle has had international crews and women crewmembers on a somewhat regular basis (Figure 6.18), but the short duration of these missions can not compare to the long-duration missions we will be facing in the future.

Culture refers to widely shared beliefs, expectancies and behavior of members of a group on an organizational, professional or national level. Besides personal space as already described, studies on pilot populations have shown significant national differences in attitudes, such as acceptance of hierarchical leadership and the necessity of adhering to rules and procedures. Another well-known cultural difference is time perception: for example, Anglo-Saxons typically emphasize schedules, appointments, segmentation, and promptness, whereas Middle East and Latin cultures are more flexible and feel more at ease with several things going on at once. Such differences obviously have the potential to cause problems in safety, performance, and interaction between crewmembers.

The lessons learned from the NASA-*Mir* program with multi-cultural crews illustrate the difficulties that can be encountered. Several U.S. astronauts have commented that under conditions of high stress such as during long-duration missions, cultural differences disrupted the harmony among the crew. They suffered from the facts that: (a) the language differences led to misunderstandings; (b) they were the sole members of a cultural group; (c) they had prolonged periods of no contact with English-speakers, even less with family; (d) they had very restricted food selection; and (e) they were

Figure 6.18. The Crew of Shuttle STS-51G (June 1985) Included Astronauts from the United States, France, and Saudi Arabia, Both Male and Female, with Military or Civilian Background. (Credit NASA).

not allowed to operate equipment. Some also complained they were treated as a guest rather than a working crewmember [Burrough, 1998].

Campbell [1985], in a review of cultural integration literature, identified a three-stage theory of adjustment to a new culture called the U-curve theory. The first stage of this theory is entry. In this stage the novelty of the environment precludes adjustment problems from manifesting themselves. The second stage is adjustment. In this stage the individual learns new ways of thinking and acting, and frustration with the environment is high. The third stage is adaptation. This stage sees the individuals reconcile their expectations with the reality of the situation.

It is expected that the adjustment of astronauts to the culture of a long-duration crew will be similar. The initial awe of being in space will give way to cultural reactions, which may include difficulties in understanding non-verbal cues, difficulties in adjusting to new work regimes, and technical language difficulties. For this reason training in each other's culture and lifestyle is an essential part of any long-duration, international space effort.

6.3.2. Selection issues

Crews are, in fact, small social systems shaped by multiple determinants, none of which, considered in isolation, can necessarily account for the variations in behavioral interactions or performance effectiveness.

Reviews of the literature on Antarctica expeditions focusing on their relevance to long-duration spaceflight have identified the leader as the single most important role in the isolated group [Stuster, 1996]. Leaders organize, direct, and coordinate followers. They also exert their influence to: (a) help the group maintain harmony and stability; (b) interpret the conditions that confront it; (c) set goals; and (d) meet challenges posed from outside. The most effective leader let crews do work with minimal interference, but recognize when group activity is needed and arrange that activity. Good leaders are also able to swing between autocratic, that is making decisions without soliciting subordinate's inputs, and participative, democratic styles of leadership as needed. Prescriptions for good leadership often dwell upon the selection and training of leaders. However, such prescriptions could also involve the selection and training of followers, and the structuring of the social settings and the group's tasks.

One potential source of conflict in today's space missions, as it is for analogs, is that the leader's right to exert his/her influence is conferred through appointment by a higher authority, not by the group itself. To counter-balance this, another key factor of long-duration missions is to have open communication among the crew and allow feedback channels. Communication is essential for it provides updated knowledge of other people's attitudes and views, which is necessary for social comparison processes and for conflict management. Also, as is evident from the ISEMSI experiment, miscommunication can contribute to interpersonal friction and conflict within the crew or between the crew and the ground personnel.

Another factor is to have clearly defined contingencies for achieving goals. Research findings are unambiguous in showing that a clear, engaging set of objectives is a powerful means for orienting members toward achieving overall organizational goals. Group goals encourage people to coordinate their activities for mutual gain, and hence are likely to affect the tone of interpersonal relations within the group. However, crewmembers must feel personally committed to these goals; it will not suffice to simply impose them from above. In addition, for long-duration missions, means must be found to maintain astronauts' interest in distant goals over prolonged periods of time. It may thus be desirable to establish a number of interim goals, which can be pursued and savored.

Finally, groups of more than two must have boundary role persons who act to interpret interests and concerns of all sides to allow activity to progress smoothly. Boundary role persons serve as agents for purposes of bargaining and negotiation. These boundary persons, with the help of the leader (see above) and the authority in Mission Control, should manage the inevitable problems and disputes that occur in real time and that threaten the overall integrity of the group, and arrange cooperative ventures with equitable outcomes for both sides [Connors et al., 1985].

6.3.2.1. Compatibility

In the context of multinational missions, one of the more important challenges is to ensure that the individuals are compatible and can work together effectively. Crewmembers may be considered compatible in that each member demonstrates qualities and behaviors that other crewmembers consider desirable and appropriate. This is challenging in the space program because individuals may have very different educational backgrounds. For example, scientists prefer their autonomy and tend to not interact and not to work well in a hierarchical command structure. On the other hand, pilot-astronauts often have military backgrounds, which lead them to prefer a more ordered command structure.

Evaluation of compatibility might be based on the results from psychological performance tests and personality questionnaires. Another more behavior-oriented approach, which has been developed in the context of industrial applications, includes the combination of a variety of behavioral exercises like role-plays, group discussions, and group exercises. The objective is to select individuals who demonstrate capabilities for effective team functioning and problem solving (Figure 6.19).

The Soviet/Russian space program has spent considerable effort developing methods to assess interpersonal compatibility for long-duration missions. These methods include attitude assessments, psycho-physiological tests, and specific group exercises. The Russian psychologists believe that biorhythms are useful in selecting specific cosmonauts for space missions. For example, when the crew works together on a complex task during a training session, they monitor their pulse. As soon as the crewmembers start helping each other their pulses synchronize to some extent. It is believed that the higher the biorhythmicity, the greater the compatibility [Bluth and Helpie, 1987] cited by Santy, 1997]. However, these compatibility tests have not been validated.

6.3.2.2. Crew composition

Obviously, the larger the group, the more chances of interpersonal conflict. In fact, it was found that larger groups react better to confinement situations. Irritations in these groups are not directed at other group members but at "things or non-personal aspects of the situation" [Smith and Haythorn, 1972]. Obviously, for space missions, especially interplanetary, the ultimate decision will be made upon propulsion considerations after calculating the total weight needed in terms of life support system mass

Figure 6.19. Individuals May Find Themselves Isolated as a Result of Poor Leadership or Not Fitting into the Group. (Source Unknown).

per person. However, one rule of thumb is that crew size and heterogeneity must be as small as possible, because the complexity of interpersonal interaction increases with crew size and heterogeneity. On the other hand, increasing crew size increases the number of possible social relationships and, among other things, options for social stimulation and developing friendships, which are favorable factors for group cohesiveness. An odd number of crewmembers is recommended over an even number to prevent the development of two equalized groups, which might hinder democratic problem solving.

A very important consideration is related to the occupational role of the crew. Traditionally, all crews in human space exploration have included one or more pilots. Some of the designers of human missions [Zubrin, 1999] state that given the demonstrated ability of guiding unmanned spacecraft safely to the surface of Mars, taking a pilot would be an unnecessary waste of resources. They argue that a scientist trained minimally to override the automatic system in case of malfunction would be enough. All schools of thought consider it essential to take along a medical doctor to cope with medical problems during the trip. Should a mechanic be included in the mission to repair malfunctioning systems? How many scientists are necessary during a pioneer exploratory mission? Or should just extremely fit individuals integrate the crew on this occasion?

One sure thing is that the role of mission commander should belong to the most qualified individual in the crew, whether a pilot, engineer or scientist, that is one whose leadership style encourages group dynamics, group performance, and morale. Consequently, the role of mission commander will not automatically fall on a pilot, as it has been the case for all space missions so far, with the exception of a couple of ISS increments.

Of prime importance are the motivational issues raised by the prospect of long-duration space occupancy. Motivation plays a critical role in maintaining individual performances and amicable social interactions over extended intervals of isolation and confinement. Duration and expected duration of missions also seem to be an important variable to consider. Taylor et al. [1968] found that when a group expects a long-duration mission there is more stress evident than a group expecting a short-duration mission.

For collective operations, the right people, well trained and properly configured (that is, with the right mix of skills, personal characteristics, task requirements, and work setting) are essential. However, this will ultimately bring differences in education, culture, and age, which may also contribute to issues in group cohesiveness and performance.

Even though there has been a significant advance of women astronauts lately, including several female shuttle pilots, again in general all crews have been predominantly male. Long-duration interplanetary missions raise unique considerations. Having an all-male crew for such a long time is at least doubtful. Married couples are definitely a possibility, and mixed crews with non-married members are also being considered. But what if two crewmembers fall in love with each other or altercate due to their relationship? What about the other crewmembers that are "left out"? Men are believed to be physically stronger, but on the other hand women are more resilient psychologically. The fact that there is no quick way to get the crew back adds to the need to consider all possible alternatives. Experiments aimed at the understanding of the psychological and social consequences of sexuality and mixed-gender groups are also needed.

6.3.2.3. External factors

It is interesting to note that there are many known factors that contribute to group cohesion and performance or to group fission (Table 6.7). For example, during long-duration missions on board *Mir*, several crewmembers reported that the arrival of an international visiting crew, staying in the station for a period of 1 week, helped to neutralize tensions among the crew. Cosmonauts on extended flights had letters and

Table 6.7. Factors that Impact Group Fusion and Group Fission.

Factors that Impact Group Fusion	Factors that Impact Group Fission
• Emergencies: when people are forced to work together for common survival • Arrival of outsiders (e.g., replacements, new personnel) • Resentment towards outsiders (e.g., mission control, authorities) • Leadership: promotes performance and minimizes conflicts • Social events (e.g., surprises, parties, holidays) • Group rituals and habits	• Power and status (e.g., leader/followers) • Differences in work demands (e.g., shifts) • Differences in responsibility (e.g., pilots/non-pilots) • Differences in motivation • Differences in personal values • Leadership (e.g., authoritarian/participative)

Figure 6.20. As a Group Ritual, Shuttle Crew-Members Play Poker on the Launch Day. They Leave the Crew Quarters only After the Commander Wins. (Credit Douglas Hamilton).

presents from home, along with special foods and fresh milk, delivered to them in space. They were also surprised by small, but apparently delightful toys, novelties, etc. The unexpected undoubtedly plays a very large role in what we see as the fullness of experience. Parties and group rituals (Figure 6.20) also help maintain morale and group interaction.

It is interesting to note that leadership belongs to both categories. That is, good leadership helps group fusion, but bad leadership can be at the origin of group fission. Obviously, the ability to be a team-leader or a team-follower should be part of the "select-in" criteria. But how do we define these criteria and others, and most importantly, how do we validate them? We will review these issues in the following section.

6.4. Crew behavior and performance

So far, the psychological selection of astronauts has focused on selecting-out candidates with psychopathological disorders. In contrast to these well established "select-out" criteria, "select-in" criteria need to be developed in relation to specific aspects of the mission, such as mission objectives, mission duration and crew composition. Once determined, the "select-in" characteristics require validation against in-flight performance measures, and need to be explored in a mission-specific manner [Sandal et al., 1996].

To date, the absence of formal criteria for astronaut performance and the limited research opportunities have made it very difficult to evaluate the efficiency of crew selection strategies. Such evaluation also requires that select-in criteria must not be used in the initial selection until they have been found to predict astronaut performance. One potential bias in validating selection criteria for astronauts and cosmonauts who have already gone through a formal selection process is related to the restriction of range in personality scores, as seen in the MMPI.

The behavioral health information derived from psychological testing evaluations into the final selection process of astronaut candidates (see Chapter 7, Section 7.2.3) is of limited use because the candidates have not yet successfully completed the training and evaluation period prior to becoming an astronaut. Additionally, it can take up to 8 years from the time a space agency hires an astronaut candidate to when the astronaut returns from his or her first long-duration mission. Therefore, to determine whether the behavioral health information collected during the hiring process is useful, the performance of the new astronauts must be observed for a period significantly longer than the year that has elapsed since their hiring.

Another issue is a how to evaluate astronaut performance. Optimally, this evaluation should be performed during training and actual space missions. Performance would then result in a re-evaluation of crew composition. This assessment is likely to increase tension between crewmembers, management, and mission controllers. For example, controllers in Mission Control in Russia were systematically keeping track of the number of errors performed by the crew on board *Mir* or by the ground personnel (Figure 6.21). Although useful for determining a change in performance throughout a mission, some astronauts might see such evaluations, as well as the psychologists who perform them, as possible threats because they fear being grounded or removed from a mission.

In recent years, however, various techniques of performance analysis have been developed. Test batteries consisting of one or a number of discrete individual tasks to measure such factors as vigilance, reaction time, tracking, limb steadiness, coordination,

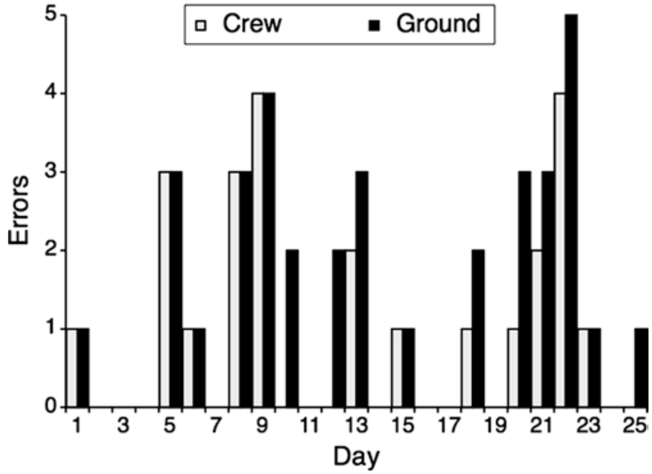

Figure 6.21. Number of Errors Made by the Crew and Ground Personnel During the Course of a 28-Day Mir Mission. (Oleg Atkov, Personal Communication).

and perceptual speed have been used during space missions. Comparison between the times required to perform the same task in weightlessness compared to ground, for example, proved useful to determine “work-efficiency ratios”, i.e., the total estimated time divided by the total number of hours available to work [Kubis et al., 1977].

The evaluation by peers proved to be an effective tool to assess both technical skills (job performance), as well as the ability of an individual to live and work with others (group living). In this type of evaluation, one crewmember is asked, for example, the following questions: “Name the five best crewmembers,” “Name the five worst crewmembers,” and “If you can’t go on a mission, who should replace you?” Using this technique in analogs, it was found that veterans of isolated and confined situations generally picked an effective crew if given a large applicant pool and time to conduct thorough interviews [Natani, 1980]. Preliminary results of peer evaluation performed by astronauts on each other during training on nine dimensions of performance (e.g., job competence, leadership, teamwork, group living, personality, communication skills) showed remarkable agreement with the ratings done by the astronauts supervisors and decision-makers [Rose et al., 1993].[4]

However, more objective and reliable methods for observing and recording the effect of space stresses upon complex performance processes must be developed. To date, no actual data have been published on astronaut performance. As Patricia Santy [1994, p. 152] wrote: “Such data are essential if behavioral scientists are to understand individual and group psychological factors as they relate to individual and crew performance in space. Without objective data to clarify these relationships, even the best guesses about what psychological criteria are critical in selecting astronauts remain only guesses.”

6.5. Psychological training and support

Let’s assume the selection process picked out the best individuals, and that the mission director, with the help of the psychologists, then picked out the best crew for a given, long-duration mission. The hazards of such a mission, and the unknown implications of stress on human behavior under stress, will undoubtedly result in group-interaction issues. Psychological training is required for preparing the crew to react to these situations. When conflicts arise, psychological support from the ground also enters into play.

6.5.1. Training

One rule of thumb is that group dynamics and group problem-solving techniques should be dealt with prior to the mission. Astronauts not only must be technically proficient in their area; they must also be aware of interpersonal dynamics and intercultural differences. Both the crew and their ground control personnel should be trained together preflight to use interactive techniques.

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[4] Mike Collins [1990] wrote: “As I used to tell John Young before *Gemini-10*, I was happy I was making my first spaceflight with him, but I wanted to fly so badly I would have gone up with a kangaroo!”.

Optimally, once a crew has been selected for a certain mission, a training oriented to that specific crew should focus on the following issues: (a) support of a team-building process within the crew that establishes a stable crew structure, develops common behavioral norms, and identifies of common mission goals; and (b) "anticipatory problem-solving" that makes the crewmembers aware of how to deal with the specific psychological problems that are most likely to arise during the course of a mission.

Three phases of training can then be identified: (a) a phase of awareness when the crew learn the basics of group dynamics and interpersonal relations and their effects on performance; (b) the group receives feedback on their newly-learned concepts by putting them into practice in role-playing and simulation exercises; and (c) these concepts are reinforced regularly to prevent backsliding [Nicholas and Foushee, 1990].

Using this type of training, issues that once caused tension between crewmembers and outside monitoring personnel have been ameliorated through "bull sessions", both in simulations and during actual space missions [Sandal, 2001]. Experts in group-dynamics who work with and are trusted by the crews are available on the ground to assist in conducting such sessions during the mission if the need arises [Palinkas et al., 2000b].

Work tasks and schedules might be planned to minimize social and psychological issues, and to ensure and maximize individual and crew performance. Future crews should also be consulted on habitat function and design, including clothing, food, layout, decor, waste management, personal hygiene, privacy, tool and equipment design, and computer hardware and software.

Psychological training is of prime importance for Russian crews. Cosmonauts are involved from the moment of their selection in a series of psychological training processes designed to prevent the occurrence of severe adjustment problems for a space mission. Cosmonauts are tested in simulators and in real-world stress situations such as parachute jumping and remote survival missions (Figure 6.22). These missions are planned so that they are as real and dangerous as possible. Roscosmos says that this type of training develops self-confidence, discipline, and steadiness during an unexpected or emergency situation.[5] Training in stressful situations is also intended to make sure the crew works together as a harmonious, well-coordinated unit.

6.5.2. Support

6.5.2.1. Soviet and Russian experience

The Soviet/Russian experience in space is extraordinary from a psychological point-of-view. The level of support that cosmonauts receive from start to post-finish is undoubtedly a factor in the success of their long-duration mission program. On the other hand, the U.S. psychological support has been minimal until the problems encountered by the U.S. astronauts during the NASA-*Mir* program (see Table 6.2).

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[5] Every cosmonaut makes day and night jumps from different altitudes, while performing tasks that become successively more difficult. For example, they may be required to carry on a radio conversation, identifying locations on the ground, *before* opening their parachute. This interest for parachuting can be traced back to Yuri Gagarin's day where the cosmonauts bailed out of the *Vostok* before landing [cited by Collins, 1990].

Figure 6.22. Astronauts Conduct an Emergency Egress Drill During Land Survival Training in the Wilderness. As Part of Generalized Stress Training, Crews Are Deposited in Extremely Hostile Environments and Survive only by Their Own Wits and Endurance. There Are No Rescue Teams to Help Out if Trainees Go into Trouble. (Credit NASA).

The psycho-social support program of the Russian Space Agency may not be used exactly as is by the other partners of the ISS because of the culture gap, but it is definitely a starting point.

From the beginning of training to postflight, cosmonauts are constantly monitored for stress and psychological symptomology. They are given a battery of psychological tests, psychiatric interviews, and are thoroughly tested for compatibility. The Psychological Support Group, a specialized cadre of psychologists, military, and civilian space personnel conduct the testing and monitoring. Drugs to regulate behavior, biofeedback, self-hypnosis, and relaxation strategies are all used in support of this effort [Kanas, 1991].

During the flight, there is an ongoing monitoring of voice communications by psychologists in Mission Control to assess crew tension, cohesion and morale, and to look for potential interpersonal problems. An analysis of voice patterns of the cosmonauts is first performed on Earth during both stressful and non-stressful activities. These are compared to vocal patterns taken on the space station to check for stress. Two-way video observations also are used to interpret facial expressions and body language for signs of stress.

In addition, cosmonauts are routinely sent personal items and different recreational materials via *Progress* re-supply capsules. They also receive constant reminders of Earth via news, books, audio, and video material,[6] and have frequent contact with family and friends over private communication links (Figure 6.23).

The psychological support does not end with the flight, either. Returning cosmonauts are helped to adjust to new fame and to reintegrate with their families after such a long absence. This is achieved through counseling, drugs, and debriefings as required [Kanas, 1991].

6.5.2.2. ISS psychological support

The NASA Psychological Services Group was established in 1994 to support the stay of the U.S. astronauts on board *Mir* during the NASA-*Mir* program. Prior to establishing this, NASA had focused far too little attention on psychological problems and their ramifications. This is partly due to the fact that there had been little need because of the short-duration of the space missions and partly because of a “technology and hardware first” attitude [Santy, 1994]. This has been changing recently, and NASA is beginning to realize the implications of an astronaut succumbing to the stresses of her/his environment. The NASA Psychological Services Group is composed of behavioral scientists and psychologists, who learned significantly from the analog environments,

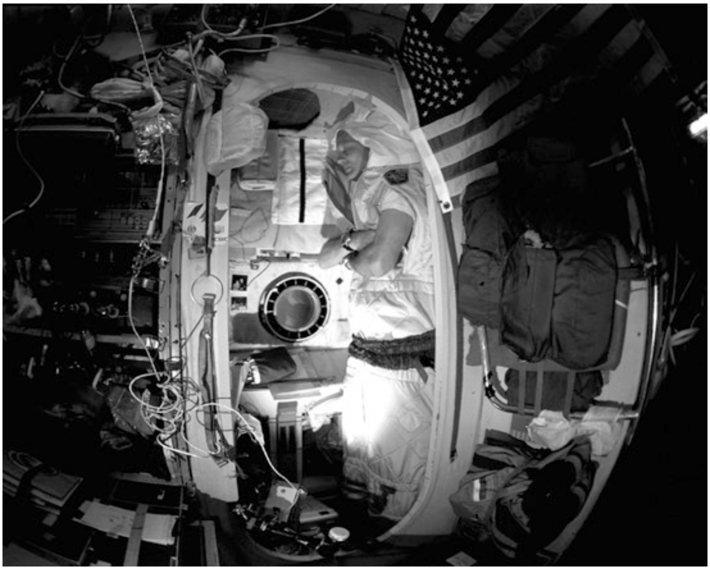

Figure 6.23. NASA Astronaut Norm Thagard in His Sleeping Compartment on Board Mir. (Credit NASA).

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[6] After 6 months spent on board the ISS, the *Expedition-6* crewmembers made an interesting description of their first sensations after their *Soyuz* landing. “When the hatch first cracked open, the smells of spring on the steppes and the sounds of birds overwhelmed us. Real earthy smells because we’d stirred up a fair amount of dirt when we landed and then we rolled and were dragged a bit. So you had this fresh dirt smell, which was just a beautiful smell… and it had a little bit of crushed grass in it, too. Then the next thing that hit us were all the birds chirping… It was just music to our ears.”

from the many years of experience of the Russian psychologists, and from sharing lessons and experience with other International Partners (CSA, ESA, JAXA).

The arrest of a NASA astronaut in February 2007 for personal actions that were the subject of criminal charges led to improvements in the behavioral health care provided to astronauts and their dependents. Since this incident, a 30-min behavioral health assessment is now conducted in conjunction with each astronaut's annual medical flight physicals. Behavioral medicine flight assessments are also now performed on crewmembers before they leave on and right after they return from a space mission.

Preflight psychological support begins when crewmembers deploy for training in Star City. Once there, tasks include advocating for improved conditions and resources, assisting with family contacts, and organizing off-hours recreation. This help is also directed toward all support personnel that follow the crewmembers with deployment.

The group is also involved in "vehicle" issues that could later affect in-flight psychological support, such as habitability and stowage, acoustics and vibration, food variety and storage, and crew quarters. Similarly, it is involved in "human" issues, such as the work and rest schedules, language training, and culture training. Crewmembers are also familiarized with potential in-flight psycho-sociological issues. Immediate family is involved in these trainings, and informal meetings serve in the preparation of off-hours onboard activities by selecting movies, books, and hobbies of interest for each crewmember (Figure 6.24).

A Family Support Office has also been created, which includes representatives from the Psychological Services Group, the Astronaut Office, and the Astronaut Spouses Group. This structure has a critical role for supporting families during all phases of a mission, and serves as a liaison role with the space agency. Through this organization, the space agency maintains regular contact with family (providing for example the assistance of a family member of another astronaut, or "escort"), and provides information about the mission, especially contingencies.

Figure 6.24. U.S. Astronaut Steven Robinson Is Relaxing While Playing Guitar and Enjoying the View from the Cupola of the ISS. (Credit NASA).

In-flight monitoring of onboard activities by the Psychological Service Group ensures that there is a balanced regime of meaningful work and rest. Monitoring of the astronauts includes a questionnaire on mood, sleep and stress, and countermeasure usage and effectiveness. There are daily private communications between crewmembers and flight surgeons and, less frequently, with psychological support personnel. Some cognitive assessment methods, and well as behavioral and fatigue assessment tools are being developed to look for potential interpersonal problems.

In-flight support activities include surprise presents and favorite foods sent up via *Progress* and the shuttle, two-way communication with family and friends on the ground via private audio-video links, special family conferences on holidays (e.g., birthdays, Mother's Day), communications with friends, scientists, actors, and artists, audio and video news and sports news, e-mail,[7] instant messaging, social networking, amateur radio communication, and onboard recreational software and audio-video material for leisure time use. A computer-based family picture album of spouses, friends, and co-workers is also proposed.

After the flight, debriefings are implemented with both the crewmembers and their family to help them readjust to their life on Earth.[8] These meetings are also used to assess the overall psychological health of the individuals and as a countermeasure for addressing residual intra-crew, crew-family, and ground crew tensions that may develop during long-duration missions. The other objective of these meetings is to assess the practical value of the current psychological preparation and support, and to obtain recommendations for improving the psychological support for following crews [Ark and Curtis, 1999] (Figure 6.25).

6.5.2.3. Unsolved issues

Despite their experience of long-duration missions, and the attention given to selection of cosmonauts, psychological training and support, numerous reviewers have pointed out that cosmonauts have faced periods of depression [Kanas, 1991]. For example, Cosmonaut Valentin Lebedev [1988], after 116 spent in orbit, wrote the following depressed thoughts in his diary: "Humming to myself, I float through the [*Salyut*] station. […] Is it possible that some day I'll be back on Earth among my loved ones, and everything will be all right?" This example shows that there are serious psychological and social disturbances during long-duration spaceflight. No psychological selection strategy by itself will exclude that possibility.

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[7] Amazingly, even though crewmembers of the ISS live and work so close together, a lot of their real communication takes the form of written words. In the information age and with computers at each work station, astronauts and cosmonauts are communicating between themselves and others more via e-mail and instant messaging that verbally [Robert Thirsk, personal communication, 2009]. This is good training because during the mission to Mars, communication with the ground using e-mail will be the least affected by the 40-min delay.

[8] Susan Helms, a crewmember of the ISS *Expedition-2,* said: "Before I went up on the ISS for 6.5 months, I moved out of my place, put all my possessions in storage, and moved into the astronauts crew quarters earlier than most people do. I didn't want telephone or credit card bills, or anything except a bank account where my paycheck could go. I figured if I didn't have a home back here to worry about, the ISS could become my home. (…) I wanted it to be like a military deployment, like Navy guys who go out on a ship for 6 months and put all their stuff in storage."

Figure 6.25. At the NASA Kennedy Space Center, the STS-133 Crew Takes a Break from the Rigors of a Simulated Launch Countdown to Have a Little Fun Hamming it up. (Credit NASA).

Another source of concern is that we don't know what is going to happen when astronauts embark on a 3-year trip to Mars or another planet. The isolation during such a mission is unique, because even the Earth will not be visible to the crew (see Figure 6.3) and there will be long delays in communication. Crewmembers will need to deal with psychiatric problems themselves with no possibility of evacuating an affected individual. One thing that we know, or should know, is that the future of space exploration will require increased input from the psychological and social science community.

Careful attention to selection, training, and organizational functions should permit small groups of individuals to live and work effectively in space for continuous periods of several months or years. But there are enormous gaps in our understanding of how the multiple, complex behavioral factors operate independently to influence the behavior of individuals and groups. It is therefore necessary to continue the research in this area, as recommended in the report by the National Research Council entitled *A Strategy for Research in Space Biology and Medicine in the New Century* [1998], and more recently, in the NASA Human Research Roadmap for exploration missions (see Chapter 7, Table 7.1).

It will be also necessary to develop more effective countermeasures to address the individual, group, and cultural issues involved in these space missions. In particular, the following countermeasures need to be addressed further:

(a) Maintaining the presence of behavior and performance specialists through all phases of space mission design.
(b) Selecting full mission crews and critical ground personnel as a team,
(c) Training the astronauts in psychological method.

(d) Embedding tests of cognitive, emotional and behavioral performance in functioning mission hardware and experiments.
(e) Greater use of simulators for training on board the mission.
(f) Further development of self-report tools like diaries, personal logs, and computer files.
(g) Developing virtual environments and telescience to address behavior and performance aspects of missions.
(h) Using ground-based analogs and simulators for selection and training.
(i) Further training of mission and ground crews together.

Behavioral and social problems have been regarded to date as obstacles or "show stoppers" to long-duration space missions. Adequate psychological selection, training, and support can minimize these problems. Some research is needed, however, because many factors involved in personal and group dynamics in a hostile environment are still unknown. Even more important from a life sciences perspective, it seems likely that entirely new principles of human interaction and group dynamics will emerge as a result of such research to ensure effective human behavior in space environments and its analogs.

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Chapter 7

Operational Space Medicine

Crew health care through all phases of spaceflight is a further assurance measure for mission success. Flight surgeons shepherd their assigned crewmembers through all mission phases, including training, medical exams, pre-launch suit-up, and post-landing recovery. These doctors are so essential that they are always first on scene for landing. If crewmembers were not mentally and physically healthy, their nominal and emergency interactions with the vehicle might be fatally compromised.

Despite careful screening, extensive training, and aggressive countermeasures against the physiological challenges encountered during spaceflight, incidents of ambulatory illness and medical emergencies are a certainty for both short- and long-duration space missions. In this chapter, strategies that evaluate the probability of medical events as well as the medical hardware, procedures, and physician and surgeon resources needed to mitigate them are explored. These risk mitigation strategies are used as the basis for design of health care procedures and facilities in space (Figure 7.1).

7.1. Space medicine: what is it?

As humans establish a permanent presence in space, whether it is on a space station or on planetary bodies, it will be imperative that health care be provided to workers, scientists, and astronauts. The required medical facilities, procedures, and expertise needed to treat these crewmembers are unique to the constraints and stresses of space (Figure 7.2), and to the physiological changes described in the preceding chapters.

One essential aspect of a health maintenance facility is its interrelation to other life sciences activities. Experience in the development of modern medicine over the past century has shown a strong correlation between optimal medical care and scientific investigation. This concept also applies to space medicine. Doing so positively affects not only the quality of care but also the quality of research in space physiology.

As in any other medical field on Earth, space medicine involves both proactive and reactive care of humans to optimize physical, physiological, and mental well being within the unique constraints of an extreme environment. Unlike on the ground, the first priority is to support the mission. Ensuring the health and safety of the crewmembers is, in a way, a secondary objective; but it is necessary for fulfilling the first. To put this principle in context, one must remember that if the primary goal were to keep a select group of individuals as healthy and safe as possible, they would be kept safely on the ground. Spaceflight is inherently risky. The closest analog to space medicine

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Figure 7.1. The Roles of Nurse Christine Chapel (Majel Barrett) and Dr. Leonard "Bones" McCoy (DeForest Kelley) Were a Vital Part of the Success of the Original Star Trek Series. (Credit Paramount Pictures).

Figure 7.2. One Astronaut Performs a Dental Examination on a Crewmate During a Skylab Mission. (Credit NASA).

would be aviation medicine as practiced by the military flight surgeon. Again, mission assurance is the first priority of all operational support [Barratt, 1995].

Therefore, space medicine is different from space physiology: many of the physiological changes to weightlessness are simply adaptive, not necessarily pathologic. Certainly there are some adaptive processes, such as bone demineralization, as well as environmental exposures, such as radiation, that may be considered pathologic, because without countermeasures they may eventually compromise health during a mission. Also, many of the adaptive responses to weightlessness, such as cardiovascular, muscular, and neuro-sensory deconditioning, become maladaptive on return to normal gravity. It has often been said that if one did not have to return to Earth, low Earth orbit would be a great place! Finally, even a non-maladaptive and non-pathologic change may alter the way in which a given illness might present and be managed, causing space medicine practitioners to creatively reassess their diagnostic and therapeutic processes [Barratt, 1995].

7.1.1. Objectives

"Il vaut mieux prévenir que guérir" ("an ounce of prevention is worth a pound of cure"). The wisdom of this adage is profound with regard to planning activities in the hostile, isolated environment of spaceflight [Holland and Marsh 1994]. Selection of the best-fit individuals is the first step of a health maintenance program. The medical requirements for the selection of astronauts will be detailed in subsequent sections of this chapter.

Once the personnel have been selected, the second component is prevention, that is, the maintenance of physical and mental health. Considerations include physiological status monitoring, nutrition and stress management, safe waste management, hygiene, medical record keeping, environmental monitoring, exercise devices and medical research facilities, assurance of a suitable sleep environment, recreation and entertainment, social support aids, and communication with family and friends.

When selection and prevention are unable to mitigate the deleterious effects of spaceflight, countermeasures are used. Countermeasures for motion sickness, post-flight orthostatic intolerance, bone demineralization and muscle atrophy, and psychological issues have been described in the previous chapters. When selection, prevention, and countermeasures are unable to prevent or mitigate illness or injury, then treatment is used.

In addition to the above, rehabilitation should be considered so as to enhance optimal crew productivity and return to operational capability. Consequently, the types of care that a health maintenance facility must provide on a minimal basis fall into these five categories: selection, prevention, countermeasures, treatment of disease and injury, and rehabilitation.[1]

7.1.2. Risk assessment

Risks are the conditional probability of the occurrence of an adverse event from exposure to the space environment. Such exposure can result in dysfunctional physiological or behavioral adaptation that could lead to increased injuries, illness, loss of life, or loss of mission objectives. Injury is the most likely debilitating or potentially

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[1] Countermeasures and rehabilitation have already been covered in previous chapters, in particular regarding the bone and muscle systems (see Chapter 5, Section 5.6) and the psychological issues (see Chapter 6, Section 6.5).

life-threatening process in young, healthy individuals. There are, however, certain medical and surgical emergencies that affect even young people, such as appendicitis, perforated ulcer, renal stones, and subarachnoid hemorrhage. The Polaris submarine experience from 1963 to 1973 revealed 269 surgical cases in 7,650,000 man-days. There have been approximately 21 cases of appendicitis, 17 of which were successfully treated with antibiotics, and four of which resulted in death [Hamilton, 2010].

When reviewing the medical experience of the U.S. Navy, the Antarctic winter-over statistics, and the Soviet/Russian space experience on long-duration missions, it can be reasonably expected that a critical medical event requiring surgery (e.g., appendectomy) in a permanent space station of six astronauts would occur every 14 years [Hamilton, 2010]. Given the fact that there has been a quasi-permanent human presence in space since 1986, first on *Mir* and then on the ISS (Figure 7.3), surgery in space could soon be a necessity. Surgery is the only alternative when antibiotics fail and is the primary treatment on Earth in a non-remote setting. If the health maintenance facility is incapable of providing surgical care, the workers and scientists, as well as the public must be aware of the possible consequences.

The goal then is to prevent surgeries by detecting the presence of potential diseases. However, most clinical tests today are used to screen pathology in patients. These tests have a poor ability for detecting disease in very healthy individuals. In addition, there are no tests that are designed to select-out the occurrence of pathology

Figure 7.3. In April 2010, Seven Crewmembers of the STS-131 Shuttle Mission Joined the Six Crewmembers of ISS Expedition-23. They Gathered for a Group Portrait in the Kibo Laboratory of the ISS. This Was the Largest Number of People in Space Ever. (Credit NASA).

over the next 3 years.[2] This is a serious problem for selecting a crew for a Mars Mission [Osborn, 1998].

In 2001, the Institute of Medicine of the National Academy of Sciences had published a report on the medical risks of long missions. The number one conclusion by the institute was sobering: “Space travel is inherently hazardous. The risks to human health on long-duration missions beyond low Earth orbit, if not solved, represent the greatest challenge to human exploration of deep space,” the report said. Furthermore, the development of solutions “is complicated by the lack of a full understanding of the nature of the risks and their fundamental causes.”

The authors of this report, a panel of 14 medical doctors, clinical psychologists, and health care specialists, were well aware that during such missions, all risks could not be predicted. They pointed out: “The successes of short-duration space missions may have led to misunderstanding of the true risks of space travel by the public. Public understanding is necessary both for support of long-duration missions and in the event of a catastrophe.” The public must be prepared for the possibility that “all countermeasures may tragically fail, that a crew may not return from a prolonged mission, or that individuals may not be able to function physically or mentally upon their return”, the study group warned.[3]

In 2005, a Human Research Program (HRP) was established at NASA to focus on investigating and mitigating the highest risks to astronaut health and performance in support of exploration missions. The goal of the HRP is to provide human health and performance countermeasures, knowledge, technologies, and tools to enable safe, reliable, and productive human space exploration. The specific objectives of the HRP are: (a) to mitigate the highest risks to crew health and performance (Table 7.1); (b) to improve human spaceflight medical, environmental and human factors standards; (c) to reduce human systems resource requirements (mass, volume, power, data); and (d) to ensure effective human-system integration across exploration mission systems.

7.2. Astronaut selection and training

7.2.1. Crew position

The first astronauts and cosmonauts were jet aircraft pilots. Physical and psychological screenings were intense, due to the hazardous nature of pioneering missions. Then the prime emphasis shifted away from flight experience toward superior academic qualifications. Some applicants were invited on the basis of their educational background alone. These were the scientist astronauts, so called because the applicants

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[2] As Dr. Arnauld Nicogossian, NASA’s director of life sciences, has pointed out: “Never before has medicine been called upon to certify that an individual will be healthy enough to perform for three years following the examination” [cited by Collins, 1990].

[3] The *Columbia* disaster seems to reveal a trend in the public acceptance of space failures. The grief and sadness were immense at the news of the tragedy. However, compared with the *Challenger* tragedy that occurred 17 years earlier, which also took the lives of seven astronauts, much less interest was given to the investigation by the media and the public during the weeks that followed.

Table 7.1. List of the 27 Highest Risks to Human Health and Performance for Human Space Exploration Identified in the NASA Human Research Roadmap. Risks Include Physiological Effects from Radiation, Hypogravity, and Planetary Environments, as well as Unique Challenges in Medical Treatment, Human Factors, and Behavioral Health Support. Without Results of Studies Addressing These Issues, NASA Will Face Unknown and Unacceptable Risks for Mission Success and Post-mission Crew Health. Source: http://humanresearchroadmap.nasa.gov/.

Risk Factor of Inadequate Nutrition

Risk of Acute and Late Central Nervous System Effects from Radiation Exposure

Risk of Acute Radiation Syndromes Due to Solar Particle Events

Risk of Adverse Behavioral Conditions and Psychiatric Disorders

Risk of Adverse Health Effects Due to Alterations in Host-Microorganism Interactions

Risk of Adverse Health Effects from Lunar Dust Exposure

Risk of Bone Fracture

Risk of Cardiac Rhythm Problems

Risk of Compromised EVA Crew Health and Performance Due to Inadequate EVA Suit Systems

Risk of Crew Adverse Health Event Due to Altered Immune Response

Risk of Degenerative Tissue Or Other Health Effects From Radiation Exposure

Risk of Early Onset Osteoporosis Due To Spaceflight

Risk of Error Due to Inadequate Information

Risk of Errors Due to Poor Task Design

Risk of Impaired Control of Spacecraft, Associated Systems and Immediate Vehicle Egress Due to Vestibular/Sensorimotor Alterations Associated with Space Flight

Risk of Impaired Performance Due to Reduced Muscle Mass, Strength and Endurance

Risk of Inability to Adequately Recognize or Treat an Ill or Injured Crewmember

Risk of Intervertebral Disk Damage

Risk of Orthostatic Intolerance During Re-Exposure to Gravity

Risk of Performance Decrement and Crew Illness Due to an Inadequate Food System

Risk of Performance Decrements Due to Inadequate Cooperation, Coordination, Communication, and Psychosocial Adaptation within a Team

Risk of Performance Errors Due to Fatigue Resulting from Sleep Loss,

Circadian Desynchronization, Extended Wakefulness, and Work Overload

Risk of Radiation Carcinogenesis

Risk of Reduced Physical Performance Capabilities Due to Reduced Aerobic Capacity

Risk of Reduced Safety and Efficiency Due to an Inadequately Designed Vehicle, Environment, Tools or Equipment

Risk of Renal Stone Formation

Risk of Therapeutic Failure Due to Ineffectiveness of Medication

who met minimum requirements had a doctorate or equivalent experience in the natural sciences, medicine, or engineering.

Since the first selection of seven U.S. astronauts for its Mercury program, NASA has selected 20 more groups of astronauts. The first astronauts were military pilots.

The first group of astronaut candidates for the space shuttle program was selected in January 1978 and included 20 scientists and 15 pilots. Six of the 35 were women. Since then, candidates were selected as needed, normally every 2 years. The backgrounds of NASA's latest group of astronaut candidates selected in 2004 include schoolteachers, doctors, scientists, and engineers.

Pilot astronauts serve as space shuttle or *Soyuz* commanders and pilots. Both civilian and military personnel are considered for the program. During the flight, the commander has onboard responsibility for the vehicle, crew, mission success, and safety of flight. The pilot assists the commander in controlling and operating the vehicle and may assist with robotics operations.

NASA Mission Specialist (MS) astronauts and Russian Flight Engineer (FE) cosmonauts work with the commander and have overall responsibility for coordinating onboard operations in the following areas: vehicle systems, crew activity planning, consumables usage, and experiment operations. MS and FE are trained in the details of the onboard systems, as well as the operational characteristics, mission requirements and objectives, and supporting equipment for each of the experiments conducted on their assigned missions. MS and FE perform extra-vehicular activities, operate the robotic arms, and are responsible for payloads and specific experiment operations.

Payload Specialists were persons other than NASA astronauts who had specialized onboard duties. They were added to shuttle crews if activities that had unique requirements were involved and more than the minimum crew size of five was needed. Payload Specialists were selected based on their scientific or technical skills (e.g., one of the 40 neuroscientists worldwide who was able to perform a microneurography on the nerve of a leg muscle at the time flew as Payload Specialist during the Neurolab mission in 1998). Invited or paying guests for a given mission, such as politician, journalist, scientist, and teacher Payload Specialists have also been classified as Payload Specialists.

The development of commercial spaceflight activities has created two other types of astronauts: Commercial Astronauts and Spaceflight Participants. Unlike the current astronauts and cosmonauts who are government-employed and trained to fly on specific spacecraft like the space shuttle, *Soyuz*, and the ISS, Commercial Astronauts are any professional astronauts trained to fly on privately owned space vehicles.[4] Spaceflight Participants, more commonly called "space tourists",[5] are people who pay for the spaceflight experience during orbital or suborbital flights and do not provide a recurring service as career astronauts. In any case, these individual become official astronauts when they reach an altitude of 100 km (Figure 7.4).

7.2.2. Physical requirements for astronaut selection

All applicants must meet certain physical requirements and must pass physical examinations with varying standards depending on classification (Table 7.2).

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[4] The first Commercial Astronaut to fly a private spacecraft was Mike Melville, who was the pilot during the flight of *SpaceShipOne* in 2004.

[5] Astronauts are selected for health; space tourists are selected for wealth.

Figure 7.4. Mission and Payload Specialists Are Performing Specific Intra- or Extra-Vehicular activities. In This Photograph, CSA Mission Specialist Dave Williams Is Being Equipped for Recording His Brain Activity During the Neurolab STS-90 Life Sciences Mission. (Credit NASA).

Table 7.2. Medical Requirements for NASA Class I, II, III and IV Astronaut Applicants. The Requirements for Spaceflight Applicants are for the Passengers of Orbital Flight to the ISS.

Item	Pilots (Class I)	Mission Specialist (Class II)	Payload Specialist (Class III)	Participants to Spaceflight (Class IV)
Distant vision	20/50 or better uncorrected; correctable to 20/20 each eye	20/150 uncorrected; correctable to 20/20 each eye	Correctable to best eye	Same as Class III
Near vision	Uncorrected <20/20 each eye	Uncorrected <20/20 each eye	Not specified	Not specified
Hearing	Each ear: 30 dBA @ 500 Hz 25 dBA @ 1,000 Hz 25 dBA @ 2,000 Hz 50 dBA @ 4,000 Hz	Same as Class I	Better ear: 35 dBA @ 500 Hz 30 dBA @ 1,000 Hz 30 dBA @ 2,000 Hz	Must hear whispered voice at 1 m (hearing aid allowed)
Height	162–191 cm	152–191 cm	Not specified	152–191 cm
Refraction/ astigmatism	Specified	Specified	Not specified	Not specified

(Continued)

Table 7.2. (Continued)

Item	Pilots (Class I)	Mission Specialist (Class II)	Payload Specialist (Class III)	Participants to Spaceflight (Class IV)
Contraction visual field	15°	15°	30°	Not specified
Phorias	Eso > 15; exo > 8; hyper > 2	Eso > 15; exo > 8	Not specified	Not specified; hyper > 2
Depth perception	No errors in 16 presentations of the Verhoeff stereopter Test	Same as Class I	Not specified	Not specified
Color vision	Pass Farnsworth lantern Test	Pass Farnsworth lantern Test	Not specified	Not specified
Blood pressure	140/90	140/90	150/90 allowed	150/90 allowed
Radiation exposure	<0.05 Sv/year	<0.05 Sv/year	Not specified	Not specified

Pilot astronaut applicants must meet the following requirements prior to submitting an application:

(a) At least 1,000 h pilot-in-command time in jet aircraft. Flight test experience is highly desirable.
(b) Ability to pass a NASA Class-I space physical, which is similar to a military or civilian Class-I flight physical.
(c) Height limitation due to the size of the space shuttle and *Soyuz* flight decks.
(d) Refractive surgical procedures of the eye (PRK and LASIK) are allowed, providing at least 1 year has passed since the date of the procedure with no permanent adverse after effects.

Mission Specialists have similar requirements to Pilot astronauts, except that the qualifying physical is a NASA Class-II space physical, which is similar to a military or civilian Class II flight physical. Height requirements for Mission Specialists correspond to the limits that the space suits (for extra-vehicular activities) can accommodate. Medical requirements for Payload Specialists were slightly less stringent [NASA, 1998, 2001].

Medical guidelines for the selection of Commercial Astronauts and Spaceflight Participants are currently being developed by expert panels [Aerospace Medical Association, 2001]. Spaceflight Participants with significant medical problems have been cleared and successfully flown to the ISS without adverse medical consequences. However, significant medical testing and preventative treatment were applied prior to medical clearance for an orbital flight. For suborbital flight, the current FAA guidelines do not require Spaceflight Participants to undergo a physical exam prior to flight, but the rule does require informed consent of the risks of suborbital spaceflight. The rule states that safety critical flight crew must have passed an FAA Class-II airman medical certificate not more than 12 months prior to the month of the launch and re-entry.

7.2.3. Selection process

During the NASA selection, discipline panels evaluate applicants who meet the basic qualifications. Those selected as finalists are screened during a weeklong process of personal interviews, thorough medical evaluations (Table 7.3) and orientation. The

Table 7.3. Medical Evaluation for Astronaut and Cosmonaut Applicants.

Examination	Astronaut Candidates	Cosmonaut Candidates
Medical history	NASA medical survey Questionnaire	Includes surgical history
Physical examination	General physical Anthropometry Muscle mass Pelvic exam and pap smear Procto sigmoidoscopy	General physical Anthropometry Rectal exam Pelvic and uterine exam
Cardio-pulmonary evaluation	History and examination Pulmonary function test Exercise stress test Blood pressure Resting and 24 h ECG Echocardiogram	History and examination Pulmonary function test Exercise stress test Blood pressure Resting and 24 h ECG Echocardiogram Phono- and mechano-cardiogram Cardiac cycle analysis
Ear-Nose-Throat Evaluation	History and examination Audiometry Typmanometry	History and examination Audiometry Typmanometry Exo- and endoscopy Vestibular function Optokinetic stimulation
Ophthalmological evaluation	Visual acuity, refraction and accommodation Color and depth perception Phorias Tonometry Perimetry and retinal photography Endoscopy	Visual acuity, refraction and accommodation Color and depth perception Night vision Tonometry Extra ocular muscles Slip lamp exam and endoscopy

(Continued)

Table 7.3. (Continued)

Examination	Astronaut Candidates	Cosmonaut Candidates
Dental examination	Panorex and full dental x-rays within last two years	Orthopantomography Electro-odontodiagnosis Vacuum test
Neurological examination	History and examination EEG at rest EEG with photic stimulation EEG with hyperventilation, valsalva and sleep	History and examination Doppler study of cranial vessels
Psychiatric and Psychological evaluation	Psychiatric interviews Psychological tests	Psychiatric interviews Psychometry Personality inventory Sleep monitoring
Radiographic evaluation	X-ray DNS Mammography Medical radiation exposure history and interview Abdominal and urogenital USG	X-ray abdomen, cranium Spine IV punction Genital system Liver scan and biliary scan Excretory urogram Abdominal and urogenital USG
Laboratory investigation	Complete hemogram Blood biochemistry Immunology Serology Endocrinology Urine analysis 24 h chemistry Renal stone profile Urine endocrinology Stool RE Occult blood Ova and parasites	Complete hemogram Blood biochemistry Immunology Serology Urine analysis 24 h chemistry Stool RE, ova, parasites Analysis of duodenal and intestinal secretions
Other tests	Drug screen Mantoux Test Microbiological, fungal and viral tests Pregnancy test Screening for sexually-transmitted diseases	Decompression and hypoxia Centrifuge for + Gz and + Gx resistance Tilt table studies LBNP Heat stress Parabolic flight

recommendations of the Aerospace Medicine Board (which consists of up to 15 physicians qualified in aerospace medicine) and of the Astronaut Selection Board (mostly composed of astronauts), which includes a list of the final candidates, are sent to the NASA Administrator. The Administrator then makes the decision of who will actually join the program. Selected applicants are designated Astronaut Candidates (known as "AsCans") and assigned to the Astronaut Office at the NASA Johnson Space Center (JSC) for a 2-year training and evaluation program. Civilian Astronaut Candidates who successfully complete the training and evaluation are expected to remain with NASA for at least 5 years. Successful military Astronaut Candidates are detailed to NASA for a specified tour of duty.

There are currently 83 "active" NASA astronauts. The Astronaut Corps is supported by 21 medical and aerospace physicians, two psychiatrists, and three psychologists who provide routine health care, annual physical and behavioral health examinations, as well as support during training exercises and spaceflight missions.

In Russia, cosmonaut selection is not a public process. The selection and training process is different for pilots, engineers, and scientist/medical cosmonauts. The Russian Air Force selects 4–5 test pilots every 3–4 years. The company Energya of Korolev (RKK), which builds Russian space vehicles, has traditionally been responsible for selecting engineer cosmonauts. Finally, the Institute for Biomedical Problems (IMBP) has traditionally been responsible for selecting scientist and medical cosmonauts. There are currently 39 cosmonauts in training.

The medical evaluation process for Russian cosmonauts is carried out in three phases: (a) an evaluation by various specialists of detailed medical history from a questionnaire decides whether a candidate is fit/unfit for hospital examination; (b) a hospital evaluation with the aim to detect any latent pathology, early disease and functional endurance capabilities of various systems, through clinical and laboratory investigations including psychological evaluation; and (c) a final selection carried out at the Yuri Gagarin Cosmonaut Training Center (GCTC), in Star City near Moscow. Basically all test results conducted so far are reviewed and involves 1-week in-patient evaluation in Moscow at the Central Military Aviation Hospital for military cosmonaut candidates and at the IMBP for civilian cosmonaut candidates.

A recent selection of six European astronauts took place at ESA in 2008, bringing the total number of European astronauts to 14. The psychological and medical selection was contracted to the German Space Agency in Cologne and the Institute of Space Medicine (MEDES) in Toulouse. 8,400 applications met the initial criteria, out of which 900 candidates were requested to undergo cognitive tests, then 190 for psychological tests, 45 for medical evaluation, 22 for job interview, and 10 for interview with ESA management. Similar selection medical evaluations apply to both the astronauts and cosmonauts (Table 7.3). After selection, the candidates also undergo annual certification examination.

7.2.4. Astronaut training

Astronaut training for ISS missions requires significant organization and coordination. About 30–40 astronauts undergo training in 1 year at five different sites: JSC in Houston, GCTC in Moscow, the European Astronaut Center (EAC) in Cologne, the

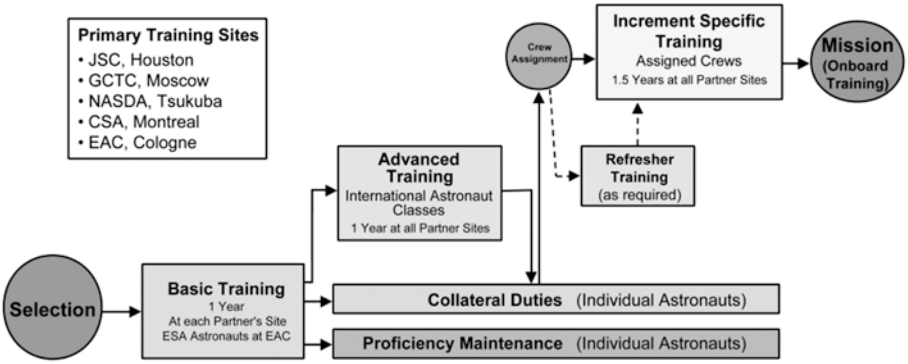

Figure 7.5. Training Flow of Astronauts and Cosmonauts Participating in ISS Missions [Messerschmid et al., 2000].

JAXA Tsukuba Center in Tokyo, and the training facilities at the Canadian Space Agency. Astronaut training is costly and requires the efforts of literally hundreds of people and numerous facilities (Figure 7.5).

Training is generally divided in three phases: (a) *Basic training* is a series of courses, following which successful candidates become regular members of the astronaut corps; (b) *Advanced training* is designed to familiarize the trainee with a feel for what it's like to work and live in space; and (c) *Mission specific training* is increment oriented and normally begins about 1 year before the scheduled launch date.

7.2.4.1. NASA astronauts

Prior to going into space, NASA astronauts receive an average 6 years of training for a space shuttle mission and an average 8 years of training for an ISS mission. Astronaut Candidates receive training at the Johnson Space Center in Houston, Texas. They attend classes on space systems, in basic science and technology. Mathematics, geology meteorology, guidance and navigation, oceanography, orbital dynamics, astronomy, physics, and physiology are among the subjects.

Candidates also receive land and sea survival training (Figure 7.6), training in scuba diving, and using space suits. All Astronaut Candidates are required to pass a swimming test during their first month of training. They must swim three lengths of a 25-m long pool in a flight suit and tennis shoes. The strokes allowed are freestyle, breast, and sidestroke. There is no time limit. They must also tread water continuously for 10 min.

Candidates are also exposed to the problems associated with high (hyperbaric) and low (hypobaric) atmospheric pressures in the altitude chambers and learn to deal with emergencies associated with these conditions. In addition, Astronaut Candidates are given exposure to the microgravity of spaceflight. Modified jet aircraft produce periods of weightlessness for 20 s (Figure 7.6). During this brief period, astronauts experience the feeling of microgravity. The aircraft then returns to the original altitude and the sequence is repeated up to 40 times in a day.

Figure 7.6. A Soyuz Crewmember Prepares to Plunge into the Water from a Mockup of a Russian Soyuz Spacecraft Descent Module as He Goes Through Water Survival Training in the Black Sea. (Credit NASA).

Pilot astronauts maintain flying proficiency by flying 15 h per month in NASA's fleet of two-seat T-38 jets. Pilots build up jet aircraft hours and also practice shuttle landings in the Shuttle Training Aircraft, a modified corporate jet aircraft. Mission Specialist astronauts fly a minimum of 4 h per month.

The astronauts begin their formal shuttle training program during their year of candidacy by reading manuals and by taking computer-based training lessons on the various spacecraft systems ranging from propulsion to environmental control. Then, they begin training in simulators, both fixed-base and motion-base, using generic training software until they are assigned to a particular mission, which happens approximately 10 months before flight. Once they are assigned to a flight, the astronauts train on flight simulators with actual flight-specific training software.

During the last weeks prior to a mission, the astronauts also train with the flight controllers in the NASA JSC Mission Control Center (MCC). A computer links the simulators and MCC in the same way that the spacecraft and MCC are linked during an actual mission. The astronauts and flight controllers learn to work as a team, solving problems and working nominal and contingency mission timelines. Total hours in the simulators for the astronauts, after flight assignment is about 300 h.

In parallel with the simulator training, several other part-task trainers are used to prepare the astronauts for shuttle and ISS missions. These trainers have varying degrees of fidelity and each serve a particular purpose. For example, the Neutral Buoyancy Laboratory (NBL) is a large water tank that helps the astronauts become familiar with planned activities and with the dynamics of body motion during extravehicular activities (Figure 7.7).

There are, however, limitations of the neutral buoyancy training. For example, the viscosity of water produces a different EVA environment than actual space: in water it is hard to initiate motion, but easy to stop; in space it is easy to initiate motion, but hard

Figure 7.7. An Astronaut Wearing a Spacesuit Is Seen Exiting the Hatch of an Orion Mockup, with a Scuba Diver Nearby for Support, in the Neutral Buoyancy Laboratory near the NASA Johnson Space Center. (Credit NASA).

to stop. Also, gravity is still present in the tank, so it is uncomfortable for crewmembers to work upside-down and some tools and other items that cannot be made neutrally buoyant are “heavy”. Finally, it is not possible to effectively simulate the transitions between day and night. Training is done in a fully lighted pool, whereas there are 90-min light-dark cycles on orbit. Finally, the thermal environment is constant in a pool, in contrast with the wide temperature extremes in space. Because of these differences, predicting the amount of time required to perform an EVA in space is difficult.

Full-sized shuttle and ISS mockups are also used to train astronauts for onboard systems orientation and habitability training. In these trainers, astronauts practice meal preparation, equipment stowage, trash management, use of cameras, and experiment familiarization. Virtual reality training is also used. Stereo video goggles and headphones allow the astronauts to “see” inside the modules of the ISS and hear in a computer-generated world. The gloves allow them to move around and grasp objects. This technology seems particularly useful for EVA training to assist in proper positioning for operation tasks while on the end of the robot arm. Crewmembers are also trained to move the robot arm to desired locations using virtual reality (Figure 7.8).

Pilots for shuttle missions receive more intensive instruction on board a jet airplane modified to perform like the shuttle during landing. Because the shuttle approaches landings at such a steep angle (17–20°) and high speed (over 500 km/h), this plane approaches with its engines in reverse thrust and main landing gear down to increase drag and duplicate the unique glide characteristics of the shuttle. Assigned pilots received about 100 h of landing training before flight, which is equivalent to 600 shuttle approaches.

All NASA astronauts receive Russian language training before transferring to the GCTC in Star City for approximately 12 months. The Russian technical training for U.S. astronauts includes theoretical training on Russian vehicles design and systems,

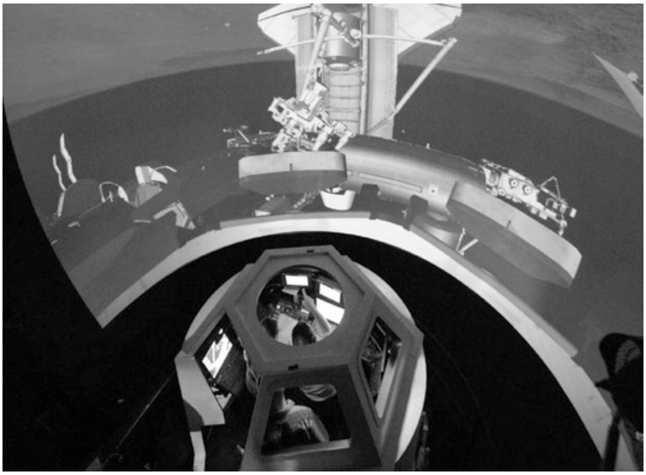

Figure 7.8. Remote Manipulator Arm Training in a Mock-Up of the ISS Cupola and a Surrounding Visual Environment Generated by Virtual Reality. (Credit NASA).

EVA training, scientific investigations and experiments, biomedical training, and Russian language courses.

7.2.4.2. Russian and European astronauts

Cosmonauts assigned for flight to the ISS using the *Soyuz* are generally trained over a 24-month period. This training first includes theoretical and active hands-on sessions on *Soyuz* and ISS simulators, as well as on the onboard life support systems. It also includes survival training, diving training sessions, and training flights that include parachute jumps and parabolic flight. A final exam determines if the candidate will be assigned as a test-cosmonaut or a research cosmonaut, the latter of which cannot be a commander or FE. It is interesting to note that this phase of training also includes 300 h of lectures and practical sessions on space physiology and medicine.

This general space training is followed by 12 months of group training aimed at improving cosmonaut's professional skills and specialization for specific types of manned space vehicles, namely *Soyuz-TMA,* and ISS. When the crew is selected for a specific mission, then the assigned cosmonauts spend 18 months learning to work as a team. Joint training sessions include detailed procedures of vehicle operations, mission tasks, onboard flight files, as well as English language classes. All cosmonauts undergo an annual medical evaluation at the GCTC in Moscow and a final pre-launch medical evaluation at the launch site in Baikonur.

Training of the European astronauts is also divided in three phases: basic training (16 months), advanced training (12 months), and mission-specific training (18 months). The first phase includes an orientation on the major space programs, ESA space laws, and inter-governmental agreements. This is followed by classroom-based learning on fundamentals, such as spaceflight engineering, propulsion, orbital mechanics, science disciplines, Earth's observation, and astronomy. Phase two includes training on the systems and operations of *Soyuz* and ISS, as well as the acquisition of special skills for

Figure 7.9. At the NASTAR Center in Philadelphia, Aspiring Space Adventurers with About $6,000 Can Find out How it Will Feel to be Launched into Suborbital Flight. (Credit Mark Greenberg).

generic robotic operations, rendezvous and docking, Russian language, scuba diving, and EVA training in neutral buoyancy. The third phase includes hands-on training in mock-ups and simulators, and a detailed study of all aspects of the ISS. For their mission-specific training the full crew and back-up crew are dispatched to the other ISS training centers.

7.2.4.3. Spaceflight participants

Training for a spaceflight participant is a condensed version of the training that professional astronauts must undergo to become acclimated to the space environment prior to a mission and be prepared to deal with in-flight contingencies. The suborbital training includes academic modules pertaining to spacecraft systems and practical modules including hypobaric, centrifuge (Figure 7.8), microgravity, and unusual attitude training. The orbital training standards are more rigorous and extensive due to the longer duration of orbital missions. Several expert groups and institutions are working with the commercial spaceflight industry to establish these standards (Figure 7.9).

7.3. Prevention: health hazards in space

In an effort to predict which medical problems might occur in orbit along with their frequency, one can look at the data from populations in analog environments that have the same age range, remoteness, and limitations of available medical resources as astronauts. Investigations of data from surface ship crew, submarine crews and Antarctica studies, however, cannot account for the specific environmental risks unique to spaceflight. The most useful data is prior experience during human space missions. Over the years, in both the U.S. and Russian space programs, several medi-

Table 7.4. Medical Problems Most Encountered In-Flight from the Most Frequent to the Least Frequent.

1. Anorexia (Loss of Appetite)
2. Space motion sickness
3. Fatigue
4. Insomnia
5. Dehydration
6. Dermatitis (skin inflammation)
7. Back pain
8. Upper respiratory infection
9. Conjunctival irritation (eye irritation)
10. Subungual hemorrhage (bruises under fingernails suit gloves)
11. Urinary tract infection
12. Cardiac arrhythmia (abnormal heart beat)
13. Headache
14. Muscle strain
15. Diarrhea
16. Constipation
17. Barotitis (ear problems from atmospheric pressure difference)
18. Bends (decompression-caused limb pains)
19. Chemicals pneumonitis (lung inflammation from EVA)

cal problems have arisen, usually with minimal impacts on the mission objectives and timeline.[6] Many of these were successfully treated using the onboard medical facility. Consequently, all of these events have influenced the selection of medical hardware for the current space program that we will review in the subsequent section.

7.3.1. Medical events during spaceflight

The most common medical problems encountered during space missions, including both U.S. and Russian, short- and long-duration missions, are listed in Table 7.4. More detailed lists of those specific medical events that occurred during shuttle missions between 1998 and 1995, and during the *Mir* missions between 1987 and 1996, as well as their frequency, are presented in Tables 7.5 and 7.6, respectively. It is important to note that the events in these last two lists were collected from postflight medical debriefings and log files.

These data show that the experience so far is that of routine disorders, such as minor respiratory infections (toxic inhalation from chemicals or products involved in

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[6] Conversely, more serious manifestations of illness have prompted the early return in at least two cosmonauts, one from *Salyut-7* (1985) for high fevers (later diagnosed as chronic prostatitis) and another from *Mir* (1987) for cardiac dysrhythmias.

Table 7.5. Medical Events in the Space Shuttle Program Reported by Frequency from Postflight Medical Debriefings with the Crewmembers. This Table Includes the Data Compiled for all Shuttle Missions from 1988 to 1995 (STS-26 to STS-74). Source NASA.

Condition	Frequency	Percent
Facial fullness	226	81.0%
Headache	212	76.0%
Sinus congestion	173	62.0%
Dry skin, irritation, rash	110	39.4%
Eye irritation, dryness, redness	64	22.9
Foreign body in eye	56	20.1%
Sneezing/coughing	31	11.1%
Sensory changes (e.g., tingly, numbness)	26	9.3%
URI (common cold, sore throat, hay fever)	24	8.6%
Back muscle pain	21	7.5%
Leg or foot muscle pain	21	7.5%
Cuts	19	6.8%
Shoulder or trunk muscle pain	18	6.5%
Hand or arm muscle pain	15	5.4%
Anxiety or annoyance	10	3.6%
Contusions	10	3.6%
Ear problems (predominantly earaches)	8	2.9%
Neck muscle pain	8	2.9%
Stress/tension	8	2.9%
Muscle cramp	7	2.5%
Abrasions	6	2.2%
Fever, chills	6	2.2%
Nosebleed	6	2.2%
Psoriasis, folliculitis, seborrhea	6	2.2%
Low heart rate	5	1.8%
Myoclonic jerks (associated with sleep)	5	1.8%
General muscle pain, fatigue	4	1.4%
Subconjunctival hemorrhage	4	1.4%
Allergic reaction	3	1.1%
Fungal infection	3	1.1%
Hoarseness	3	1.1%
Concentrated or “dark” urine	2	0.7%
Decreased concentration	2	0.7%
Dehydration	2	0.7%
Inhalation of foreign body	2	0.7%
Subcutaneous skin infection	2	0.7%
Chemical in eye (buffer solution)	1	0.4%
Mood elevation	1	0.4%
Phlebitis	1	0.4%
Viral gastrointestinal disease	1	0.4%

Table 7.6. In-Flight Medical Events for Cosmonauts in the Mir Program from February 7, 1987 to February 29, 1996. Source NASA.

Medical Event	Initial Events (n=169)	Recurrences (n=135)
Superficial injury	34	2
Arrhythmia/conduction disorder	30	98
Musculo-skeletal	29	NR
Headache	16	8
Sleeplessness	10	9
Tiredness	10	4
Conjunctivitis	4	2
Contact dermatitis	4	3
Erythema of face, hands	4	NR
Stool contents (preflight)	4	NR
Acute respiratory infection	3	NR
Asthenia	3	2
Surface burn, hands	3	NR
Dry nasal mucous	2	NR
Glossitis	2	1
Heartburn/gas	2	NR
Foreign body in eye	2	NR
Constipation	1	NR
Contusion of eyeball	1	NR
Dental caries	1	NR
Dry skin	1	1
Hematoma	1	NR
Laryngitis	1	5
Wax in ear	1	NR

NR none reported.

investigations, pyrolysis products from fire, propellants), skin disorders such as contact dermatitis, and minor trauma. All these events are extremely common in the industrial setting, and are observed in about the same proportion during Antarctic studies (Table 7.7). Medical reports of medical officers at a South Pole station indicate that over a period of 1 year they see an average of three cases per day in a population of less than 300 during the summer months, and 0.4 case per day on a population of 40 during the winter months. During the year 2000, there were two medical evacuations, seven hospitalizations, 35 accidents or injuries, and three deaths [Nielsen, 2001].

Spaceflight, however, is also characterized by microgravity-specific disorders, such as space motion sickness, musculo-skeletal problems, cardio-vascular events, and foreign bodies in the eye (particles do not “settle out”). Based on past incidence, it is

Table 7.7. Illness and Injury in Antarctica. Data Compiled from Stays in Antarctica Between 1988 and 1997. Group Categories Are Based on the International Classification of Diseases, 9th Revision. Adapted from Lugg [2000].

Group	Number of Cases	Percent
Injury and Poisoning	3,910	42.0%
Respiratory system	910	9.7%
Skin and subcutaneous tissue	899	9.6%
Nervous system and sense organs	702	7.5%
Digestive system	691	7.4%
Infections and parasitic disease	682	7.3%
Muscle, bone, and connective tissue	667	7.1%
Other illness	335	3.6%
Mental disorders	217	2.3%

expected that the rate of musculo-skeletal injuries will be of 8.3 per person/year, skin rashes of 3.3 per person/year, and eye injury of 2.5 per person/year [Jones, 2010].

Medical evacuations have occurred on orbit, therefore are highly likely during the operational lifetime of ISS or an exploration mission. Based on the U.S. and Russian spaceflight data, military aviator data, submarine crew data, and polar research station data, the risk of a significant illness or injury requiring equivalent of emergency room visit or hospital admission is of 6–7% per person/year. The risk of a significant illness or injury that would require advanced life support is of 1–2% per person/year [Hamilton, 2010].

7.3.2. Sleep

Believe it or not, sleep disorders, fatigue and insomnia rank respectively third and fourth in the most commonly encountered disorders during spaceflight. In fact, sleeping aids are the most frequently used medication on shuttle missions. Actigraphy and self-reporting are currently used to measure to what degree spaceflight results in disruption of sleep during long-duration missions. Many astronauts experience sleep difficulties, averaging only about 6 h of sleep a day in contrast to the 7 or 8 h they get on the ground. These disorders could be related to the psychological stress related to isolation and confinement (see Chapter 6, Section 6.1.1), to their heavy work schedules, or to the noisy environment (Figure 7.10). It was observed that sleep quantity is reduced even more prior to undertaking critical mission operations, such as EVAs. Ground-based studies have consistently reported performance impairments under conditions of acute or chronically reduced sleep.

Sleep structure (i.e., sleep quality) may also be altered in space. Several polysomnographic studies found that sleep is more fragmented, e.g., the latency to the first rapid eye movement (REM) episode is shorter and slow wave activity (SWA) is redistributed and reduced in-flight and postflight compared to preflight [Dijk et al., 2001].

Figure 7.10. With His Body Tucked Away in a Sleeping Bag, an ISS Crewmember Poses for a Photo near Two Spacesuits in the Airlock of the ISS. (Credit NASA).

This suggests that not only is sleep quantity reduced during spaceflight, but also that the restorative component of sleep may be disrupted in space, which may further increase the likelihood that waking neurobehavioral performance deficits will occur [Bonnet et al., 2005].

Interestingly enough, the change in sleep pattern that typically comes with aging is early waking and fragmented sleep. Optimal alertness during the day and sound sleep at night, valuable qualities on Earth and in space, require proper synchronizing of the human circadian pacemaker commonly known as the "body clock". Thus, researchers seek to better understand how aging and spaceflight affect the mechanisms governing circadian rhythms. The examination of astronauts' circadian alertness using sleep diaries, brain activity (see Figure 7.4), and oral temperature rhythms suggests that the endogenous circadian pacemaker seemed to function quite well up to 90 days in space [Monk et al., 2001]. However, after about 3 months in space, the influence of the endogenous circadian pacemaker on oral temperature and subjective alertness circadian rhythms is considerably weakened, with consequent disruptions in sleep. While researchers think that aging changes the properties of the body clock, they are not precisely sure how these changes occur.

Any natural lighting to which crews are exposed on a spacecraft may impact their circadian adaptation. The ISS orbits the Earth every 1.5 h, resulting in 16 sunrises and sunsets every 24 h, causing the natural lighting cues surrounding the ISS to vary greatly from the terrestrial 24-h day and night cycle. Indeed, astronauts are no longer exposed to the natural 24-h day and night cycle of the Earth but, rather, rely on cues from artificial lighting in addition to those from any of the sunrises/sunsets. Thus, the astronauts' circadian rhythms may be altered by these changes in light exposure.

Slam shifting, which is an acute shift in the sleep/wake schedule to accommodate a docking or critical task in-flight is another risk factor for circadian desynchronization. In 2,000 days of ISS operations (2000–2006), slam shifts occurred 13% of the time, typically before and during critical operations like docking and undocking, spacecraft relocation, and EVAs [Leveton and Dinges, 2006]. Such changes in schedule force critical mission operations to occur against the body's natural circadian rhythm and after sleep deprivation. Slam shifting can result in sleep loss and fatigue for astronauts, and in the ground teams when these teams are working overnight.

Shuttle and ISS missions typically operate on 23.5-h days, and astronauts exploring Mars will experience a natural 24.65-h day. Research has shown that bright light can reset the body clock. In a normal day/night sleep cycle, the level of melatonin, a hormone that regulates the body's sleep activities, will rise about 2 h before an expected sleep period to help the body prepare for rest. The levels are even higher during sleep and low during the day. When subjects are in dim lit conditions, such as in a spacecraft, and on a different day schedule, such as working night shift or during jet lag, the melatonin cycle loses its normal rhythm. Levels are often high when the person is awake and low when she is trying to rest. This factor makes it difficult to sleep at the scheduled time. A treatment to adjust the internal clock that was originally developed for aging people has more recently proven useful to astronauts preparing for spaceflight [Wright and Czeisler, 2002].

Objective feedback on sleep quantity is important information to provide to flight surgeons and astronauts who are preparing for critical mission activities. This will be particularly true for the more autonomous exploration planetary missions.

7.3.3. Immune system

In normal conditions, when challenged by pathogens the immune cells in bone marrow and lymphoid organs initiate and regulate lymphocyte and antibody responses. These cells thereby control the production and function of cells in the blood and connective tissues. Many factors could contribute to a suppression of the immune system in space, including microgravity, cosmic radiation, and highly stressful living conditions.

More than 50% of the Apollo and Skylab astronauts had experienced either bacterial or viral infection during their flight. A depression of T-cell lymphocyte activation was also observed during shuttle missions. The lymphocytes exposed to microgravity tend to lose their capability to react in their normal defensive role. Studies on animals conducted in space also indicated reduced killer cell activities and a higher susceptibility to viral infections. This suppression is thought to happen because the organization of the cells is geared to gravity; without it, the cells become disoriented and fail to function normally (see Chapter 2, Section 2.2.2).

The results of blood analyses during more recent studies on board the ISS indicate that the adaptive immunity[7] is not affected by spaceflight [Chouker et al., 2008]. This

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[7] After the first line of defense that constitutes the skin and mucus barriers, the T-cells in the blood recognize the invaders and either directly attack them or activate fellow T- or B-cells, which produce antibodies that either help destroy the microorganisms or mark them for attack. After the first exposure to a microorganism, "killer" B- and T-lymphocytes are able to recognize that microorganism so that on the second encounter, the response is targeted to that specific germ, allowing more rapid and more efficient action and elimination. This adaptive immunity is the principle behind the efficacy for vaccination [Chouker et al., 2008].

is in contrast with the confinement studies, which have shown inhibition in this immune response to stress (Table 7.8). Also, the occurrence of serious infections in space has been very uncommon. In Antarctica, once the polar station closes and vehicles bringing new visitors and new microbes stop coming for 6 months, there are no new diseases for the occupants to catch. The immune system of the winterers is therefore less challenged. Perhaps the fact that the astronauts in orbit continue receiving regular visits of crewed and uncrewed (but not sterilized) vehicles during their 6-month increments explains this difference. When a new ISS crew arrives, the astronauts have not been exposed to each other's germs and have not yet developed the immunities they need, so their immune system is kept challenged. This situation will be different for the mission to Mars when the crew will start "to function like one organism with one big immune system, and in a way, one nervous system, too!" [Nielsen, 2001].

However, spaceflight is known to result in significant reductions of both plasma volume and red blood cell mass within days (see Chapter 2, Section 2.2.2). Abnormalities in human and animal lymphocyte numbers and morphology are also observed. Prior specimen studies had shown that lymphocytes do not respond to stimuli that normally cause division, suggesting an impaired ability to proliferate in space. This could have profound implications for the immune and red blood cell formation systems in humans for missions of very long duration.

By analogy, aging also depresses the human immune response (though the change in space is presumably temporary while the change due to aging is not). It is not clear, however, whether aging or other factors that typically accompany aging, such as declining activity, cause this immune system depression. Models of age-related changes in immune function are difficult to find, so microgravity may be a very useful model system to use to enhance our understanding of changes due to aging.

Table 7.8. Physiological Response to Isolation and Confinement in Antarctica.

Cardio-vascular function

- Increase in weight
- Increase in lipids
- Increase in blood pressure

Immune function

- Delayed reactivity to bacteria
- Increase in virus shedding
- Decrease in T-cell function

Thyroid function

- Increase in TSH
- Increase inT3 production or clearance

Other

- Decrease in hydroxylation of vitamin D (decrease in UV-B radiation)
- Increase in PTH
- Decrease in testosterone

Also, cosmic radiation, combined with other stress factors such as microgravity and mission-oriented stress, can have an aggravating effect on the immune system during a interplanetary mission. The bugs' ability to cause disease is also subject to change. In fact, the virulence of specific bacteria, such as *Salmonella typhimurium*, has been shown to intensify in orbit. Complex proteomic and genetic analyses revealed that changes in protein synthesis and gene transcription resulted from spaceflight conditions.

Emerging methodology in biomedicine has allowed immunologists to further study relationships between the organ systems and the immune responses. In addition to controlling infections and eliminating germs, immunologic responses are also responsible for eliminating non-functional or dysfunctional tissue-cells (e.g., tumor cells). Failure to maintain adequate immunity may result in autoimmune diseases (e.g., rheumatoid arthritis), acute and life threatening infections, overwhelming systemic immune responses (e.g., septicemia), or the development of cancer. A current study on board the ISS is focused on using small monitoring devices to watch for how and when immune changes become a health risk to better target prevention and therapy [Chouker et al., 2008].

7.3.4. Medical aspects of extra-vehicular activity

Because of the complexity of the ISS and the need for repairing or maintaining satellites in orbit, the requirement for extra-vehicular activity (EVA) is evident. The EVA astronaut becomes analogous to the commercial deep-sea diver or the Antarctic field researcher, each facing their respective environmental hazards protected by technology in what are now routine excursions. One difference, though, is that the body of the astronauts at the time of the EVA is undergoing some adaptive changes to weightlessness, as discussed in Chapters 3–5, which may alter their physical condition. Also, the design of the space suit influences many secondary decisions, such as spacecraft or station cabin pressure, medical hardware inventory, and power and consumables requirements (Hills, 1985).

Alexei Leonov performed the first EVA in 1965. It lasted 12 min and almost ended in disaster when the cosmonaut was unable to re-enter the vehicle because his spacesuit had expended. He had to bleed air from the suit to get back into the airlock. After Leonov finally managed to get back into the spacecraft cabin, the primary hatch would not seal completely. The environmental control system compensated by flooding the cabin with oxygen, creating a serious fire hazard in a craft only qualified for sea level nitrogen-oxygen gas mixes. This flight preceded the *Apollo-1* disaster by several years. Since then, nearly 200 astronauts and cosmonauts, including 11 females, have performed over 700 EVAs. The total EVA duration in the vacuum of space is more than 5 months, including one week for 30 female crewmembers. Nearly half of these EVAs have been performed during the last 10 years for the construction of the ISS. Also, among these EVAs, 28 were made on the lunar surface by 12 astronauts, for a total duration of about 80 h.

Many EVAs were not without problems. The most significant were the following: (a) astronauts were blinded for several minutes due to an eye irritation caused by drink bag leak that mixed with the helmet anti-fog solution; (b) improper boot fit caused severe pain with skin breakdown; (c) nitrogen coolant leaked and sprayed

Table 7.9. Advanced EVA System Wish List for Space and Planetary Surface Extravehicular Activity.

Space EVA

- No pre-breathe – diminished pressure differential between cabin and suit
- Modular design with low on-orbit maintenance and servicing capability
- Durability – maximum time between ground maintenance checkouts
- Regenerable – non-venting systems for heat rejection and CO_2 scrubbing
- Rapid, automated check-out
- Flexibility of crewmember fit, mission capability
- Real-time video and telecommunication display
- Rapid donning and doffing
- Enhanced worksite restraint system
- Increased mobility, manual dexterity
- Comfort level allowing repeated EVAs for 6–8 h each

Planetary Surface EVA

- Dust controlled workplace for suit cleaning and servicing
- Easy replacement of shorter-life components
- Discardable covers for gloves, knees, outer visors, other high-wear areas
- Enhancement of manual dexterity – gloves, optimal suit pressure, tool design
- Increased number of suits per crewmember – minimize impact of malfunction
- Augmented reality

crewmembers, who were required to execute the decontamination routine outside while baking off in the sun; (d) suit visors steamed up; (e) suits ripped at the helmet or the cuff, and the astronauts developed sunburn; (f) there was a shoulder injury during lunar drilling; and (g) hypothermia and finger frostbites. Except for the coolant leak and shoulder injury, all of the other medical effects were due to a spacesuit component malfunction. Following the recommendations of the NASA Human Research Roadmap, research is currently ongoing to improve the reliability and comfort of EVA spacesuits (Table 7.9).

As is always the case in space medicine, the first step is prevention. When planning for EVAs, teams take into account mission parameters, estimated duration, ISS altitude and inclination, plus information on space weather conditions (e.g., solar activity, geomagnetic field conditions, proton flux) that are anticipated for that day. Also, to prevent any adverse trends as early as possible during an EVA, the space suit and physiologic parameters are monitored by crewmembers within the spacecraft and controllers on the ground. These parameters include suit pressure, temperature, O_2 consumption, CO_2 partial pressure, electrocardiogram, heart rate, and radiation exposure.

In the event of a medical emergency, the patient is not immediately accessible to medical treatment. He/she must be moved to the airlock and re-enter in the spacecraft, possibly requiring the aid of a fellow crewmember, undergo the re-pressurization

Figure 7.11. Astronauts in the Airlock of the ISS Preparing for an EVA. (Credit NASA).

cycle, and finally have the bulky space suit removed to whatever degree is necessary to accommodate emergency treatment (Figure 7.11).

Barratt [1992a] explains, "A simple but vital concept when discussing closed gas system is that the biological responses of most gases are dependent on their partial pressures, not their overall concentrations. At sea level, where total pressure equals 760 mmHg or 101.3 kPa with an O_2 concentration of 21% and a partial pressure of O_2 (ppO_2) of 21 kPa (158 mmHg), the respirable atmosphere is said to be normoxic. The same 21% is hypoxic at altitude, where ppO_2 diminishes in step with total pressure, and hyperoxic in hyperbaric atmospheres. Either of these conditions may be detrimental. Similarly, the toxic effects of CO_2 are partial pressure dependent; thus, what may be an acceptable concentration at sea level, e.g., 3%, may be toxic at hyperbaric pressures of a few atmospheres".

In general, the operating pressure inside a space suit is 30–40 kPa, whereas the cabin pressure is 101.3 kPa. The O_2 concentration is 100% in the suit, whereas it is only about 30% in the cabin. The use of lower pressure in the space suit has the advantage that the joints are more flexible. However, this system requires extensive pre-breathing with higher cabin pressures (for more details on this procedure, see Eckart, 1996).

A malfunction of the space suit or a failure in the pre-breathing procedure could have severe consequences on the crewmember. For example, a slow leak and partial depressurization of the space suit could result in hypoxia, with such symptoms as loss of color vision, followed by confusion and eventual loss of consciousness.[8] Telemetry

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[8] During the STS-37 mission in April 1991, an EVA crewmember upon returning to the shuttle after an EVA with no notable events noticed a blood spot on the inside of a glove where a pinhole leak had developed and induced a small skin injury.

will of course alert the controllers before serious symptoms occur, but the onsite medical facility must be prepared to deal with the consequences.

The transition from the ISS to the suit pressure is the equivalent of ascending from sea level to approximately 9,144-m altitude in an unpressurized aircraft [Heimbach and Sheffield, 1985]. Therefore here is the potential for nitrogen bubbles to move into the tissue and generate localized limb and join pain, a symptom known as decompression sickness, or "the bends." Pre-breathing with 100% O_2 prior to initial depressurization during exercise on the cycle-ergometer, along with a final in-suit pre-breathe just prior to final depressurization is currently used to limit this problem. The increased cardio-vascular circulation while breathing 100% O_2 rapidly purges the blood stream of excess nitrogen. A rather short period of this exercise replaces many hours of the standard oxygen pre-breath. However, should the bends occur in orbit, the cabin atmosphere would need to be re-pressurized to the maximum cabin atmosphere (110 kPa) immediately with the astronaut continuing on 100% O_2 [Newman and Barratt, 1997]. The suit pressure would be increased to 160 kPa to provide some hyperbaric oxygen. Executing this procedure would prevent the suit from being used again. Over-inflating a spacesuit compromises its integrity. Return to Earth would be performed as soon as practical if symptoms did not resolve [Hamilton, 2010].

At sea level, prolonged exposure to 100% O_2 eventually leads to pulmonary O_2 toxicity, manifested by chest discomfort, cough, decrease in tidal volume, and eventually serious pulmonary and respiratory problems. Also, following loss of suit ventilation, high levels of CO_2 (greater than 2 kPa) could induce headache, increased respiratory rate, and decline in exercise performance.

Thermoregulation was problematic in the early days of EVA, but has been solved operationally with the introduction of the liquid-cooling garment (LCG). By controlling water inlet temperature, this system offers individual control to accommodate the wide variation in heat production during changing workload requirements. Since the water temperature is monitored, it is possible for the controllers on the ground to decide to terminate an EVA before detrimental heat storage occurs [Newman and Barratt, 1997]. According to the transmitted biomedical data (heart rate, respiratory rate, rate of O_2 absorption, CO_2 level, water temperature in the LCG, body temperature measured from a sensor located behind the ear) the average metabolic expenditures of an astronaut during an EVA range from 175–250 kcal/h. However, during extensive effort for a limited duration the metabolic expenditures rate can go up to 400 kcal/h [Bagiana et al., 1993].

As previously discussed, cardiac dysrhythmias have been occasionally observed on crewmembers during EVA (see Chapter 4, Section 4.3.3). Although, none of these dysrhythmias have led to the interruption of an EVA, they signify alterations in cardiac function that were not detected prior to the spaceflight. The psychological stress associated with the EVA, the heavy workload, and the dehydration that follows could be responsible for these symptoms.[9]

The most common medical events associated with EVA, though, are mostly localized aches and pains, such as finger bruises, resulting from the rigidity of the suit and the physical work (see Tables 7.4 and 7.5). Perhaps some of these symptoms are

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[9] During a space walk, astronauts can drink from a drink bag located inside the space suit by means of a straw.

related to decompression sickness. Fortunately, no serious injury has occurred, despite the hazards of people locomoting, or being moved on robotic arms between massive objects, some with sharp angles. Perhaps the forces that lead to such events terrestrially, such as vehicle accidents and falls, are not present up in orbit. Crush injuries and ankle or knee ligament injuries are, nevertheless, a possibility.

From a operational point of view the EVA rules of thumb are the following: (a) each EVA crewmember should check out his or her own suit; (b) always use "Make before break" tether protocol – EVA crewmember and equipment must remain tethered at all times; (c) "slower is faster" – slow and deliberate motion provides much greater stability than quick, jerky motions; (d) "EVA is an art" – needs procedures, techniques, knowledge, skills and creativity; (e) Don't use the glove as a hammer; and (f) body positioning is 90% of the task.

7.3.5. Conclusion on space health hazards

At present it is not possible to certify any physiological system to be unaffected by several years in microgravity or to preclude any as a fruitful area of research. We cannot assume that as spaceflight increases from months to years, unanticipated malfunctions will not appear. For this reason, scientists recommend that a reliable database must continue to be established so that new phenomena can be recognized and addressed by research before proceeding to longer flights. To accomplish this, the approach of incremental exposure of humans to microgravity should be continued with careful surveillance during and after exposure.

So few data on space medicine are currently available that any projection for human space missions of 1 year or more is only tentative. The physiological effects of short-duration spaceflight are tolerated, or compensated for, by the state of current countermeasures. However, the long-term effects of microgravity or the reduced gravity of Mars on bone and muscle metabolism and on cardio-vascular function remain poorly understood.

The more general problem of the ability of human beings to interact and perform well in a closed, stressful environment assumes novel importance and exigency with extended spaceflights. In addition to the problems of weightlessness and heavy ion radiation, the crew may have to deal with increased microbial density in the cabin air, organic and inorganic toxins (outgassing products), nutritional limitations, and the problems of health care delivery in space. These physical stresses will exacerbate the severe emotional stresses associated with working and living in confined quarters. Many of these problems cannot be studied in terrestrial analogs, and many scientists think that they must be understood in much greater depth during space missions in LEO before a human mission to Mars.

7.4. Treatment: space medical facilities

Because the onboard medical facility cannot be equipped for all possible eventualities, the supplies and equipment included in its design must be carefully selected for maximum utility. A major task involves ranking candidate diseases and injuries according to their potential impacts during a space mission. Typically, the risk associated with an event is defined as the product of its frequency and its consequences. Where an event may have a variety of consequences, an aggregate risk is defined as the sum of the risks of each of the consequence types in common units [McCormick, 1981; Laurence, 1997].

A universal maxim in medicine is that "common things occur commonly." This maxim definitely applies to space missions, as indicated by the frequency of minor medical events reported during space missions (see Tables 7.4 and 7.5). This supports the premise that the bulk of the on-orbit medical care will be directed toward more "general symptoms" or routine disorders [Nelson et al., 1990]. Space medicine here is an analog to the environmental medicine for employees in industrial settings where consideration is given to the environmental hazards that may cause sickness, impaired health, or significant discomfort. These include hazards like chemical, physical, biologic, and ergonomic problems. It is obvious, however, that even minor medical problems may have a major mission impact, considering the cost and risk of maintaining an orbital work force.

In examining the less common but more severe medical problems that might occur, more mission-specific parameters are evaluated. For instance, any toxic substance required operationally must be accompanied by the means to treat inadvertent exposure to it. This includes the toxicity of chemical substances (e.g., hydrazine) or their mixture, as well as the likely failures of environmental control life support systems and their medical implications. The onboard medical doctor or an individual trained for medical procedures must be able to recognize, diagnose, and treat these disorders quickly (Figure 7.12).

Figure 7.12. ISS astronauts Participate in a Medical Training with the Onboard Medical Kit and a Mannequin Representing a Fellow Crewmate in Need of Emergency Care. (Credit NASA).

We must also remember that each illness or injury is occurring on top of the physiological adaptive changes affecting the multiple physiological systems as have been previously discussed. Consequently, signs, symptoms, or the presentation of various diseases and their treatment may be altered by fluid shifts, electrolyte changes, hemodynamic changes, and so on. Finally, it is a fact that manpower is in short supply aboard spacecraft and space station. The crew is on its own with the available equipment and limited support from Earth [Barratt, 1992b].

There are basically two health care systems available during space missions. The first system is a facility that provides simple first aid, with one or all members of the crew trained in basic care, and minimal equipment. Medical kits used on board the space shuttle and the ISS include an emergency medical kit and a medications-and-bandages kit. Such items as a stethoscope, blood-pressure cuff, sutures, disposable thermometers, and injectible medications are in the emergency pack. Band-aids, adhesive tape, gauze bandages, and oral medicine are in the medications-and-bandages kit. The third kit is an instrumentation pack, which includes a respirator, an intravenous fluid system, and a defibrillator.

The second level of health maintenance is a dedicated area for first aid and exercise, which will eventually include equipment for treatment of hypobarism. The objective is to stabilize the injured patient until a rescue happens, treat minor injuries, and even carry out some minimal invasive diagnostic studies and simple diagnostic testing. Such a facility requires extended crewmember training. Symptoms and clinical signs can be described to physicians on the Earth, who direct treatment by giving instruction to the medical doctor or the crew medical officer on board ISS.

7.4.1. Crew health care system

To support the medical needs of crewmembers during ISS assembly and operations, NASA has developed the Crew Health Care System (CHeCS). The CHeCS consists of three primary elements: the Health Maintenance System, the Environmental Health System, and the Countermeasures System. The latter includes a treadmill, a cycle ergometer, and an advanced resistive exercise device as previously described (see Chapters 4 and 5) for the crewmembers to exercise and minimize the effects of spaceflight on the body.

7.4.1.1. The human research facility

The primary purpose of CHeCS is to provide for and monitor the well being of the astronauts in orbit. However, components of CHeCS occasionally may be used to support life sciences research. Similarly, CHeCS may require occasional use of research equipment for periodic assessment of crew health. The CHeCS is thus complemented by the Human Research Facility (HRF), which houses equipment to investigate the effects of microgravity on human physiology. The HRF is composed of two racks, which provide services and utilities to experiments and instruments installed therein. These include electrical power, command and data handling, cooling air and water, as well as pressurized gases and vacuum. Computers are also used to transmit data from environmental experiments that measure radiation, contaminants, and microorganisms. They also transmit data from life sciences experiments and crew psychological surveys (Figure 7.13).

Figure 7.13. An ISS Crewmember Performs an Ultrasound Examination of the Eye of His Crewmate Using the ADUM Instrument of the Human Research Facility in the ISS Destiny Laboratory. (Credit NASA).

The Advanced Diagnostic Ultrasound in Microgravity (ADUM) instrument is the only medical imaging device currently available on the ISS (see Figure 4.1). Ultrasound technology is now deployed in many trauma centers around the world as a first-line diagnostic procedure. Results have been accurate, even when performed by non-radiologists. Hence, it is used on the ISS.

The ultrasound imaging system located in the HRF rack provides image enlargement of the heart and other organs, muscles and blood vessels. This generic diagnostic research tool is capable of high-resolution imaging in a wide range of applications, both research and diagnostic, such as:

(a) Echocardiography, or ultrasound of the heart;
(b) Abdominal ultrasound, deep organ;
(c) Gynecological ultrasound;
(d) Thoracic ultrasound;
(e) Muscle and tendon ultrasound;
(f) Vascular ultrasound;
(g) Small parts ultrasound.

The ISS crewmembers, acting as operators and subjects, have used the HRF ultrasound machine to scan the heart, lungs, liver, spleen, kidneys, and bladder, as well as mouth, teeth, gums, facial bones, sinuses, bones, and eyes (Figure 7.13). Using visual cue cards, written procedures, and verbal directions from ground-based trained radiological personnel, ISS astronauts were able to obtain diagnostic-quality imagery for assessing health problems in the eyes and bones, as well as sinus infections and abdominal injuries.

In addition, the crew assessed the on-board proficiency enhancer (OPE), a software application that is used to train crewmembers on the methods that are employed for each ultrasonic scan. Minimally trained ISS crewmembers were able to capture high-fidelity images of the thoracic, cardiac, and vascular systems with guidance provided remotely from the ground. This investigation has laid the groundwork for using ultrasound as a diagnostic tool in medical contingencies during space missions and remote locations on Earth when a physician is not readily available. A scientific paper discussing these results was submitted by the crewmembers directly from orbit [Foale et al., 2005].

Also housed in the HRF is the Gas Analyzer System for Metabolic Analysis Physiology (GASMAP). GASMAP is used for periodic assessment of crew aerobic capacity. It analyzes human metabolics, cardiac output, lung diffusing capacity, lung volume, pulmonary function, and nitrogen washout in subjects at rest and during exercise. Other equipment stowed in the HRF includes sample collection kits, a continuous blood pressure device, a foot force platform, and a lower body negative pressure device. The HRF also hosts the Space Linear Acceleration Mass Measurement Device (SLAMMD) for measuring on-orbit crewmember mass (see Figure 5.11), and a refrige-rated centrifuge for processing blood samples.

The equipment used for daily exercise on board the ISS for maintaining aerobic capacity, and muscle and bone strength was described in Chapters 4 and 5, respectively. Compared to the equipment previously flown on *Skylab*, *Mir*, and the space shuttle, this new generation of exercise equipment collects information on protocols and forces that are used, stores individual settings and performances, and downlinks this information to the ground. This equipment is not simply used as training exercise, but also as research tool acquiring supplemental data for studies of muscle and bone loss and cardio-vascular health during long-duration spaceflight.

The NASA equipment includes: (a) the Advanced Resistive Exercise Device (aRED), which provides versatile exercise capabilities and collects data such as loads, repetitions, and stroke (see Figure 5.21); (b) the Cycle Ergometer with Vibration Isolation System (CEVIS), which provides the ability for aerobic exercise during recumbent cycling; and (c) the Combined Operational Load Bearing External Resistive Exercise Treadmill (COLBERT), which collects data such as body loading, duration of session, and speed for each crewmember (see Figure 4.20).

In the Zvezda module are another treadmill and cycle ergometer (see Figure 4.20), as well as the Chibis lower body negative pressure (LBNP) device (see Figure 4.21). The Muscle Atrophy Research Exercise System (MARES) is also used for research on musculo-skeletal, biomechanical, and neuromuscular human physiology to better understand the effects of microgravity on the muscles (see Figure 5.22). This instrument is capable of assessing the strength of isolated muscle groups around joints by controlling and measuring relationships between position/velocity and torque/force as a function of time.

ESA just recently evaluated a Percutaneous Electric Muscle Stimulator (PEMS) as a countermeasure for muscle atrophy caused by reduced use. This stimulator delivers electrical pulse to non-thoracic muscle groups of the astronaut subject, thereby creating contractile responses from the muscles. It provides single pulse or pulse trains according to a preadjusted program. The results of this stimulation are currently being analyzed.

7.4.1.2. The health maintenance system

The examination of the factors for health hazards during spaceflight has led to the development of specific facilities for the Health Maintenance System (HMS). Unlike the HRF that focus on the prevention and monitoring of crew health, the HMS includes equipment that is used during emergency situations: (a) a defibrillator; (b) an ambulatory medical pack; (c) a respiratory support pack; (d) an advanced life support pack; (e) a crew medical restraint system; and (f) a crew containment protection kit.

During spaceflight, the accessibility and use of the HMS strongly influences the success of a mission or even the survival of an individual. Some issues are analogous to clinical medicine of Earth. For example, medical waste like sharp needles must be carefully disposed of and medications must be tracked and discarded when their shelf life is exceeded. In addition, the absorption of oral medications may be sensitive to the adaptive changes of body function to microgravity, such as fluid shift or digestive function. Also, alternate means of administration such as intramuscular injection, intravenously, or as a nasal spray may be better than on Earth for some drugs.

Finally, due to microgravity, some of the equipment or procedures must be adapted to the environment of space. Let us now review some of the unique elements of the HMS:

Body Restraint System. If the medical hardware is not in close proximity, then it is either transported to the patients, or the patient is transported. For transport and medical care in microgravity, proper restraint is required. For maximal efficiency, the restraint function is integrated with the diagnostic and therapeutic systems. A crew medical restraint system can be secured to the ISS structure within two minutes to either provide a patient restraint surface or to perform emergency medical procedures, such as during advanced life support (see below). It can also be used to restrain two crewmembers during their delivery of medical care (Figure 7.14).

Cardiac Defibrillator. Early electrical defibrillation correlates best with survival in the event of cardiac arrest. On Earth, applying the charged paddles to the patient's chest normally requires a weight of 11 kg, which is provided by the weight of the rescuer leaning over the patient's chest. In microgravity, the rescuer has no weight, so self-adhesive defibrillator pads are used. To protect the other crewmembers and sensitive avionics, insulation from delivered voltage and electro-magnetic interference (EMI) shielding are used.

Advanced Life Support Pack. This large soft pack stores emergency life saving medications and medical equipment in an easily accessible form. Solving the problems of providing emergency cardiac care during spaceflight sometimes requires new and innovative life-saving techniques. For example, under normal conditions, cardiopulmonary resuscitation (CPR) involves repeated applications of force to the patient's

Figure 7.14. CSA Astronaut Robert Thirsk Is Demonstrating CPR in Microgravity on Board the ISS. Note the Body Restraint System on the "Floor" of the Module. (Credit NASA).

chest while ventilating the lungs. In space, however, both patient and rescuer are free-floating. Being unable to stabilize the patient on a surface and with no force of gravity to provide weight, the rescuer could not easily perform CPR as is done on Earth (Figure 7.14). This problem has been resolved by a modification of the conventional technique. In the microgravity environment, the patient is secured on a restraint and the rescuer is held in place over the patient with a simple harness attached to the restraint. The harness prevents the recoil force of the chest compressions from propelling the rescuer away from the patient, and conventional CPR can be performed.

7.4.1.3. The environmental health system

The Environmental Health System is used for monitoring the internal environment of the ISS, including toxicology, water quality, microbiology, and the radiation environment. The radiation environment is monitored with a variety of dosimeters located inside and outside the ISS. The toxicology system includes a volatile organic analyzer, a compound-specific analyzer for combustion products, and a compound-specific analyzer for hydrazine. A water sampler and total organic carbon analyzer enables crewmembers to assess water quality. A surface sampler kit, a water microbiology kit, and a microbial air sampler enable microbiology assessments.

It is important to remember that a substance might be physiologically ineffective at a very low dose, therapeutic at an intermediate dose, and toxic at a high dose. Also, below a given threshold, a high dose of a substance usually has a greater effect than a low dose; this is known as the "dose-response curve". For space missions, a threshold limit value (TLV) and a permissible exposure level (PEL) have been determined for each substance. Furthermore, there is a maximum allowable concentration authorized for each substance in human spacecraft (Substance Maximum Allowable Concentration, SMAC).

Toxicological issues for human missions include accidental contact with chemicals used in the life support system (leaks or spills) or the fuels for the attitude control system (hydrazine and nitrogen tetroxide). These fuels are toxic when absorbed through skin or by inhalation and provoke immediate and violent irritation of nose, throat, eyes, and the respiratory tract. Longer exposure can result in respiratory arrest; lung, kidney, and liver damage; and possible death. For example, 1 mL of hydrazine vaporized in the shuttle cabin will produce 11.8 ppm (part per million), whereas the SMAC for a 7-day space mission is only 0.04 ppm. Decontamination procedures are especially difficult in microgravity, where the contamination has to be contained. Skin surfaces and eyes must be washed thoroughly upon exposure. The wash water must be contained and controlled as well (Figure 7.15).

On board the ISS, the Lab-on-a-Chip Application Development-Portable Test System (LOCAD-PTS) is a handheld device used for the rapid detection of biological and chemical substances on board the ISS. Astronauts swab surfaces in the cabin, mix the swabbed material in a liquid form to the LOCAD-PTS, and obtain results within 15 min on a display screen. This procedure effectively provides an early warning system to enable the crew to take remedial measures if necessary to protect themselves. The handheld device is used with three different types of cartridges for the detection of endotoxin (a marker of gram-negative bacteria), glucan (fungi), and lipoteichoic acid (pram-positive bacteria). Lab-on-a-Chip technology has an ever-expanding range of applications in the biotechnology industry. Chips are in development that can also detect yeasts, mold, and gram-positive bacteria, identify environmental contaminants, and perform quick health diagnostics in medical clinics.

The radiation hazard for humans in the space environment is measured using various techniques. The Matryoshka experiment is a phantom torso made of plastic, foam, and a real human skeleton (see Figure 2.27). The torso is equipped with dozens of

Figure 7.15. ESA Astronaut Jean-François Clervoy Washing His Eyes with a Blob of Water in Microgravity. (Credit NASA).

radiation sensors that are placed in strategic locations throughout its surface and interior to measure how different organs and tissue may be susceptible to radiation damage experienced by astronauts in space outside and at various locations inside the ISS. The systematic investigations using this tool started in 2004 and will continue incrementally for several years to come. The results will provide information on the radiation dose distribution inside the body for a better correlation between skin and organ dose and for better risk assessment in long-duration spaceflight.

The Anomalous Long-Term Effects in Astronaut's Central Nervous System (ALTEA) system experiment is a helmet-shaped device holding six silicon particle detectors used to measure the effect of cosmic radiation on brain activity and visual perception (Figure 7.16). Visual perception is evaluated by asking astronauts to report perceptions of light flashes behind their close eyelids as a result of high radiation. Because of its ability to be operated without a crewmember, it is also being used as a portable dosimeter to provide quantitative data on high-energy radiation particles passing in the ISS. JAXA also uses passive dosimeters that record the personal dose radiation of its astronauts. The dose records are used to assess a radiation exposure limit of each astronaut.

7.4.1.4. The human physiology research facilities

Human physiology research on board the ISS is coordinated by an international working group that coordinates experiments and share data. An astronaut or cosmonaut can participate in as many as 20 physiology experiments during his/her stay on the ISS. The equipment for this research is located in the various ISS laboratories. The partners of the ISS share the use of this equipment based on collaborative agreements and memorandum of understanding.

In the *Columbus* module, the European Physiology Module (EPM) is a double-rack designed for studies in neuroscience (multiple EEG recording), cardio-vascular, bone, and muscle physiology, as well as investigations of metabolic processes. Another

Figure 7.16. ALTEA Is Used for Health Monitoring of Crewmembers Regarding the Effects of Exposure to Radiation During Their Stay on Board the ISS. Radiation Shielding Can Also Be Studied by Comparing the Efficacy of a Variety of Special Material. (Credit NASA).

rack-mounted Pulmonary Function System (PFS) includes analyzers to measure the gas composition of an astronaut's breath (which is also useful to evaluate cardiac output), the capability to make numerous different measurements of lung capacity and breath volume, as well as a system to deliver special gas mixtures that allow astronauts to perform special tests of lung performance. A small portable version of the system, called Portable PFS, can also be used in conjunction with the various exercise equipments in other laboratory modules. Research hardware in neuroscience include systems for studying H-reflex, body motion, eye movements, hand-eye coordination, visual perception, and mental representation of space.

In the Zvezda module, the Russian Human Life Research system includes a Cardiovascular System Research Rack, a Weightlessness Adaptation Study Kit, the Immune System Study Kit, and a Locomotor System Study Facility. In the Kibo module, The Human Research Hardware for JAXA includes a portable digital holster ECG recorder for 24-h electrocardiogram monitoring of cardio-vascular and autonomic function of the astronauts. The recorded data are downlinked to the scientists on the ground.

7.4.2. Telemedicine

In orbit, astronauts can communicate with and be advised by their ground medical support team, which includes flight surgeons, biomedical engineers, nurses, and consultants, using audio and video telecommunications links. The on-orbit facility is part of a larger integrated health system consisting of the medical facility itself, the onboard doctor or crew medical officer, ground medical personnel, and a telemedicine link. All elements must function in a coordinated fashion. The general philosophy is that the onboard crew medical officer serves more of a technician and procedural role, with ground personnel providing decision-making support; essentially a "brains on the ground, hands in orbit" approach.

The telemedicine link not only connects the crewmember with the most qualified consultants, but it also provides real-time downlink of video and diagnostic procedural images such as ultrasonic images. Using the onboard system, video imaging of the eye, ear, nose, throat, and skin is possible. In case of illness or disease, continuous biomedical monitoring of parameters including ECG, heart rate blood pressure, and O_2 saturation, is performed and the data are downlinked in real time to ease the burden on the crew medical officer. The primary medical procedure document, called the Medical Checklist, is a text-based reference with illustrations that provides procedures to guide astronauts, whose training may be in non-medical disciplines, through medical tasks ranging from examination to emergency procedures. This document also provides reference materials such as contents lists of onboard medical kits and information about the various medications and instruments available [NASA, 2006].

Such telemedicine systems have been and are being utilized in remote terrestrial settings, such as Antarctica stations or ships, during which medical specialists on the ground were able to review cases and provide therapeutic and procedure advice.[10]

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[10] In a remarkable book called *Ice Bound*, Dr. Jerri Nielsen describes her experience when she diagnosed and treated her own breast cancer during wintering over a South Pole station [Nielsen, 2001]. Her true story is also full of interesting observations on the medical and psychological issues related to isolation in extreme environment.

Computerized medical databases and medical diagnostic programs are being evaluated for incorporation into the onboard medical facility. In recent years, small steps have been made in the fields of diagnostic imaging upgrade and miniaturization. However, a giant leap is still needed for an autonomous care system to support Mars exploration missions. Large toxicology databases are already utilized during space missions, accommodating rapid search and information retrieval to offer immediate advice in treating exposure to toxic substances. Future customized medical data management systems could include medical databases, diagnostic software, and crew medical records with medication allergies, ill-effects history, and environmental exposures into an integrated health care tracking network [Barratt, 1992].

However, the technology and sophistication mentioned above must be balanced against the capabilities and proficiency of the onboard crew medical officer. New technologies may be very demanding in terms of time required, power needed, and complexity required to use them. A well-trained clinician may immediately dismiss an entire pattern of diagnostic considerations, which the automated system feels it must process, and even the best video images may not transmit what the crew medical officer can detect at a glance. Technology can never completely substitute for skills in physical diagnosis. For this reason, the level of training of the crew medical officer is a vital consideration in the integrated health system [Barratt, 1992].

However, during long distance space missions such as Mars exploration, communications to Earth are subject to significant time delays so that Earth-based support will most often be asynchronous. This means that astronauts will need to be self-reliant, making optimal use of available on-board resources and prior medical training to effectively handle medical events. While it is anticipated that every mission will include at least one physician, this individual may herself be in need of medical attention or may have to care for medical disorders with which she is relatively unfamiliar or out of practice.

7.4.3. Emergency and rescue

There is a trade-off between the capability for emergency transportation back to Earth and the capability for emergency treatment in space. If emergency rescue is impossible or impractical, then emergency care capability must be provided, meaning that there must be a physician for in-flight care. This person could also be a trained astronaut capable of performing a physical examination of a patient and, along with the direction and assistance of the ground-based physician, recognizing and responding to potential medical issues. As in terrestrial medical care, the response to a medical event during a space mission then depends on five factors: (a) the severity of illness or injury; (b) the capability of the onboard medical system; (c) the ability of surgeon to assist during medical event; (d) the level of skill and training of crew medical officer; and (e) the ease and feasibility of medical evacuation to Earth.[11]

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[11] An easy way to remember these five factors is "SCALE," with the letter S for severity, C for capability, A for ability, L for level of skills, and E for ease [Hamilton, 2010].

7.4.3.1. Crew medical officer

There are six crewmembers aboard the ISS for stays that last between 90 and 180 days. One mission safety rule states that the crew shall be able to return to Earth in less than 24 h. A *Soyuz* vehicle is permanently docked to the ISS, and is ready to leave given just a few minutes notice. Two astronauts of each ISS Expedition crew are trained as a crew medical officer (CMO). The CMOs on ISS are usually not physicians. They receive 34 h of medical training completed at least 6 months prior to flight. The other crewmembers (non-CMOs) only receive 17 h of preflight medical training. When on board, the CMOs have 1 h per month of in-flight computer-based refresher training, and must complete one emergency simulation per mission. In addition they receive an optional "Space Emergency Medical Training" course at a local community college (20 h in classroom, 50 h in clinical setting).

As stated earlier, the CMO must recognize, treat, and stabilized acute injury, as well as prepare the patient for transport in case of an emergency return. CMOs receive cross training in different disciplines so that they could provide surgical assistance, anesthesia support, and diagnostic capability, such as in the laboratory or imaging areas. However, due to their limited training, it is imperative that the CMOs have access to consultation with other medical specialists on Earth. Communications from the ISS allow this telemedicine link. However, the medical events during interplanetary missions require a more substantial capability than low Earth orbit, where rapid return to Earth is a viable option.

During a mission to Mars the astronaut physicians and CMOs, as well as the flight surgeons on console, will take on different roles. The crew will have greater responsibility because of time latency. They will need a greater baseline depth of knowledge and technical skill than dictated by current program requirements. They will need a broader medical and surgical skill set or will have to accept higher risk. Although there will be more need to "treat in place", the mass and volume for medical capabilities will be more constrained than on board the ISS. Medical officers will presumably be limited to medical kits onboard the transit spacecraft and rovers. Also, longer missions result in lower proficiency, so there will be a need for "just-in-time training" and telementoring. Flight surgeons on the ground will be crucial advisors to onboard medical officers, but will be challenged to lead resuscitations or other major interventions due to time delays.

Today's discussions focus on how to prepare for these missions when the overarching mission is poorly defined: What preflight training should be provided to the onboard of physicians and backup CMOs? What residency training is optimal for exploration mission? Is it aerospace medicine, emergency medicine, occupational medicine, general surgery or something new? Should they need in-flight proficiency training and tools? And what level of support can they get when at much greater distances from home? [Jones, 2010].

7.4.3.2. Surgery in space

Spacecraft are closed ecosystems with everything recycled, including the air. In the absence of gravity, microscopic particulate matter is dispersed in the air, rather than settling to the "ground". Surgical procedures must therefore be protected from this increased level of air contamination, and the solution to date has been to create canopies or tents to protect the operative site. Indeed, during open surgery in space, surgical debris would disperse throughout the spacecraft rather than being contained by gravity into the peritoneal cavity.

For those missions where surgery may be necessary, procedures must be developed to allow the surgeon to operate in microgravity. For example, both the patient and the surgeon must be restrained to prevent floating away from the operating table (Figure 7.17).

New training techniques must also be developed for instrument deployment and fixation as well as to ensure a sterile environment. Cleanliness is particularly important, given that, as mentioned earlier, there is an increased population of antibiotic resistant bacteria in space. Furthermore, a decrease in the immune function in space has been documented. Other factors that may affect surgical procedures in space are the level of lighting (operating theaters in hospitals are equipped with very bright lighting to ensure the best possible exposure in all directions) and the possible decreased in proprioceptive sensitivity from the muscles, skin, and joints.

Simulations performed during parabolic flight have demonstrated the ability to perform endotracheal intubation, mechanical ventilation, CPR, intravenous access with infusion of fluids and medications, intravenous anesthetic techniques, suturing, and cleansing of wounds, splinting and casting of limbs, and the insertion of urinary and nasogastric catheters, using either training mannequins or animal models in microgravity. Open surgical procedures on anaesthetized animal models in 0 g have included exploratory laparotomy, mesenteric vein ligation and repair, and incision and repair of renal artery, carotid artery, and aorta. Endoscopic procedures have included laparoscopic surgery and thorascopic techniques. The ability to carry out these procedures has depended on a number of ingenious systems designed to restrain the patient, surgeons, surgical, and anesthetic equipment [Jones, 2010].

Figure 7.17. Lesson Learned: When Performing Surgery in Microgravity, Both the Patient and the Surgeons Must Be Restrained. (Credit Douglas Hamilton).

Figure 7.18. A Crewmember of the NASA Extreme Environment Mission Operations (NEEMO) Project Evaluates the Use of Telementoring for Emergency Treatment of Medical Conditions That Could Arise During a Space Mission, Including Surgery. (Credit NASA).

For long-duration space travel, "just-in-time" training, robotic surgical procedures, mentored-surgery performed by non-surgical personnel, or other techniques may be the only alternatives. In many instances, minimally invasive techniques can provide protection. These procedures can be conducted and viewed through a video monitor, which permits the opportunity now for telementoring, and, in the future, the potential for remote robotic telesurgery (Figure 7.18). There is, however, the issue of time delay in communications for interplanetary missions (40-min round-trip between Mars and Earth).

It is expected that a Mars mission will benefit from current general trends in medicine. Advances in microelectronics have enabled smaller, lighter, and less power-intensive components such as cardiac monitors, ultrasound imaging systems, and pulso-oximetry (the little pulse measuring device that the nurse puts on the end of your finger). There is also a trend toward less intensive therapies. Once major surgical procedures are being replaced by fiber-endoscopy approaches, vastly simplifying problems of sterile field maintenance and blood handling, which are magnified in microgravity [Campbell et al., 2001]. Ultrasonic pulses applied externally are being employed in the process known as "lithotripsy" to treat kidney and gall bladder stones. Another more quiet revolution is in the area of advanced pharmaceuticals. In recent years new class of broad-spectrum antibiotics has been developed, which can be taken in pill form, replacing more complicated therapies that previously required intravenous administration. For example, the number of surgical procedures for peptic ulcer disease has been drastically reduced by the use of several classes of highly effective anti-ulcer medications [Barratt, 1992].

These innovative solutions applied to perform surgery in remote sites could lead to discoveries for new surgical applications on Earth for remote or small villages or less experienced medical personnel. By having such a critical need to provide medical and surgical support to space missions, space agencies will continue to push the envelope in leading edge surgical technologies and training techniques.

7.4.3.3. Evacuation

Studies at NASA based on nine categories of medical conditions and on medical review surveys, including such factors as on-orbit environment and medical facilities, have ranked the likelihood for medical conditions that would require an evacuation from the ISS [Billica et al., 1996]. The results of these studies suggest that an evacuation of a crew of seven could take place every 5 years of a permanent utilization of the ISS. The most likely causes of evacuation besides a medical emergency are a radiation dose event, collision with a micrometeorite, orbital debris, or major system failures.

In the past, several missions were aborted and required medical evacuations from space. In 1976, the crew on board *Salyut*-5 experienced chronic headaches secondary to life support problems, and the station was abandoned after 49 days. In 1985, the crewmember of *Salyut*-7 became ill with prostatitis and developed urosepsis, which required return to Earth after 56 days of a 216-day mission. In 1987, a crewmember of the second *Mir* mission developed persistent dysrhythmia, and the mission duration was shortened from 11 to 6 months with a safe return in *Soyuz*. Also, in the 15 years of the *Mir* existence, three events could have prompted an evacuation: an O_2 candle fire, a collision with the *Progress* vehicle and the depressurization that followed, and an attitude control and power loss.

The experience in Antarctica indicates that there are about 70 events prompting a medical evacuation per 2,000 person-years. A medical evacuation of the ISS is therefore a possibility. The *Soyuz* is currently the ISS evacuation vehicle, should such problems occur. However, flight surgeons are concerned because the *Soyuz* capsule has obvious limitations as a medical evaluation vehicle: it is small and not equipped with medical assistance equipment (Figure 7.19). With a crew of three, there is no room on board *Soyuz* for medical equipment. Therefore, in a medical evacuation (med-evac) role, the *Soyuz* third seat would be required for stowage of medical

Figure 7.19. During Nominal Operations, Three Crewmembers Share the Cramped Confines of a Soyuz Capsule for Two Days Before Docking with the ISS and for About 6 h During the Return to Earth. (Credit NASA).

support hardware. This limits the emergency return capability of the *Soyuz* to a two-person rather than a three-person crew. In addition, *Soyuz* could return a sick or injured crewmember only if he/she is strapped into the couch (see Figure 4.8), approximating a fetal position, as was the case of a cosmonaut at the end of the *Soyuz T-14* mission in 1985. Consequently, leg or spinal injuries cannot be accommodated. Fortunately, this type of injury is only a remote possibility [Hall and Shayler, 2004].

Finally, during re-entry the deceleration of the *Soyuz* returning the crew from the ISS can climb up to nearly 4 g as the atmosphere slows the lightweight craft down. Due to software or human error, the capsule may follow an even steeper descent path, known as ballistic re-entry. As a result, the crew is subjected to about 8–10 g. In this situation, the vehicle can miss the targeted landing site by several hundreds of kilometers. Lately, ballistic re-entries have accidentally occurred on three *Soyuz* missions returning from the ISS. After one of them, it took the three crewmembers of *Expedition-6* more than 1 h to drag themselves out of the hatch under the oppression of Earth's gravity following 6 months in weightlessness. They erected a folded communications antenna to assist the search planes and helicopters to find them, which happened several hours later (Figure 7.20).

A medical evacuation from the ISS may take a minimum of 6 h to ensure that the *Soyuz* lands in a safe area, but it could be up to 24 h before the evacuation is complete. Consequently, the emphasis is on advanced trauma life support capability, stabilization, and medical transport. Evacuation from a Moon or a Mars base is in the order of several days or 9–12 months, respectively, so the emphasis will be more toward

Figure 7.20. One of the Crewmembers of Soyuz TMA-11 Is Chatting with a Member of the Recovery Team After Landing. His Capsule Unexpectedly Followed a High-g Ballistic Re-entry Trajectory and Ended up Landing 400 km Off-Course. (Credit Novosti Kosmonavtiki).

broadly trained physician(s) as part of the crew, onsite treatment, and telemedicine as augmentation.

For a *Soyuz* returning from the ISS, the search and rescue team is at the expected landing site nominally 5 h before landing. During the re-entry of the *Soyuz* capsule, aircraft, helicopters, and all-terrain vehicles are in motion criss-crossing the 800 km projected landing path in the desert heading towards the landing area. After the capsule has landed, the rescue and recovery teams move together across the steppe to the landing point. Ground personnel then secure the landing area, erect a scaffolding around the capsule if the hatch is on top, and recover the crewmembers from the capsule. The astronauts are seated in lounge-type chairs near the spacecraft and are surrounded by a crowd of onlookers, including space agency managers, other astronauts, as well as other officials (see Figure 1.21). They are then carried to an inflatable tent where medical personnel perform medical and psychological check-ups. Following another series of ritual routines, the cosmonauts are transported by helicopter to the nearest airport and returned to Moscow or Houston. Obviously, none of this will happen after a landing on Mars!

7.5. Challenges for exploration missions

The chain of medical care for space medicine in low Earth orbit includes the following links: selection, prevention, diagnostic, treatment, stabilization, transportation, and transfer to a terrestrial definitive care medical facility. For a Mars mission, the chain is limited to: prevention, diagnostic, treatment, and rehabilitation. All links are equally important for mission success, because for both types of missions, the chain of medical care is only as strong as its weakest link.

Some options of medical requirements are unique to a human mission to Mars mission. Indeed, there is an increased risk of disease or injury with long-term habitation for a relatively large number of crewmembers. The amount of EVA work in a 0.38-g environment involving high-mass hardware will dramatically increase further compounding potential risks to trauma (Figure 7.20). If and when a serious medical situation does arise, rapid emergency transportation may not be available or appropriate. Also, rapid return of the patient to Earth for life-saving treatment is not an option. Consequently, there are significant potential impacts of the medical care options on design and operations of a human Mars mission.

The medical capabilities envisioned to support exploratory class missions must address the ALL requirements, for Autonomous, Lightweight (modular), and Lean (Low power). This includes the development of portable, remote and automated diagnostic capability, computer-based treatment algorithms (virtual consultant), non-invasive monitors/sensors, medical suite in habitats and pressurized rovers, telerobotics, and emergency surgical capability. There is plenty of work for all that are interested in medical technology development!

This, then, is space medicine in a nutshell. As a new field of medicine, it has developed quickly in a highly technical arena. It has caused us to redefine much of what we know about human physiology and performance for a new and challenging environment, and it will keep in step with the continued projection of humanity off the home planet.

Figure 7.21. **The Star Trek Sick Bay.** Memorable Citations from Star Trek Doctors Include the Following: "He/She's Dead, Jim." (Various Episodes); "I Signed Aboard This Ship to Practice Medicine, Not to Have My Atoms Scattered Back and Forth Across Space by This Gadget." (Television Original Series: "Space Seed"); "Shut up Spock, We're Rescuing You!" (TOS: "The Immunity Syndrome"); "Do You Want to See Just How Fast I Can Put You in a Hospital?" (TOS: "This Side of Paradise"); "By Golly, Jim – I'm Beginning to Think I Can Cure a Rainy Day!" (TOS: "The Devil in the Dark"); "A Child Could Do it… a Child Could Do it…" (TOS: "Spock's Brain"); "Well Jim, I Hear Chapel Is an MD Now. Well, I'm Gonna Need a Top Nurse, Not a Doctor Who'll Argue Every Little Diagnosis with Me. And They Probably Redesigned the Whole Sick Bay Too! I Know Engineers, They Love to Change Things!" (Star Trek: The Motion Picture); "The Bureaucratic Mentality Is the Only Constant in the Universe. We'll Get a Freighter." (Star Trek IV: The Voyage Home); "Because I'm a Doctor, That's How I Know!" (TOS: "Friday's Child"); "Jim, You Don't Ask the Almighty for His ID!" (Star Trek V: The Final Frontier); and of Course "Live Long and Prosper!".

Like the ship's surgeon of a sixteenth century vessel of exploration, the crew medical officer of the first human Mars expedition will be equipped according to the best information possible and at the same time constrained by space and resources. He will, like his earlier counterpart, also have other duties, but will be responsible for the health of the crew. He can be expected to observe many effects for the first time and must be prepared to adequately describe new medical findings and adequately react if they are hazardous. And as always through history, he and all the crew will be anxiously awaited back at the homeport to share the discovery [Barratt, 1995] (Figure 7.21).

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Chapter 8

Life Support Systems

It is certainly true that robots like the Mars *Pathfinder*, Spirit, and Opportunity have shown that a lot of scientific information about a planet's surface can be gathered by sending robots instead of people. As well, it can be done significantly cheaper. But imagine that you wanted to go to Paris. Would you be satisfied with a robot… taking very good pictures of the Eiffel Tower and chemically sampling the French food?

As humans, we are really going into space because of the fundamental human drive to explore and to understand. It's an intrinsically human thing. It is part of the human experience in the broadest sense and science is just one piece of that experience. Learning about the universe is only part of the equation; learning how the astronauts who participate in this exploration change and evolve is of equal importance. However, before humans can embark in such a voyage, it is necessary to re-visit the current concepts of life support systems on board space vehicles (Figure 8.1).

8.1. Human needs for space missions

When asked, "Why should humans go to Mars or anywhere else?" there are at least six reasonable answers: (1) To increase our knowledge of the universe and to answer questions such as "Are we alone?" and "Does life exist elsewhere in the universe?" (2) To explore and discover new frontiers; (3) To advance the engineering practice and generate new technologies that might be useful for Earth, knowing that there is a 9:1 return on investment by way of spin-offs from space technology; (4) To enable the commercialization of space by using seemingly limitless, untapped resources, which could prove to be "profitable"; (5) So we don't destroy each other or planet Earth. It is known that cooperative peaceful endeavor unites the people of the world; and (6) Humans need to push the boundaries of our species or risk extinction, given that the current projections for severe energy and resource shortages by 2,100.

8.1.1. Environment

Earth's atmosphere is made up of 78% nitrogen, 21% O_2, 0.5% water vapor, along with very small amounts of argon, CO_2, neon, helium, krypton, xenon, hydrogen, methane, and other trace gases. We depend on the correct mixture of gases in the atmosphere to sustain our lives. We also depend of the pressure of our atmosphere to be able to breathe (at sea level, atmospheric pressure is 1 atm = 760 mmHg = 101.1

G. Clément, *Fundamentals of Space Medicine*, Space Technology Library 23,
DOI 10.1007/978-1-4419-9905-4_8,

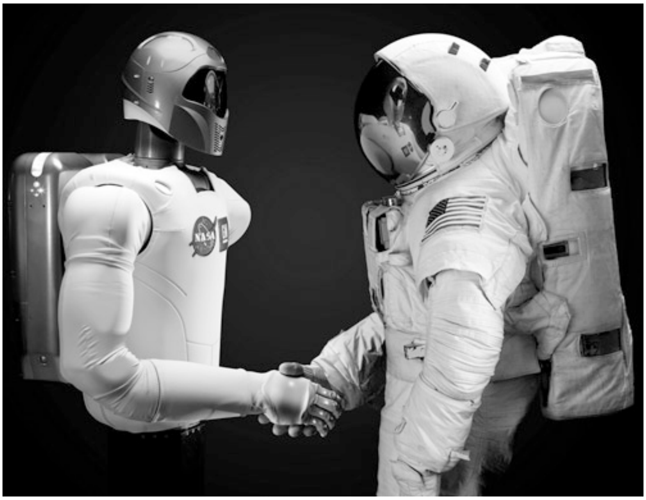

Figure 8.1. Robonaut 2, a Dexterous Humanoid Robot, Will Fly to the ISS on Board STS-133. After Operational Tests and Eventual Upgrades, It Will Help Spacewalking Crew-Members with Tasks Outside the ISS. (Credit NASA).

kPa = 14.7 psi). Therefore, space travelers must carry along their own pressurized atmosphere with the correct mixture of gas.

Because spacecraft are completely closed environments, CO_2 must be actively removed from the atmosphere. CO_2 levels should be lower than 0.01%. If not, high CO_2 levels increase heart rate and respiration rate and cause problems with the acid–base balance of the body. In today's spacecraft, the air is filtered through canisters of white, granular lithium hydroxide (LiOH) to remove the exhaled CO_2. The canisters also contain a layer of charcoal to trap odors in the air. Fans throughout the habitat pull the clean air constantly through screens that catch debris, such as lint, hair, dead skin, and crumbs.

Although the Mars spacecraft will be assembled in a "clean room" where dust particles have been filtered out, bacteria will nonetheless pervade all of the equipment and no doubt a colony of them will grow and accompany our crew on their voyage. In all likelihood, no virulent strains will find their way on board, but it is possible that in the radiation and microgravity environment of space, some genetic mutations might develop and produce new forms of bacteria that humans have never encountered before. Just as Christopher Columbus had to fight scurvy and syphilis, so might the first Mars crews find that a new disease awaits them far from their homeport [Collins, 1990].

High humidity can promote the rapid growth of microbes or fungus. Low humidity can cause drying of the eyes, skin, and the mucous membranes of the nose and throat, thus providing less protection against respiratory infections. Temperature is also an important aspect of the body heat balance, and should ideally range from 18°C to 27°C.

8.1.2. So, how long will we live?

Try the following thought experiment. Imagine yourself in a lecture hall with 100 other people. Now, imagine that the door is blocked and the room is completely sealed.

What will be the first complaint of the people trapped inside? How long would they live? If asked these questions the responses of the trapped people would invariably include the need for water, air, or food. In reality, the first complaint of people will be that they need to go to the bathroom after a couple of hours. Waste management is an important component of a life support system!

If the system providing the fresh air suddenly stopped functioning, the reserve of air in a volume of, say, 1,200 m^3 would allow a six-person crew to survive for about 10–12 days before symptoms of hypoxia (lack of oxygen) or hypercapnia (CO_2 toxicity) become lethal. If the loss of air was due to a collision with a piece of orbital debris or a micrometeorite, crew survival would depend on the rate of pressure loss, i.e., the size of breach, the initial module pressure and volume, and the ability of the environmental control system to compensate, and the access of the crew to emergency breathing equipment. In case of a sudden loss of oxygen, the time of useful consciousness goes from 20 to 30 min for an oxygen level equivalent to an altitude of 5,000 m to about 9–12 s for an altitude of 15,000 m. Experience with people stranded in desert environments indicate that people can survive 9–11 days with as little as 1 L of water, provided they stay in the shade where the external temperature is around 21°C. For an external temperature of 37°C, the survival duration drops by half to 5 or 6 days.

8.1.3. Human needs

It is clear that the basic human requirements include atmosphere, food, and water. In 1 year, a 75–kg individual requires four times his/her weight in oxygen, three times his/her weight in food, and 17 times his/her weight in potable water. A much larger quantity of water is needed for hygiene, sanitation, than for nutritional requirements. Table 8.1 shows the perfect balance between the inputs and outputs that are needed to sustain human life. However, simple things like food dislikes, external temperature, and stress can dramatically disturb the equation.

Table 8.1. Average Values for Most Human Inputs and Outputs. Potable Water Is Used for Drinking and Preparing Food; Hygiene Water Is Used for Maintaining Hygiene, Toilet Flushing, Doing Laundry, and Washing Dishes.

	One Day (Per Person)	One Year (Per person)	% of Total Mass
Inputs			
Oxygen	0.83 kg	303 kg	2.7%
Food	0.62 kg	226 kg	2.0%
Potable Water	3.56 kg	1,300 kg	11.4%
Hygiene Water	26.0 kg	9,490 kg	83.9%
Total	**31.0 kg**	**≈11,400 kg**	**100%**

(Continued)

Table 8.1. (Continued)

	One Day (Per Person)	One Year (Per person)	% of Total Mass
Outputs			
Carbon dioxide	1.0 kg	363 kg	3.2%
Metabolic solids	0.1 kg	36 kg	0.3%
Water	30.0 kg	10,950 kg	96.5%
Including:			
Metabolic/urine			12.3%
Hygiene/flush			24.7%
Laundry/dish			55.7%
Latent			3.6%
Total	**31.0 kg**	**≈11,400 kg**	**100%**

8.2. Contamination

In the past, several contamination events have occurred during missions on board various spacecraft, including faulty fiberglass insulation (*Apollo-10*, 1969), CO_2 build-up (*Apollo-13*, 1970), propellants entering via vents during re-entry (*Apollo-18*, 1975), acrid odors (*Soyuz-21/Salyut-5*, 1976), eye irritation from LiOH canisters and payload chemicals, and formaldehyde and ammonia from an overheated refrigerator motor (the space shuttle), as well as ethylene glycol and fumes from a fire (*Mir*).

Sources of physical, chemical, and microbiological contaminants include humans and other organisms, food, cabin surface materials, and experiment devices. One hazard is the outgassing of vapors from plastics and other items on the ISS. Although this is a minor hazard, the accumulation of these contaminants in the air can prove dangerous to crew health. The air sampling systems on the ISS periodically check the air for potential hazards. Advanced high efficiency particulate air (HEPA) filters and periodic filter cleanings have proved successful in keeping harmful vapors out of the air.

Spacecraft also build up a diverse array of microorganisms that directly interacts with the crew. Most micro-organisms are harmless or even beneficial to the crew. However, the presence of medically significant organisms appearing in this environment could adversely affect crew health and performance during long-duration missions. Microorganisms can be responsible for infectious diseases, toxin production, allergies, food spoilage, plants diseases, material degradation, and environmental contamination.

New collection and analysis techniques have been developed to improve the quality of the environment on board the ISS. These studies use modern molecular biology, advanced microscopy, and immunochemical techniques to examine air, surface, and water samples for bacteria and fungi, pathogenic protozoa, allergens, and microbial toxins (Figure 8.2). Air samples are collected through a novel gelatin filter to improve collection efficiency. These filters can retain particles that are as small as viruses. Water and surface samples are analyzed in-flight for bacterial fingerprinting, bacterial

Figure 8.2. An ISS Crewmember Conducts a Surface Sampling in the Destiny Laboratory of the ISS for an Onboard Microbiological Analysis. (Credit NASA).

and fungal ribosomal identification, and identification of specific genes that can produce microbial toxins. For example, the volatile organic analyzer (VOA) is an atmospheric analysis device on ISS that uses a gas chromatograph and an ion mobility spectrometer to detect, identify, and quantify volatile organic compounds (i.e., ethanol, methanol, and 2-propanol) that are harmful to humans at high levels in a closed environment. Some samples are also returned to the ground and evaluated using electrophoresis for the identification of bacteria without any amplification of organisms with growth on media [Vesper et al., 2008].

During one recent study of the ISS atmosphere, 12 bacterial strains were isolated and fingerprinted from the water system. These bacteria consisted of common strains and were encountered at levels below 10,000 colony-forming units/10 cm^2, i.e., well below the minimum level of bacteria that would cause illness. These data indicate that the lessons learned from previous *Mir* and *Skylab* missions were implemented and have been effective in keeping the ISS a safe place in which to live and work [Castro et al., 2004].

Microbial examination of the drinking water in various stages, from preflight assembly to the ISS ports, has revealed that the biocide treatment has effectively removed pathogenic microbes. Studies on ISS air quality found that the active (VOA) and passive (HEPA filters) controls are effective in controlling trace contaminants of volatile organic [La Duc et al., 2004]. In another analysis, 39 mold species were identified in the dust collected from the HEPA filters on board the ISS. Because some molds pose health risks, including infections and allergic reactions, and others break down organic substances that could compromise parts of the ISS hardware, understanding the mold populations on the ISS is important [Vesper et al., 2008].

Planetary protection of the Earth and other Solar System objects from a possible contamination source is another major issue. The living bacteria found on one camera of the *Surveyor-3* probe on the Moon (see Chapter 2, Section 2.1.1) is evidence that contamination can also occur with unmanned vehicles. Careful mission design and

Figure 8.3. The Quarantine for the Apollo Astronauts Returning from the Moon Was Only Used After the First Two Lunar Landing Missions. (Credit NASA).

planning are essential to prevent contamination. Spacecraft and their components must be cleaned very carefully, and sometimes sterilized. After cleaning, a spacecraft must be tested to ensure that cleanliness requirements have been met and can be maintained until launch. Sterilization of the entire spacecraft may be required for landers and rovers with life detection experiments, and for those landing in or moving to a region where terrestrial microorganisms may survive and grow, or where indigenous life may be present. For other landers and rovers, the requirements would be for decontamination and partial sterilization of the landed hardware (Figure 8.3).

Future Mars explorers will need to monitor and restrict biological contamination before, during, and after their extra-vehicular activities. Despite careful screening and quarantine, a crewed spacecraft always contains plenty of biological material, and it can't all be eliminated. Quick bio-monitoring tests of spacesuits such as LOCAD-PTS (see Section 4.1.3) can be used to ensure that humans are not about to taint the Red Planet and its potential life forms with human microorganisms. Not only would this lead to a contamination of the Mars environment, but it would also complicate the search for extra-terrestrial life that might exist in ecological niches. Conversely, returning humans or soil and rock samples from Mars might contaminate species on Earth, although scientists regard the possibility as extremely remote.

Because of these possibilities, several nations have signed the Outer Space Treaty and agreed that "State Parties to the Treaty shall pursue studies of outer space, including the Moon and other celestial bodies, and conduct exploration of them so as to avoid their harmful contamination and also adverse changes in the environment of Earth resulting from the introduction of extra-terrestrial matter and, where necessary, shall adopt appropriate measures for this purpose". The Outer Space Treaty resembles the Antarctica Treaty, which has shielded Antarctica from all sorts of exploitation, including mining and nuclear testing. According to the Antarctica Treaty people can face large fines or imprisonment back in their home countries for bringing contaminants (including personal items such as fragrances) to the Antarctic islands, for harming or harassing wildlife, or for taking rocks or shells as souvenirs. Obviously, human missions to Mars include plans for drilling, using in-situ resources, searching for life, and bringing back rocks and samples. There is a plenty of work for lawyers and policy makers to ensure that these activities will comply with the Outer Space Treaty!

8.3. Major life support system functions

The major functions of a life support system for space missions are listed in Table 8.2. The importance of each subsystem clearly depends on mission duration. For example, water production, treatment of waste, food storage, and trace contaminant monitoring and control are not absolutely necessary for missions of less than 12 h. Water can still be resupplied for missions lasting up to 1 week, but water production would save a lot of mass. Protection against radiation and environmental contaminants are then required. For missions ranging from 12 days to 3 months, water recycling, monitoring of water quality, nutritional control, dust removal, and a thermally conditioned storage quality become of paramount importance. Finally, for a mission longer than 3 months, the waste management system must be fully operational, including treatment and degradation of waste, and the recycling of byproducts. Plant growth facilities would also significantly contribute to food production and water recycling.

8.3.1. Atmosphere management

The function of the atmospheric revitalization and control subsystem is to continuously control temperature and humidity, and to regenerate the atmosphere. It also

Table 8.2. Major Functions of a Life Support System.

Atmosphere Control

- Gas storage, recovery and generation
- CO_2 removal
- Trace contaminant monitoring and removal

Temperature and humidity control

- Cabin ventilation
- Equipment cooling

Water and food management

- Processing, storage and distribution
- Microbial control

Waste management

- Collection and storage of human waste
- Trash

Crew safety

- Fire detection and suppression
- Radiation shielding

monitors and removes the harmful trace contaminants that are generated by the crew and the equipment. The latter function was discussed in Chapter 7, Section 7.4.3.1.

The primary source of oxygen is water electrolysis, which is the process that uses electricity from the ISS solar panels to split water into hydrogen gas and oxygen gas. The hydrogen is vented into space. Eventually, a system that combines the hydrogen with excess carbon dioxide from the air in a chemical reaction that produces water and methane will be used. The water would be used to partially replace the water used to make oxygen, and the methane would be vented to space. Other uses for the methane are being considered, including expelling it to help provide the thrust necessary to maintain the ISS in its orbit. The ISS also has large tanks of compressed oxygen mounted on outside that serve as a backup oxygen supply.

In case of failure of the electrolysis system, the crew can also breathe oxygen from "perchlorate candles", which produce oxygen via chemical reactions inside a metal canister. This is exactly the same technology that is used in commercial aircraft when the oxygen mask drops down. Each canister releases enough oxygen for one person for 1 day.

Carbon dioxide is removed from the air by a machine on the *Zvezda* Service Module, the basis of which is a material called "zeolite", which acts as a molecular sieve. The removed CO_2 is vented to space. In a regenerative system, CO_2 is not discarded, but reduced to produce useful components inside the system. Thus, the output from the CO_2 concentration subsystem is used as the input for the CO_2 reduction subsystem. Currently the main competing regenerative subsystems for CO_2 reduction are the Bosch process and the Sabatier process that will be operational on board the ISS in the near future. Other technologies that are being considered for CO_2 reduction are the reactor systems, electrolysis, and superoxides.

In addition to exhaled CO_2, people also emit small amounts of other gases. Methane and carbon dioxide are produced in the intestines, and ammonia is created by the breakdown of urea in sweat. People also emit acetone, methyl alcohol, and carbon monoxide in their urine and their breath. All of these chemicals are byproducts of metabolism. Activated charcoal filters are the primary method for removing these chemicals from the air [NASA, 2000].

8.3.2. Water management

The onboard water management system supplies the metabolic and wash water needed by the crew and collects atmospheric condensate and wastewater. The basic processes fall into two categories: distillation and filtration. While the distillation method is mainly considered for urine recovery, the filtration method processes hygiene and potable water.

It is anticipated that very long-duration space missions will include two water recycling and storage subsystems: one subsystem will process concentrated feeds, such as urine and flush water, and the second will process a more dilute feed, such as laundry or shower water. Potable water will probably be recycled using a phase change process while lower quality water will be recovered by filtration.

In addition to the subsystem designed specifically for reclaiming space habitat waste water, by-product water is derived from other space habitat subsystems, such as

Figure 8.4. The ISS Expedition-19 Crewmembers Hold Drink Bags with Special Commemorative Labels and Celebrate with a "Toast" the Drink Water That the New ISS Recycling System Has Purified. (Credit NASA).

H_2O_2 fuel cells, CO_2 reduction and the space habitat condensing heat exchanger used for cabin humidity control. Water from CO_2 reduction is of high quality because it is derived from a high-temperature process that destroys harmful bacteria. Also, the feed gases used for CO_2 reduction are clean. Water derived from fuel cells and the condensing heat exchanger may require post-treatment to remove chemical and biological impurities prior to being reused.

Life support systems on board *Mir* recycled the cosmonaut's sweat and water that condensed from exhaled air. Since May 2009, astronauts aboard the ISS drink water that has been recycled from their sweat and urine (Figure 8.4). The $250 million urine recycling system uses a process of distillation (with artificial gravity), filtration, ionization and oxidization "to turn yesterday's coffee into today's coffee." By producing about 2,700 l of potable water each year, this water recovery system is expected to cut the amount of water carried up to the ISS by 65%.

8.3.3. Food management

According to the values in Table 8.1, an astronaut needs about 0.62 kg (dry weight) of food per day. However, this amount may vary depending on the activity level at which he/she is operating. The caloric requirements are determined by the following formula for basal energy expenditure (BEE):

$$\text{Women BEE} = 655 + (9.6 \times \text{weight}) + (1.7 \times \text{height}) - (4.7 \times \text{age})$$

Table 8.3. Nutritional Requirements for a Typical Shuttle Mission. Note that these Numbers Represent the Nutrients Provided, not Consumed Calories [Phillips, 1997].

Nutrient	Quantity
Protein	0.8 g per day per kg (minimum recommended)
Carbohydrate	350 g per day
Lipid	77–103 g per day (less than 30% of calories)
Kilocalories	2,300–3,100

$$\text{Men BEE} = 66 + (13.7 \times \text{weight}) + (5 \times \text{height}) - (6.8 \times \text{age}).$$

Based on the activity levels of the astronauts, the estimated required energy ranges from 2,300 to 3,200 kcal/day. An additional 500 kcal/day are needed on EVA days. Diets for space missions are generally planned at caloric levels close to those needed for normal activity on Earth (Table 8.3). For missions lasting from 30 days to 1 year, the energy provided by each food group (nutrient breakdown) is the following: protein = 12–15%; carbohydrate = 50–55%; fat = 30–35%; fiber = 10–25 g/day; and fluid = 1.5 mL/kcal (>2 L/day).

Crewmembers assigned on a mission can select food from 150 items, (see Table 1.3 in Chapter 1). Most of the food onboard the ISS is frozen (i.e., most entrees, vegetable, and dessert items), refrigerated (includes fresh and fresh treated fruits and vegetables, extended shelf-life refrigerated foods, and dairy products), or thermostabilized (heat-processed, canned, and stored at room temperature) and does not require the addition of water before consumption. However, many of the beverages are in the dehydrated form. NASA's beverage package is a modified commercial-off-the-shelf package made from a foil laminate. Other types of food, such as fresh food and natural form food (ready-to-eat foods like peanuts), are also flown.[1]

All space foods are stored under ambient storage conditions and must safely maintain a shelf life of 9 months to 5 years. Whereas shuttle food was required to have a minimum shelf life of 9 months, ISS foods require a 1-year shelf life. All rehydratable and bite-sized food destined for ISS is overwrapped with an aluminum foil laminate and vacuum sealed to improve barrier properties, increasing shelf life (Figure 8.5). The food system for planetary outposts will require a 5-year shelf life because of the planned mission lengths. Each menu weights about 1.7 kg, out of which 0.5 kg is packaging. ISS food packaging waste is heavier, because of the additional aluminum foil laminate to increase shelf life. Thermostabilized pouches are used more frequently on the ISS than in shuttle missions, also adding additional food package weight.

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[1] The history of space food and the methods of food preservation and preparation used by NASA are described in a .pdf document "Space Food and Nutrition. An Educator's Guide With Activities in Science and Mathematics", EG-1999-02-115-HQ, which can be downloaded from the NASA web site at http://search.nasa.gov/search/edFilterSearch.jsp?empty=true [Accessed 8 October 2010].

Figure 8.5. Astronaut Koichi Wakata Is Pictured near Food and Drink Containers Floating Freely in the Harmony Node of the ISS. (Credit NASA).

Despite this variety, observations during long-duration missions suggest that individuals do not crave a continual variety in foods, but rather tend to select foods in the same small range or limited number over months, stretching out to a lifetime. In absence of in-flight diet logs (who has eaten what and when), caloric consumption is generally derived by assessing food that has disappeared, assuming an equivalent intake by each crewmember. Where data is available, it appears that crewmembers consume fewer calories than provided and recommended. Perhaps the dietary intake is inadequate. Some nutritionists claim that it represents only 60–70% of the recommended energy requirements [Lane and Schoeller, 1999]. This could explain in part the weight reduction in astronauts (see Chapter 5, Section 5.3.1).

The food system on board the ISS provides a 6–10 day menu cycle. Before each mission, crewmembers participate in food-tasting sessions, and dietitians plan menus using crew choices that best fulfill the defined nutritional requirements for spaceflight. In-flight, crewmembers are asked to record their dietary intake once per week using a Food Frequency Questionnaire (FFQ) designed to obtain a near-real-time estimate of intakes of energy, protein, water, sodium, calcium, and iron, as well as to collect information about vitamin supplement use and any crew comments. The questionnaire inputs from the astronauts are transmitted to the ground, and results are calculated and reported to the flight surgeon. As described in Chapter 5 (Section 5.3.1), body mass is also measured preflight, in-flight, and postflight, while body composition is determined pre- and postflight using laboratory measurements. Blood and urine samples are also collected pre- and postflight for analysis of whole blood, plasma, serum, and other components.

Data collected on several ISS missions are in agreement with those previously obtained on *Mir*: (a) the intake of energy (relative to World Health Organization standards) generally decreases over time during missions, body weight decreases during flight; (b) antioxidant capacity decreases during flight, leading to increased susceptibility to genetic damage from radiation; and (c) blood concentrations of some nutrients, such as vitamin D, continue to be low even when astronauts receive supplements during flight [Smith and Zwart, 2008].

In the past, many athletes and astronauts were convinced that high protein intake builds muscle and strength. However, the physiological evidence indicates that protein is increased in muscle only when needed for the muscle hypertrophy required by continuing physical activity; excess calories of any kind are converted to and stored in the body as fat. In addition, numerous previous studies unrelated to space have indicated that increasing the protein intake increases the urinary excretion of calcium. Because this would add to the bone demineralization and the potential for kidney stone formation, the level of protein in the diets of astronauts, therefore, needs to be monitored [Smith et al., 2005]. Some degree of uncertainty exists as to whether the high phosphate content of meat is partially protective against the effect of high protein intake to increase urinary calcium. At the same time, there is concern not to accentuate the negative nitrogen balance associated with muscle atrophy in weightlessness by encouraging too low a protein intake. Because a negative nitrogen balance in space has occurred at daily protein intakes of 85–95 g, the recommended intake should not fall below this level [Phillips, 1997].

A clinical nutritional assessment study is currently ongoing on all ISS crewmembers by means of blood and urine collection (Figure 8.6). On ISS missions earlier than *Expedition-14*, it was not possible to assess nutritional status during flight because blood and urine could not be collected, stowed frozen, and returned. In addition to monitoring crew nutritional status during flight, in-flight sample collection allows for better assessment of countermeasure effectiveness. For example, additional markers of bone metabolism and insulin-like growth factor are measured to better monitor

Figure 8.6. Astronaut Robert Thirsk Inserts Urine Samples into the Minus Eighty Degree Laboratory Freezer for ISS (MELFI) as Part of a Nutritional Status Assessment Study in the Kibo Laboratory of the ISS. (Credit NASA).

bone health and countermeasure efficacy. The array of nutritional assessment parameters was also expanded to include markers of oxidative damage, serum folate, plasma pyridoxal 5'-phosphate, and homocysteine to better understand changes in folate, vitamin B6 status, and related cardio-vascular risk factors during and postflight. Additionally, stress hormones and hormones that affect bone and muscle metabolism are also measured for more accurate recommendations to be made for crew rehabilitation Smith, 2010].

It is well known that under time pressure, astronauts often prefer to consume snacks, i.e., foods rich in carbohydrate, at their workplace rather than a full meal in the galley. However, carbohydrates are of special concern because any dietary carbohydrate that elicits the secretion of insulin can, unless consumed with adequate amounts of protein, increase the synthesis and release of the brain neurotransmitter serotonin. This substance makes people drowsy and interferes with optimal performance. Menus and the time of consumption of particular items, especially snacks, might not be appropriate to the tasks required, particularly if they are complex and prolonged. It is possible that other food constituents also affect behavior, mood, and cognition. As carbohydrates are the likely products of future chemical synthetic systems, it is important to determine the type and maximum amount of carbohydrate that should be reasonably contained in a human diet.

Because no studies have yet been made on the effects of spaceflight on the metabolism of any of the trace elements, no comment can be made other than that care should be taken that space diets contain trace elements in the amounts recommended by the nutritional standards.

The important vitamin during long spaceflights is vitamin D, the "sunshine vitamin". Enclosure in a space vehicle prevents the normal conversion in the skin of the vitamin-D precursor to vitamin D. This is normally accomplished by exposure of the face and arms to as little as 20–30 min of sunlight a day. Because vitamin D is essential for facilitating calcium absorption from the intestine, as well as other calcium-related effects in kidney and bone, a surplus of this vitamin needs to be supplied to astronauts. The space recommended dose is 10 μg/day, whereas the Earth recommended dose is 5 μg/day.

Other vitamins are not so critical because it is expected that an adequate amount is taken in the diet, provided it is "balanced" and the vitamins are not degraded by the methods of food preservation in use. It has become customary, however, to provide astronauts with daily vitamin supplements.

In the early days of planning for human spaceflight, scientists believed that diets should be low-residue in character so that bowel movements would be small and infrequent. It was observed especially in longer flights that bowel function in microgravity is essentially normal. Hence diet is normal in residue, and adequate bulk is available to afford relatively easy passage of stools once or twice a day.

The ISS experience will help to make sure that there will be adequate and satisfactory food selection and storage for the 3-year flight of a human mission to Mars. The lessons learned form the ISS will also provide guidelines for future completely closed ecological life support systems and in particular for quantities of food to be produced by these systems.

8.3.4. Hygiene

Skylab had a shower: while standing in a collapsible, cylindrical cloth bag, the astronauts squirted warm water on themselves using a water gun and scrubbed with liquid soap. In practice, the shower was a failure because the two other crewmembers had to spend valuable time vacuuming water that escaped into the air and equipment. There is no shower on the shuttle or the ISS, and there will probably not be a shower on the spacecraft en route to Mars. Instead, crewmembers use sponge baths. According to the training procedure, astronauts draw a curtain from the toilet door to the side of the galley for privacy. A washbasin on the side of the galley provides warm water and a soap dispenser. Above the basin are a mirror and a light, and on the wall are strips of tape to attach towels, washcloths and personal hygiene items. One cloth is used to wash, and another to rinse. At the rear of the basin is a fan that pulls the excess water toward a drain that leads to the wastewater tank under the floor. The washcloths and towels go into the bag hanging on the bathroom door.

As there is no washing machine on board, trousers (changed weekly), socks, shirts, and underwear (changed every 2 days) are sealed in airtight plastic bags after being worn. Garbage and trash are also sealed in plastic bags.

The toilet (or waste collection system) is in a private room. To remain seated, the user must insert his boots into foot restraints and snap together the seatbelt waist restraint. There are also handholds. Instead of water to flush away solid wastes, this toilet relies on a fan that draws away the “wastes” from the user and sends “them” to a compartment below. There, it is dried and disinfected. Urine is drawn into a contoured cup and flexible hose by airflow and the fluid is pumped into the wastewater tank under the floor.[2]

8.3.5. Radiation shielding

Our life on Earth has a most bittersweet relationship with radiation. Our human existence has been vitally shaped by solar radiation by providing us with food and energy. Visible and non-visible radiation from the depths of the universe is responsible for illuminating us with a glimpse of our origins. Radiation also has a deadly face as seen by human use of atomic bombs in past history, by nuclear reactor disasters, and by the fear of skin cancer caused by ultraviolet radiation. Perhaps for these reasons it is often claimed that radiation provides the greatest obstacle (“show stopper”) to interplanetary missions.

In low Earth orbit, crewmembers are protected from ionizing radiation by the Earth’s magnetic field. However, they will be exposed to significant heavy ion radiation during interplanetary missions or while inhabiting a Moon or Mars base. This exposure could have disastrous effects on the central nervous system, because heavy ion radiation has been shown to inflict “single hit” damage, even death, on non-dividing cells. These aspects are reviewed in the following section.

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[2] The Russian supplied toilet paper is not like what one normally thinks of as toilet paper. It consists of two layers of coarsely woven gauze, 10 by 15 cm in dimension sewn together at the edges with a layer of brown tissue sandwiched in-between. According to the astronauts, “it works very well for its intended purpose” [Pettit, 2003].

8.3.5.1. Space radiation environment

Space radiation, including its physics and the concepts of radiation dose and protection, has been reviewed in details in Eckart [1996] book. We will only summarize the sources here, to introduce the section on the medical issues of space radiation.

There are basically three sources of naturally occurring space radiation that can be hazardous to human spaceflight: the geomagnetically trapped proton and electron environment in the Van Allen belts, galactic cosmic radiation, and solar particulate radiation (see Figure 2.22).

The Van Allen belts consist of high-energy protons (approximately 1 keV to several 100 MeV) and electrons (approximately 1 keV to several MeV) trapped in the geomagnetic field. The proton belt extends to an altitude of approximately 20,000 km, with peak intensities occurring at approximately 5,000 km. The electron belts extend to an altitude of 30,000 km with peaks at about 3,000 and 15,000 km. Models of the trapped proton and electron environments have been developed from satellite measurements.

Galactic cosmic radiation (GCR) consists of extremely energetic (up to 1,013 MeV) ionized nuclei (or HZE particles, for “high charge and energy ions”) ranging from hydrogen to uranium and originating outside the Solar System. Models of the GCR environment have been generated from geostationary satellite and high-altitude balloon measurements.

Solar radiation, or solar particle events (SPE), consists of high-energy particles, predominately protons ejected from the Sun usually during solar flares. Solar activity has an 11-year cycle, during which a tenfold variation in the frequency of SPE has been observed. No reliable physical model can predict the timing or magnitude of solar flares occurrence with acceptable accuracy. This feature makes SPE a significant hazard in long-duration space travel. Additionally, solar flare activity can substantially increase the fluence of HZE particles, at least up to energies of a few 100 MeV per nucleon.

Radiation exposure in low Earth orbit, where the shuttle and ISS orbits lie, comes primarily from the proton and electron belts and GCR. Trapped-radiation exposure increases with altitude and varies with orbital inclination. GCR exposure also varies with orbital inclination. The geomagnetic field provides some degree of protection from SPE, depending on the orbital inclination; flux is almost totally eliminated for a 28° orbit and reduced to about 30% of the free space flux for polar orbit.

Exposure at geosynchronous (GEO) altitude will be primarily from bremsstrahlung (x-rays) created by the trapped electrons as they interact with spacecraft shielding (see Figure 2.23). The electron environment at GEO has a diurnal fluctuation, and intensities can increase by several orders of magnitude with magnetic storm activity. GEO is also susceptible to the full exposures from GCR and SPE, as are lunar and interplanetary missions.

8.3.5.2. Spacecraft radiation environment

In addition to specific lifetime radiation limits, medical standards specify that radiation doses that are achieved by astronauts should be as low as reasonably achievable (ALARA). To create new and improved shielding for EVAs, researchers must know the type and flux of radiation inside and outside the spacecraft.

Incoming radiation from space is modified as it passes through the body of a spacecraft and any additional shielding that may be present (see Figure 2.23). The biological effects of radiation must be determined, therefore, by starting with this modified spectrum. The physical principles by which radiation interacts with matter are well known, but the way to combine these principles to form a good model of the resulting secondary spectrum is not. HZE and SPE can also cause problems in electronic components (the so called "single event upset").

A substantial amount of data obtained from various forms of dosimetry on board Apollo, *Skylab*, the shuttle, *Mir*, and ISS missions (such as the phantom torso described in Chapter 2, Section 2.5.2) has provided measurements of radiation exposures. Models derived from these biodosimetry measurements suggest a high level of accuracy in predicting dose-equivalent for a human Mars mission (Figure 8.7).

Interactions of ionizing radiations with the ISS structure and its contents create a somewhat different radiation field at each location inside the ISS modules. This is in part due to a large contribution from the secondary radiation that is created by particles colliding with the spacecraft materials. Four types of detectors are used on board the ISS: (a) thermo-luminescence dosimeter chips; (b) CR39 nuclear track detectors with and without converters; (c) a silicon dosimetry telescope; and (d) four silicon mobile detector units. Crewmembers have used the mobile detector units as personal dosimeters. They have provided the ability to measure spectral composition with respect to nuclear charge, energy, rate of energy deposition, as well as to estimate the absorbed dose from galactic radiation, radiation belt particles, and solar particle events.

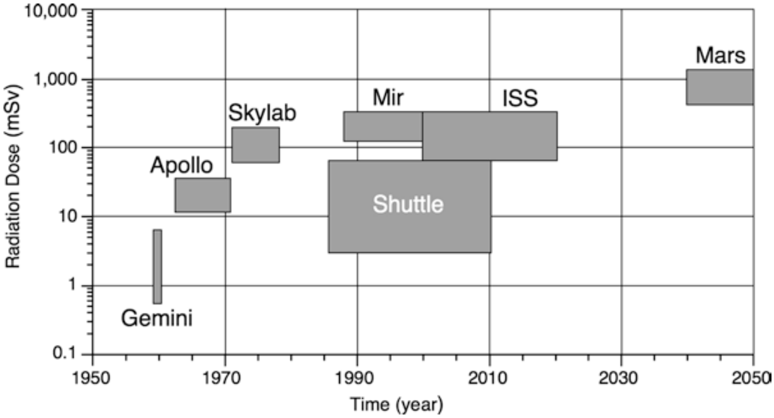

Figure 8.7. Average Radiation Biological Dose-Equivalent for Astronauts on all NASA Space Missions, and Prediction for a Human Mars Mission. The Standard Unit (SI) of Absorbed Dose Is the Gray (Gy) with 1 Gy = 100 rad. One Gray is the Amount of Ionizing Radiation Corresponding to 1 J Absorbed by 1 kg of Material. Note That 1 Gy from High-Energy Protons Is the Same as 1 Gy from X-Rays (One Chest x-Ray = 1 mGy). Because the Biological Effects Are Different for the Various Types of Radiation, the Concept of Dose Equivalent Unit Has Been Introduced, Which Takes into Account a Quality Factor Depending on Tissue Interactions with Various Radiations. The Sievert (Sv) Is the Dose-Equivalent SI Unit for Humans (1 Sv =100 rem). (Sources: Comet, 2001; Durante, 2002; Cucinotta et al., 2008).

In general, radiation damage to the human body is indicated by the amount of energy that is deposited in living tissue, modified by the type of radiation causing the damage; this is measured in units of Sv. The background radiation dose that is received by an average person in the U.S. is approximately 3.5 mSv/year. An exposure of 1 Sv/h can result in radiation poisoning, and a dose of 5 Sv/h will result in death in 50% of exposed individuals [Reitz et al., 2005]. The average radiation dose received for a 6-month stay on the ISS ranges from 72 to 330 mSv. The majority of radiation energy that is deposited in human tissues (~85%) is due to galactic cosmic radiation. The remaining 15% of the tissue-damaging dose (effective dose) is from the short-ranged neutrons and protons that are created within the spacecraft materials. Post-mission biodosimetry assessments of chromosomal damage in lymphocyte cells from ISS astronauts who flew near the solar maximum and near the solar minimum, indicated that the solar maximum decreased the GCR levels [Cucinotta et al., 2008].

By comparing the radiation dose as measured by instruments aboard the ISS and by those of the Odyssey's Martian radiation environment in orbit around Mars, it was calculated that the accumulated total radiation in Mars orbit is about two and a half times larger than that aboard the ISS (Figure 8.8).

Outside the spacecraft, the EVA Radiation Monitoring (EVARM) experiment has investigated the dose that is received by different parts of the body, including skin, eyes, and blood-forming organs during an EVA. This is accomplished by measuring dose rate based on the time and position of EVAs as compared to the orbit, altitude, and attitude of the ISS. Spacewalkers wore dosimeters that were placed inside the suit, around the calf, and above the eye. Dosimeters were tiny silicon chips that build up a positive charge when exposed to ionizing radiation. The results from EVARM have shown that EVA doses are more elevated from those inside the ISS, but not significantly.

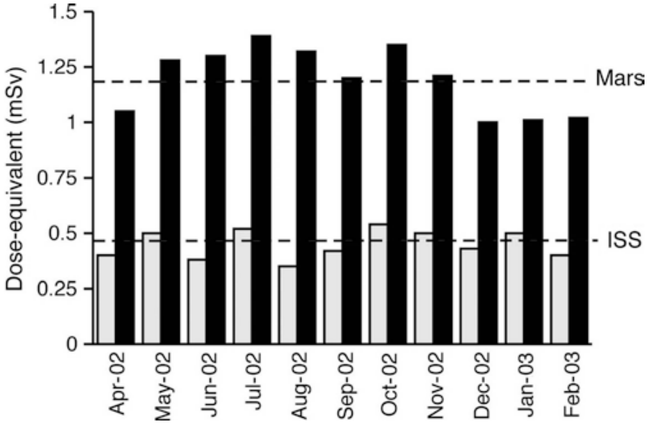

Figure 8.8. Comparison Between Radiation Dose Equivalent on the ISS and in Mars Orbit for an 11-Month Period. The Accumulated Total in Mars Orbit Is About Two and a Half Times More Than That Aboard the ISS. About 10% of the Dose Equivalent at Mars Is Due to Solar Particles. Note the Increase in Radiation in Mars Orbit During the Summer 2002 When the Sun Was Particularly Active. (Source: http://www.spaceref.com/news/viewsr.html?pid=8355).

During increased geomagnetic activity, doses were increased due to elevated levels of electrons in low Earth orbit. These electrons are easily shielded by spacecraft materials and, thus, not measured inside the ISS. Fortunately, proper positioning of the spacecraft can dramatically reduce the radiation field that is encountered during EVA missions [Badhwar, 1997]. The data also indicates an average radiation quality factor (a measurement of how damaging a type of radiation is to tissue) of 2.6; these quality factors do not appreciably change with depth in the body.

8.3.5.3. Medical effects of radiation exposure

When highly charged particles, for example electrons or protons, contact living tissue, they have the ability to ionize molecules like water or oxygen. This reaction produces highly reactive products called free radicals, which can inflict much damage to cellular components. The most significant effects stem from interaction with DNA and other "controlling" macromolecules. There are primarily two effects of radiation, a short-term and a long-term effect. The short-term, also known as the "acute radiation syndrome," may cause nausea, a decrease in blood count, or even death if the dose is high enough. The long-term effect is known as a stochastic risk and predominantly involves cataract or cancer formation.

Tissues vary in response to immediate radiation injury. The tissues with higher cell turnover are the most vulnerable. Here is a list of susceptible tissues arranged in descending order of vulnerability: lymphoid, gonad system, bone marrow, epithelial cells of the gastro-intestinal system, epiderm, hepatic tissue, pulmonary alveoli, and biliary epithelium. The DNA effects include decreased mitotic (division) rate, and impaired synthesis with abnormal progeny cells and cell lines (cancer). However, a high enough dose will induce necrosis in any tissue.

Acute Radiation Syndrome – Although most space radiation doses will be low, a very large solar particle event can expose astronauts to high-dose radiation, which can produce clinically significant effects. These effects are non-stochastic: the severity of the effect increases with dose above some effective threshold. The Acute Radiation Syndrome (Table 8.4) at sub-lethal doses is characterized early on by transient anorexia, nausea, vomiting, and diarrhea. Later, the survivors may suffer temporary or permanent sterility and cataracts, as well as cancer. Lethal doses lead to bone marrow suppression and immune system malfunction, which leads to death in 30–60 days. These high doses lead to severe gastrointestinal disturbances in 1 day to 1 week. Extreme doses can produce central nervous system derangement in a matter of hours. The Acute Radiation Syndrome has been studied extensively in animal models, but the human clinical experience is extremely limited.

Long-Term Effects – There are very severe implications when cellular DNA (the "blue prints" of the organism) is affected by either free radicals or by the radiation particle itself. If certain regions of DNA are damaged, then that particular cell may undergo uncontrolled cell division, which later manifests itself in the gross scale as cancer. There are two major compensatory mechanisms that attempt to avoid this outcome. The first method is that if the cell is damaged enough, then it undergoes a morphological set of events from nucleus shrinkage, condensation, and ultimately DNA fragmentation. This sequence, called apoptosis, is basically a mode of carefully orchestrated cell death.

Table 8.4. Symptoms and Time Course of the Acute Radiation Syndrome.

Dose (Sv)	Probable Medical Effects
0.1–0.5	No effects except minor blood changes
0.1–1	5–10% subjects experience nausea or vomiting; fatigue for 1–2 days; slight reduction in white blood cells
1–2	25–50% nausea and vomiting, with some other symptoms; 50% reduction in white blood cells
2–3.5	75–100% nausea, vomiting, fever, with anorexia, diarrhea, and minor bleeding; 75% reduction in all blood elements. 5–50% subjects will die
3.5–5.5	100% nausea, vomiting, fever, bleeding diarrhea, and emaciation. Death of 50–90% in 6 weeks. Survivors require 6-month convalescence
5.5–7.5	100% nausea and vomiting in 4 h. 80–100% die
7.5–10	Severe nausea and vomiting for 3 days. Death within 2.5 weeks
10–20	Nausea and vomiting within 1 h. 100% subjects will die within less than 2 weeks
45	Incapacitation within hours. 100% subjects will die within 1 week

The other mechanisms involve natural molecular level processes, such as the p53 gene. This gene is known as the "guardian of the genome" because it codes for a protein making the cell to pause before it undergoes mitotic division. This pause allows for the DNA repair mechanisms to function so that any damage can be repaired before the ensuing DNA replication and following cell division. But if this gene is damaged, then cancer may result. The cancer projection model of NCRP Report No. 132 [NCRP, 2000], which can be applied to the effective measured doses in Figure 8.7, indicates Risk of Exposure-Induced Death (REID) values approaching 1% for many astronauts who have flown on *Mir* or the ISS [Cucinotta et al., 2001].

8.3.5.4. Exposure limits

The biological effects of ionizing radiation have been extensively studied for almost a century. The data come from studies of controlled irradiation of cell cultures, small and large animals, and non-human primates, as well as from retrospective studies of humans exposed to nuclear weapons blasts, radiation used for medical treatment, and nuclear occupational hazards. However, most of the information has been obtained with low linear energy transfer (LET) radiation such as x-ray, gamma ray, and electron radiation. Separated clusters of ionization along the path of the primary photon or electron characterize the low-LET radiation. In contrast, high-LET radiation, such as stopping protons, secondary-stopping protons from neutrons, alpha particles, and energetic heavy multicharged particles, is densely ionizing.

It has been known for decades that a given amount of energy deposited by high-LET radiation could be several times more damaging than the same amount of energy deposited by low-LET radiation. Because of the higher relative biological effectiveness of high-LET radiation, a quality factor (QF) is applied to occupational doses (in physical units) to obtain a weighted unit for assessment of radiological health risk (or dose equivalent). For example, the QF for neutrons from a nuclear reactor would be about ten.

More generally, the assumed linear relationship between absorbed dose and observed biological effect has come into question for HZE particles or high-LET particles in general. Since the manner in which energy is deposited in tissue by HZE particles is so different from that of low-LET particles, this linearity may not apply to HZE particles. Of current interest has been the "microlesion" concept. This theoretical model of the interaction of heavy particles with biological tissue has raised the question of a whole new spectrum of biological damage, including damage to non-dividing cells, particularly the central nervous systems. It appears that the microlesion concept is worthy of further investigation, as there may be significant consequences in long-duration spaceflight (>3 years) if an accidental underestimation of the effect of HZE particles is made.

The assessment of the health risks for various missions and thus the operational limits for such missions are dependent on QF, which in turn will be greatly dependent on the evaluation of biological damages (life shortening, tumor induction, chromosome abnormalities, mutation, and so on). The database using space-type radiation for such assessments is very small. Also, the current knowledge of the GCR hazard is inadequate because of the poor understanding of the effects of HZE particles on biological tissue.

Table 8.5 shows the best currently available estimates of cancer risks for the effects of 1 Sv of radiation spread over 10 years. These radiogenic cancer risk estimates have served in part as the basis for the set of astronaut radiation exposure limits being recommended to [NASA, 2005]. These limits are shown in Table 8.6.

The female astronaut brings special concerns for several reasons. In general, her overall body size and organ sizes are smaller than those of her male counterpart (thus her radiation doses will be higher, given the same amounts of administered activity and similar biokinetics); her gonads are inside of her body instead of outside, and are located nearer to several organs often important as source organs in internal dosimetry (urinary bladder, liver, kidneys, intestines); her risk of breast cancer is significantly

Table 8.5. Cancer Morbidity and Mortality by Age Group and Gender, with and without Radiation. A: Lifetime Incidence (%) Unirradiated; B: Additional Incidence (%) from 1 Sv; C: Lifetime Mortality (%) Unirradiated; D: Additional Mortality (%) from 1 Sv. The Risk of Developing a Fatal Cancer Increases by 1–3% with a dose of 1 Sv (Sv) of Radiation Spread over 10 years. 1 Sv at 0.1 Sv/year for 10 years Starting at Indicated age. Source: U.S. National Council on Radiation Protection [2000].

Gender	Age	A	B	C	D
Male	25	34.9	3.10	18.5	1.99
	35	35.2	1.84	18.7	1.20
	45	35.5	1.38	18.9	0.92
	55	35.4	1.12	18.7	0.75
Female	25	35.6	6.24	15.7	2.93
	35	35.2	3.50	15.5	1.70
	45	33.9	2.22	15.1	1.19
	55	30.8	1.73	13.9	0.99

Table 8.6. Astronaut Ionizing Radiation Exposure Limits for Non-Cancer Risks (in Sv).

Depth	BFO	Skin	CNS	Heart	Lens
30-day limit	0.25	1.5	0.5	0.25	1
1-year limit	0.5	3	1	0.5	2
Career limit	1–4[a]	6	1.5	1	4

BFO blood-forming organs, *CNS* central nervous system.

[a] The career dose-equivalent is based upon a maximum 3% lifetime risk of cancer mortality. The total dose equivalent yielding this risk depends on gender and on age at the start of exposure. The career dose equivalent limit is approximately equal to 2 + 0.075 (age 30) Sv, for males, up to 4 Sv maximum; and 2 – 0.075 (age 38) Sv, for females, up to 4 Sv maximum [NCRP, 2006].

higher than that of her male counterpart; and in the case of pregnancy, very little is known about how much activity may cross the placenta and expose the embryo/fetus and the nursing infant.

Within these dose limits, the risk a crewmember developing cancer from space radiation during his or her lifetime is 3%. However, the genetic effects for crewmembers of childbearing age (especially women) become increasingly possible.

In low Earth orbit, it is unlikely that any astronaut will receive 1 Sv over a career. However, in a high orbit or during interplanetary travel, where a rapid evacuation is not possible, an Acute Radiation Syndrome could result from a solar particle event without adequate shielding. It is estimated that the 1 Sv value will be approached during a 3-year Mars mission, given currently used quality factors and average shielding of 10 g/cm^2. During a Mars mission, the total dose could reach 0.8–2 Sv, including 0.2–0.8 Sv per year due to GCR and 0.3 Sv per year due to one large SPE.

It is obvious that the threat of cancer to astronauts after a prolonged mission is a serious issue (Figure 8.9). In Zubrin's opinion, every 0.6 or 0.8 Sv (female and male values respectively) of radiation absorbed over extended periods of time only adds a 1% increased chance of fatal cancer later in life to a 35-year old adult [Zubrin, 1996]. Thus, based on these results, a spacecraft with today's technology in terms of shielding and having a safe-haven interior shelter for the crew in times of solar flares would be able to house a crew to Mars within acceptable radiation limits. On the other hand, experiments have shown that DNA damage repair occurs at a reduced rate in yeast in microgravity [Pross et al., 1994]. These results magnify the radiation risk.

Other stochastic effects involve cataract formation in the eye lenses of astronauts and central nervous system effects. To date no Russian cosmonauts who have undergone long-duration missions have had cataracts, but the problem is still a potential risk. As a countermeasure, antioxidants in the diet of the astronauts could be extremely helpful of warding off the ill effects of radiation. Vitamin E, vitamin C, and beta-carotene are well-known and effective antioxidants. Novel and new flavanoids, such as venoruton, have also been shown to decrease cataract formation in rat models [Kilic et al., 1996].

Calculations have been made that indicate that the cell nucleus in every single cell in the body would be hit by a proton once every 3 days, given a nuclear area of 100 mm^2, as a result of the background cosmic radiation [National Research Council, 1996].

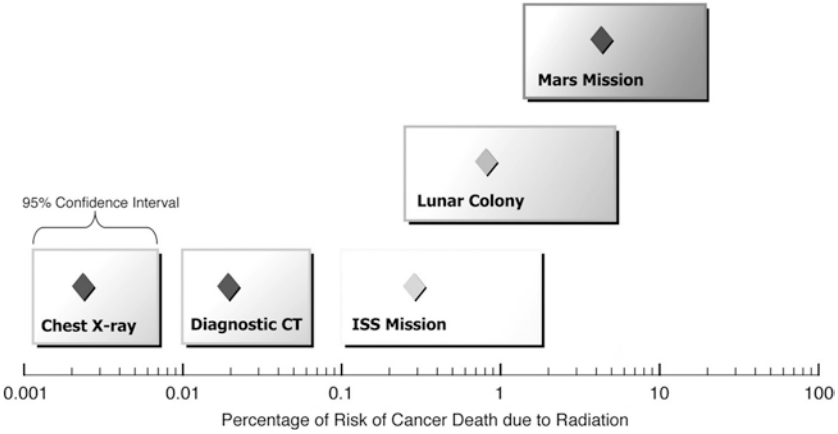

Figure 8.9. Current Estimates of Cancer Risks (*Diamonds*) and 95% Confidence Bands for Adults of Age 40 years (Which Is the Typical Age of Astronauts on Space Missions) for Several Terrestrial Exposures and Missions on the ISS as Well as Projections for a Lunar Colony and a Mars Mission. Uncertainties in Risk Projection for Terrestrial and Space Exposures. (Adapted from Cucinotta et al. [2008]).

The effects of this are unknown, but there is concern that there may be substantial effects on the nervous system due to changes in transcription rate and function of proteins.

Not much research can be done safely on Earth to investigate these radiation effects, because cosmic rays are difficult to generate, and no one would consent to being exposed to a theoretically fatal dosage. The ISS provides a good testing ground, given that a large number of astronauts are exposed to modest amounts of radiation during their 6-month tours of duty. However, a full investigation might require waiting decades until these astronauts retire and die either of natural causes or of cancer. Obviously Mars mission advocates have no intention of waiting that long. It actually makes the most sense to accept the radiation risk on the Mars mission. After all, it is a journey into the unknown and the risk of radiation is mild compared to the dangers that explorers on Earth have faced in the past, and overcome [Reifsnyder, 2001].

8.3.5.5. Radiation countermeasures

Prevention – Various solution strategies exist or have been proposed that attempt to counteract the deleterious effects of radiation: (a) as a preflight measure, a bone marrow sample could be obtained from the astronaut so that it could be used to regenerate the bone marrow, should the astronaut be inflicted with cancer at a later time; (b) another possible problem is that children conceived postflight might have a larger risk of birth defects due to their parent's higher radiation dosage. Thus, a proposed solution could be to cryogenically preserve the ova or sperm, from the female and male astronauts, so that they could be used in the future if and when desired; (c) another idea as a measure to decrease an astronaut's chance of getting cancer may be through astronaut selection. Given that certain oncogenes have hot spots that are especially vulnerable to damage and that cancer is not a one-mutation process, but is instead a multiple hit process, then the following potential solution could be considered. As molecular biology techniques are quickly advancing, it is not hard to imagine that certain loci on genes, which are especially vulnerable to becoming oncogenic, may be isolated. It then follows that astronaut candidates who have already had a mutagenic hit on this gene, may have a greater likelihood of getting cancer, and thus may be jeopardizing their future by embarking on an interplanetary mission; (d) other solutions include the use of radioprotective drugs. Some of these drugs have side effects, such as vomiting and vasodilatation, which result in hypotension, so that would pose a problem during spaceflight. New drugs that bind DNA and protect neural tissue may provide hope in terms of pharmacological solutions.

Monitoring – As already mentioned in Chapter 2 (Section 2.5.2), passive dosimeters are available on ISS to determine the space radiation dose at specific locations inside. At present, the information from these readers is returned to the ground and analyzed in a laboratory to obtain the LET spectrum. The LET spectrum is then combined with the dose information to determine a corrected total dose. Active dosimeter systems are also available on ISS for real time monitoring. Small chambers for biological specimens may be attached to the sensor unit. A tissue equivalent proportional counter and a charged particle directional spectrometer also have the capability for real-time data collection and viewing. They are mounted both inside the habitation module and outside.

Satellite Solar Flare Advanced Warning – In the event of a solar flare, protection of the crew and early detection are of extreme importance. Solar observatory satellites such as SOHO observe particles of solar, interplanetary, interstellar, and galactic origins; thus solar winds and flares, as well as cosmic radiation. Because these satellites are closer to the Sun than the spacecraft in LEO or en route to Mars, a solar event would be first sensed by the satellite and then the warning could be relayed directly to the crew onboard. This would provide life preserving valuable time to the crew, which would then undertake the necessary precautions, as will be discussed in the next section. During a solar flare, the electromagnetic radiation (x- and gamma rays) travels at the speed of light from the Sun towards the planets, so the satellite data would arrive too late. However, because the high-energy charged particles that inflict the bulk of the damage do not travel at the speed of light, a satellite-warning signal would be most useful.

Radiation Damage Repair – Recent evidence obtained by the cancer research community indicates that the multiphase process of biological damage (carcinogenesis) can be interrupted at various stages. For example, at the DNA damage or initiation phase, vitamin E and possibly vitamin A, beta-carotene and vitamin C (ascorbic acid) can protect (Figure 8.10). Several of the trace elements also have an antioxidant effect; these include copper, iron, manganese, selenium and zinc. Some data indicate that the promotion phase, in which a radiation-damaged cell changes to a potentially cancerous cell cluster and then goes on to the progression phase yielding a tumor, can be interrupted by agents such as dimethylsulfoxide or protease inhibitors. Implementation of the results of studies directed toward early detection of cancer could help improve the prognosis for crewmembers unfortunate enough to contract cancer. Before a Mars

Figure 8.10. Fresh Fruits Brought to the ISS by Progress or Soyuz Vehicles Are Rich in Vitamins That Can Protect Biological Damage Caused by Space Radiation. (Credit NASA).

Table 8.7. Time (in Hours) for Radiation Exposure to Reach the 30-Day Limit in the Blood-Forming Organs (BFO) and at the Skin and Eye Lens Levels Using Various Thickness of Aluminum Shielding.

Shield Thickness (g/cm^2 Al)	BFO	Skin	Lens
0.2	6.0	3.0	1.9
1.0	6.3	3.5	2.4
5.0	8.9	8.0	6.5

mission, mutagenesis and teratogenesis by high-LET radiation must be extensively studied. Mutation and developmental abnormalities are, like cancer induction, stochastic effects: the severity of the effect is independent of dose, but the probability of occurrence increases with dose. The mutation risk to future generations from the expected space radiation on Mars is apparently fairly low, but the available information is largely inadequate for assessing the teratogenic risks to fetuses [Bhardwaj, 1997].

8.3.5.6. Strategies in radiation shielding

In the prevention of high-dose acute radiation exposure, special shielding is the most commonly considered modality. Mass shielding is just the passive ability of bulk mass to inherently shield radiation (Table 8.7). A fundamental property of mass shielding is that the thickness must increase enormously as the energy of the radiation particle increases [Wilson et al., 1997].

In situations where it is not possible to de-orbit or lower the altitude of the spacecraft to a protected region of space, such as during the mission to Mars, the vehicle will most likely include a “storm shelter” or “safe haven,” where the crew will stay until the radiation has subsided to acceptable level. For such shelter, the use of food racks and water tanks packed around the walls to absorb the radiation, or a water-filled collapsible cocoon has been proposed. Fortunately most of a solar flare’s energy is in alpha- and beta particles that can be stopped with a few centimeters of shielding.

Cosmic rays are a different story. They are constantly present, coming from all directions. The radiation consists of heavy, slow moving atomic nuclei that can do far more damage to more cells than alpha and beta particles. This radiation requires several meters of shielding for complete blockage, and because the nuclei come from all directions at all times, unlike the brief solar flares that last only a few hours or days, a storm shelter would be insufficient to protect the crew.

Another solution for shielding is to create a magnetic field around the spacecraft capable of deflecting solar radiation. Technology using low temperature superconductor coils seems inadequate because it is too costly in terms of energy. However, new high temperature superconducting coils are promising because they can produce a high energy, low intensity magnetic field [Goldman, 1996]. One possible concern with this mode of protection is that there are still lingering concerns about the effects of magnetic field exposure to human tissue, especially neural cells.

For added protection in case a very large solar event occurs, partial body shielding of a small amount of bone marrow stem cells can be very effective in raising the lethal threshold. For example, in one study, monkeys that had 1% of their stem cells protected survived a dose that killed all unshielded animals. In the future, ex vivo cell storage techniques may allow a bank of shielded bone marrow to accompany astronauts on a long-duration mission.

It should be noted, however, that a 100% efficient radiation shielding system might not be desirable. It is possible that a minimum level of ionizing radiation is necessary to keep the biochemical repair cellular mechanisms in functioning order. This beneficial effect of a low-level exposure to an agent that is harmful at higher levels is called hormesis. Obviously, the shielding technology needs improvement for interplanetary travel, but there may be a non-zero optimum value [Bhardwaj, 1997].

8.3.5.7. Conclusion on radiation issues

In space medicine, radiation is often seen as a “show stopper” for a mission to Mars. However, when evaluating all the risks involved in such a mission, it might not be the worst. In addition, technological leaps are being made in the fields of molecular biology and superconductors, which could provide valuable countermeasure solutions in the near future. Bhardwaj [1997] concluded his essay by the following interesting thought: “the essence of our physical life form originated from matter ejected from supernovae, which is *radiation*. The engine of evolution, which transformed a unicellular organism into a human being, was fuelled by nothing but galactic cosmic rays, which also is radiation. The day might come when life will not be possible on planet Earth, because of the dreadful radiation of a nuclear bomb. When exploring other planets as a possible refuge, [humankind will] again be confronted with radiation. Ironically, the spacecraft carrying the human crew to Mars will also probably use some sort of nuclear propulsion!”

8.4. Methods for life support systems

8.4.1. Open loop and closed loop

There are two fundamental approaches for designing life support systems: open loop and closed loop. The first approach brings all life support resources from Earth and discards them after they are converted to a non-useful form. Systems which employ this method are called "open loop" to signify the continuous flow of material into and out of the system. In this scenario, all food, water and oxygen are from stored sources (Figure 8.11). Oxygen can be transported as a cryogenic fluid or a high-pressure gas. High-pressure storage is ready-to-use, but introduces risk of tank rupture and has decreasing delivery pressure. Open loop technologies tend to be simple and highly reliable and have been extensively used in human spaceflight to date. The big disadvantage to open loop systems in general is that resource requirements continue to increase linearly as mission duration and crew size increase. Using the numbers in Table 8.1 we can see that in 3 years a crew of four will use 2.7 (metric) tonnes of food, 3.6 tonnes of oxygen, and 129.5 tonnes of water! And that is without packaging.

The second approach for designing life support systems is to bring an initial supply of resources from Earth and then process the non-useful waste products to recover useful resources. These types of systems are called "closed loop" because once a resource enters the system it does not leave and the non-useful forms of material are recycled. The major advantage of closed loop systems is the one-time transport to orbit of the processing hardware and initial resource supply with minor subsequent re-supply of expendables. The disadvantages are lower technology maturity and increased power and thermal requirements. However, when mission duration becomes long enough, or re-supply is not possible (e.g., on a trip to Mars) there is a time when closed loop technologies provide the most cost-effective solution.

Figure 8.11. Astronaut Susan Helms Is Photographed in Front of the Potable Water Storage on Board the ISS. (Credit NASA).

8.4.2. Physical-chemical or biological (bioregenerative)

In physical-chemical life support systems, the human is the only biological component. Physical-chemical processes include use of standard engineering mechanical components such as fans, filters, etc., physical separation processes such as molecular sieves, reverse osmosis, or electrolysis, and chemical separation and concentration processes. These processes are well understood: engineers feel comfortable with them; they are relatively compact and low maintenance and have quick response times. Biological processes employ living organisms such as plants or microbes to produce or breakdown organic molecules. They are less well understood: they make engineers nervous, and they tend to be of large volume, power and maintenance intensive, with slow response time [Doll, 1999].

There are many Earth-based technologies that are capable of providing the five major life support functions. These include providing and maintaining a comfortable and breathable atmosphere, providing oxygen, food and water, and managing waste. These methods have been extensively described in Peter Eckart's book [1996]. Traditional heating, ventilation and air-conditioning systems can control temperature and humidity and provide air distribution. Sophisticated contaminant removal systems are used commonly for clean room applications. Atmosphere regeneration techniques purify air and provide oxygen on submarines and municipal facilities routinely process water and waste.

A closed ecological life support system is the ultimate closed-loop system. Such a system can use physical-chemical, or biological (also called bioregenerative) methods, or a combination of both (hybrid). The most effective closed-loop and bioregenerative systems will include both plants and animals for air, water and waste management, as well as food processing. Such systems are much more than a "greenhouse in space", however. It must be a multi-specific ecosystem operating in a small closed environment. Duplicating the functions of the Earth without the benefit of its large buffers, i.e., the oceans, atmosphere, and landmasses, is extremely challenging. Several experiments have been attempted, including the Biosphere-two project, with limited success (Figure 8.12). The main question is how small can the requisite buffers be and yet maintain extremely high reliability over long periods of time in a hostile environment. Also, by necessity, space-based systems must be small, and therefore a high degree of control must be exercised.

One of the major challenges of adapting or improving these technologies to be used for space applications is related to the nature of the space environment itself. For example, because there is no gravity, there is no convection for mixing of gases or for natural convective cooling, and phase separation of gases and liquids requires special devices. There are severe power, weight, and mass constraints on hardware design as well as extremely limited local resources (Figure 8.13). Because life support is a critical system for survival of the human space travelers and it is operating in a totally isolated environment, safety and reliability requirements are also very strict. Ingenuity, an understanding of the space environment, and familiarity with multi-disciplinary tasks are key characteristics for successful life support system engineers.

Figure 8.12. The Biosphere-Two Project Supported a Crew of Eight Inside a Large Glass Building Resembling a Giant Terrarium in the Arizona Desert. It Included a Rainforest, Savanna, Ocean, Desert, Human Habitat, and Intensive Agriculture. The Full Spectrum of Biological Life Support Agents Was Used, with Plants Producing Food, Oxygen and Clean Water, People and Animals as Consumers, and Microbes Decomposing Waste Materials and Metabolizing Airborne Contaminants. The Living Biomass Was Approximately 70 t! This System, However, Had Severe Problems Maintaining the Atmosphere Levels and Food Required for the Eight-Person Crew. (Source Unknown).

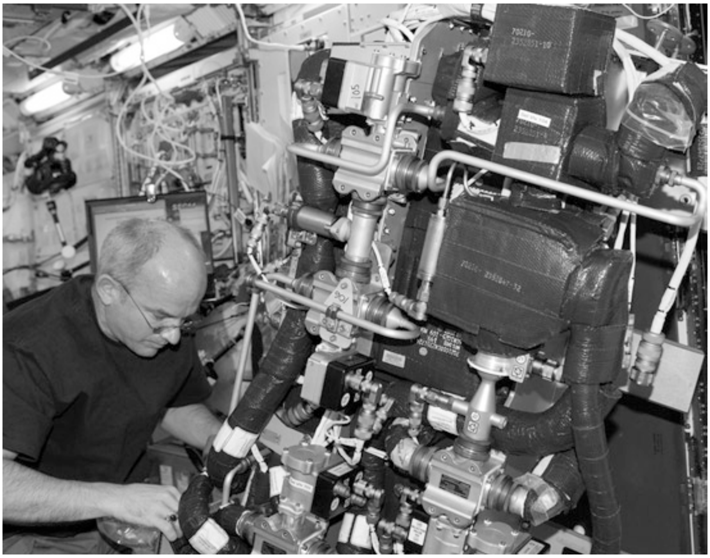

Figure 8.13. An ISS Crewmember Is Cleaning the Carbon Dioxide Filter in the Kibo Laboratory of the ISS. (Credit NASA).

8.5. Closed ecological life support system

A closed ecological life support system (CELSS) attempts to create an integrated self-sustaining system capable of providing food, potable water, and a breathable atmosphere for space crews during missions of long duration.[3] The control of these parameters is obviously an engineering question. The failure of any one component, however, immediately involves the medical support group.

8.5.1. CELSS for exploratory missions

For very long-duration missions in low Earth orbit or for exploratory missions, it becomes too expensive or impractical to rely on stored supplies. For a Mars mission, it is also impossible to depend on re-supply from Earth. The life support system must instead rely on regenerative system to regenerate food and oxygen, recycle waste, and purify air and water. Advanced life support systems for these missions will likely rely on plants to serve as sources for food, and to purify air and water. However, this solution has several drawbacks. For example, the introduction of plants and humans to a closed environment increases the chances of unwanted, potentially dangerous microbial contamination. Microbes are resilient organisms, capable of adapting to harsh environments, and able to colonize any surface that contains adequate nutrients and moisture. It is then far more desirable to monitor microorganism levels in a CELSS. Biochemical tests must be developed, which can be simply done by the crew or automated, not dangerous and low time-consuming. For example, computer algorithms could be used to identify a suspected organism by comparing its rRNA sequences with those of known organisms, the so-called “DNA chip” technique [Sanz et al., 2001].

On Earth, animals breathe in O_2 from the air and breathe out CO_2 as a waste. Plants absorb this CO_2 from the air, and using the energy of sunlight plus water and materials from the soil and air produce sugar, starch and other things, based on a process called photosynthesis. Plants emit O_2 as a waste. That completes the animal-plant cycle. In this cyclic manner, animals and plants are mutually dependent upon each other. Plants produce both food and O_2 for animals. In turn, animals produce CO_2 for plants. In addition, animals produce excrement wastes, which enrich the soil. Dead plants also enrich the soil and are not wasted.

$$\text{Photosynthesis: } CO_2 + H_2O + \text{light} \rightarrow (CH_2O)n + O_2$$

$$\text{Respiration: } CH_2O + O_2 \rightarrow CO_2 + H_2O$$

This natural cycle can be moved to space, in whole or in part. Early Soviet experiments in the 1950s and 1960s focused on recycling air using algae, not food crops. Flat

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[3] The use of this acronym in the literature is sometime confusing. Typical NASA engineers use ECLSS for Environmental Control and Life Support System, i.e., a group of devices that allow a human being to survive during a space mission. The scientific community uses CELSS for Closed (or Controlled) Ecological Life Support System, i.e., a type of scientific endeavor to create a self-supporting life support system. It is this second definition that is being used in this book.

tanks of algae were put under artificial light in order to absorb CO_2 that humans had exhaled in closed chambers, and emitted the O_2 for the humans to breathe. It was found that each human required about 8 m^2 of algae for equilibrium. (The alga tanks were generally stacked as shelves so that they took much less than 8 m^2 of floor space.)

More recent research has expanded this to include production of edible food, and recycling of animal or human excrement wastes and dead plant wastes in the food cycle. Studies are required for defining the conditions required for optimum rates of dry matter production. Although most research has been done with open systems, experiments with closed systems are currently ongoing (e.g., the "Melissa" project at the University Autonomous of Barcelona, Spain; the CEBAS Minimodule developed by OHB-System in Bremen, Germany; the "Aquatic Biosphere" developed by Paragon Space Development Corp. in Tucson, Arizona). However, the only artificial ecosystems that were tested in microgravity, the one from OHB on the shuttle and another from Paragon on the ISS, included only aquatic species, including swordtail fish, cichlid fish, snail, shrimp, and other crustaceans, and algae or horn weed plants.

Using humans in the loop, a "Biomass Production Chamber" has been developed at the NASA Kennedy Space Center, which consists in a sealed large steel chamber approximately 3.5-m in diameter and 7.5-m high, with two floors. Each floor has multiple racks and lamp banks, duct work for airflow, and various equipment for controlling temperature and humidity. Total chamber plant growing area is 20 m^2. Wheat, soybeans, potatoes, sweet potatoes, strawberries, rice, peanuts, radishes, and other foods were grown in the facility. Instrumented test subjects were placed inside the chamber for limited duration. Human subjects were periodically enclosed while exercising on electronic cycle ergometer in order to evaluate gas exchanges in various conditions. Adjacent laboratories were used for converting wastes into plant nutrients, plant fertilizer, carbon dioxide, and water. At every stage, careful and detailed measurements of many kinds were made in an attempt to understand the processes in depth. Results indicated that a minimum surface of 40 m^2 of crop field was required per human for total recycling of oxygen and food [Doer, 2001].

Some factors that must be considered in establishing a CELSS for food production are using crops that provide a dependable yield, have a high edible biomass yield, are of small size, provide dietary variety, and can be combined to form a nutritionally complete diet. Based on consideration of primarily agricultural plant species, a small number have been selected for further investigation. These include wheat, potato, soybean, and tomato. It may well be that some of the plants will be genetically modified to increase levels of certain micronutrients, essential lipids or amino acids. An additional factor is that very intensive agriculture will be practiced to grow a maximum quantity of usable raw food in an area as small as possible. Although the development and growth of plants seem little affected by the space environment (both radiation and microgravity), at least during the first couple of generations (Figure 8.14) (see Chapter 2, Section 2.4.2), no experiments have yet been performed in microgravity at full scale to determine if current systems can function in space. In short, a considerable increase in research efforts is required to reach the desired goals of a closed ecological life support system.

The challenges for long-duration interplanetary mission is to design closed life support systems that are: (a) closed-loop, i.e., except energy, no material needs to be added

Figure 8.14. An ISS Russian Cosmonaut Proudly Poses for a Photo with His Microgravity Plant Growth Experiment. (Credit NASA).

to the system for it to function; (b) bio-regenerative, i.e., everything is recycled biologically instead of through physical or chemicals means; (c) non-polluting, i.e., it does not result in any toxic byproducts; (d) self-sustaining, i.e., it is productive and functions independently for long period of time using only the materials available from within the system; (e) intensive agriculture system, i.e., it produces high yields with diverse crops; and (e) pathogen-free, i.e., is utilizing "good" bacteria only [Poynter, 2006].

Until all aspects of closed ecological life support systems are better known during the conditions of spaceflight, the best solution for a life support system is hybrid, i.e., a combination of physical-chemical and bioregenerative methods. The design and evaluation of such a life support system combines the expertise of various fields, including mechanical, electrical and thermal engineering, life sciences, material sciences, physics, chemistry, and agriculture. Multiple factors enter into play, such as mission duration, system mass, reliability, maintainability, power and thermal cost, as well as the number of interfaces with other systems and subsystems. Like for space biology, physiology, and medicine, the research on life support systems will be an important area in preparation for the human Mars missions.

8.5.2. Terraforming

Planets are places, not vehicles. Surviving there will be different from camping in a spacecraft flying into space. An effort to build human communities either on other planets or on artificial new worlds might begin with altering the existing climate and atmosphere to resemble more closely that of Earth. The process of transforming a planet to create a more Earth-like habitable living environment is called terraforming.[4]

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[4] The (debated) options to manipulate Earth's environment to specifically counteract the effects of global warming are called geo-engineering rather than terraforming.

Any terraforming process is likely to take the candidate world on a path from initial sterility through a continuum of improving habitable states.

"Full" terraforming (the achievement of an entire environment suitable for Earth-like humans, animals, and plants) is likely to remain a distant, although not impossible, goal. Indeed, terraforming an entire planet into an Earth-like habitat would almost certainly need to be done over several centuries or even millennia. On the other hand, the initial stages of terraforming might take only several decades. For example, humans could begin by living in transparent domes. The domes would have radiation shielding that protects plants and animals. This would permit the construction of ambient pressure dwellings and the replacement of pressure suits with simple breathing gear. Such solutions could allow human habitation well before full habitability of a planet is attained.

Earth was once terraformed. In the beginning, there was no oxygen in the atmosphere, only carbon dioxide and nitrogen, and the land was composed of barren rock. Using photosynthesis, organisms transformed the CO_2 in Earth's atmosphere into O_2, in the process completely changing the surface chemistry of our planet. The evolution of aerobic organisms then modified Earth still more, colonizing the land, creating soil, and drastically modifying global climate. Once the biosphere had extended, humans accelerated its development rate by using irrigation, crop seeding, weeding, and domestication of animals [Zubrin, 1999].

Terraforming Mars would use the same principle, but using the greenhouse effect would accelerate the process. The first step would be to set up factories to produce artificial greenhouse gases (e.g., perfluoromethane, CF_4) for release into the atmosphere (Figure 8.15a). Zubrin [1996] predicts that if these gases were produced at the same rate as chlorofluocarbon (CFC) gases are currently produced on Earth (about 1,000 tonnes per hour), the average global temperature of Mars would be increased by 10°C within a few decades. This temperature would cause CO_2 to outgas from the regolith, which would warm the planet further due to the greenhouse effect (Figure 8.15b).

This effect could even be amplified by adding bacteria releasing methane and ammonia, two very strong greenhouse gases. The net result of such a program would

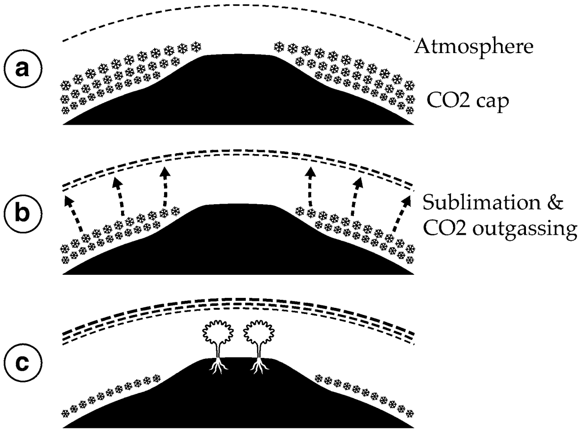

Figure 8.15. Principle of Terra-Forming Mars as Proposed by Zubrin [1996].

be a planet with acceptable atmospheric pressure and temperature, and liquid water on its surface (Figure 8.15c). Even though the atmosphere would not be breathable by humans, space suits would no longer be required when outdoors (just breathing gear). Crops could grow in the fields and aquatic life could flourish in lakes oxygenated by algae. Humans would live in closed habitats until plants released enough oxygen in the outside atmosphere. A Japanese company, Obayashi Corporation, recently proposed a design concept for such a Mars habitat, including a farm and terrarium in an area of about 400 m × 500 m. It is envisioned that by the year 2057, i.e., for the 100th anniversary of *Sputnik*, this habitat could host 150 pioneers.

At the same time, the environment of space will also influence Earth-like biological and physiological processes. Organisms might begin evolving into forms suitable for the local environment. It is not certain that the gravity of Mars will be sufficient to prevent the bone demineralization and muscle atrophy observed in microgravity. It might be much healthier for crews to provide artificial gravity for long-duration habitation, assuming that they plan to come back to Earth. Artificial gravity could be achieved by exposing the crew to intermittent centrifugal force generated by a centrifuge or a slow rotating room inside the Mars habitat (Figure 8.16).

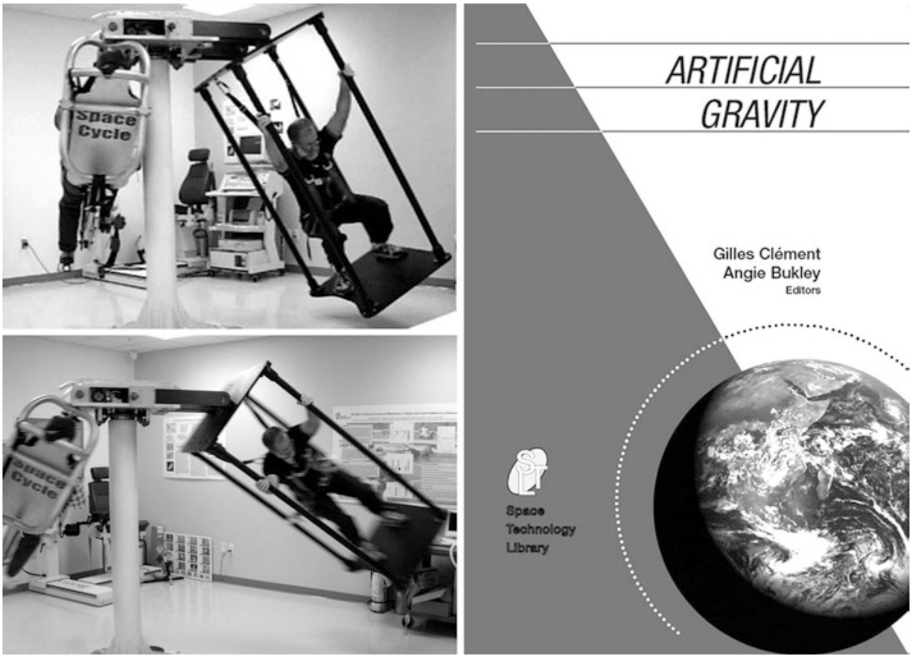

Figure 8.16. To Avoid Some of the Physiological Problems Created By Reduced Gravity, a Continuous or Intermittent Rotating Environment Could Provide an Artificial Gravity Environment, the Level of Which Is Still to be Defined. One Method to Achieve Intermittent Artificial Gravity in the Mars Habitat Is the Space Cycle Proposed by the University of California, Irvine. For More Details, See the Book *Artificial Gravity* by Clément and Bukley [2007].

How much artificial gravity and for how long are questions that need to be answered by investigations during long-duration space missions. For small habitats, rotating them to produce artificial gravity results in some very noticeable differences with real gravity due to the Coriolis effect. Ground-based experiments have led to guidelines for a "comfort zone" in artificial gravity, bounded by values of the radius of the rotating structure, head-to-foot acceleration gradient, rotation rate, and tangential velocity. However, this comfort zone is essentially terrestrial, since very little is known about artificial gravity in space or planetary surfaces with less than 1 g [Clément and Bukley, 2007]. On the other hand, it might be better to facilitate biological adaptation to reduced gravity instead.

These thoughts also bring interesting questions, which go far beyond the area of space life sciences. For example, what are the costs and benefits of encouraging some or all organisms to adapt to the local environment of space rather than trying to make that environment Earth-like? What are the ethical concerns of whatever we do and to whom/what we have ethical obligations? For example, do intelligent beings only deserve ethical concern? Or all "life" forms (whatever "life" is)? And do nonliving environments (e.g., fossils, rocks) have rights or deserve ethical concern? And finally, what are the possible sequences in extraterrestrial settlement and expansion?

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Chapter 9

An Investigator's Guide

In past years, hundreds of space life sciences investigations have been conducted on board the space shuttle, *Skylab*, and Spacelab. Experiments are now conducted on board the ISS, where special laboratory equipment and experimental procedures are specifically designed for use in space. In addition, flight experiments must fit within physical limits of the spacecraft and its resource constraints. Yet, as many experiments as possible are to be conducted on each mission to achieve maximum scientific return. This chapter reviews the constraints of space life sciences missions and the step-by-step procedures "to fly" an experiment.

9.1. Resources and constraints

For many reasons, progress in human physiological research in space has been limited. The dearth of flight research opportunities reflects the low priority given to life sciences research in general. There was a long absence of flight opportunities between the *Skylab* and shuttle programs. There was yet another delay between the last Spacelab mission in 1998 (Figure 9.1) and the time when ISS became fully operational. The ISS is equipped with state-of-the-art laboratories, and a crew of six persons spending several hours per day on science activities. Nevertheless, the nature of the current space program is such that there is much to do and only a few flight opportunities that must be shared. In addition, these flight experiment opportunities are constrained in a number of ways, such as mass, volume, power, re-supply of consumables, and crew time. Finally, stringent reliability constraints are imposed on the space experiments competing for the limited opportunities. Both the hardware and the protocol must be evaluated and tested to guarantee that they will function properly in orbit. Consequently, experiments that might take weeks on Earth take years to plan and execute in space.

9.1.1. Opportunities for space life sciences experiments

Three types of flight experiments are currently solicited: (a) on-orbit experiments that can be implemented on the ISS, *Soyuz*, or biosatellites; (b) pre- and post-mission studies involving data collection and analysis of biological specimens prior to and on return from space missions; and (c) laboratory ground-based investigations (Figure 9.2).

G. Clément, *Fundamentals of Space Medicine*, Space Technology Library 23,
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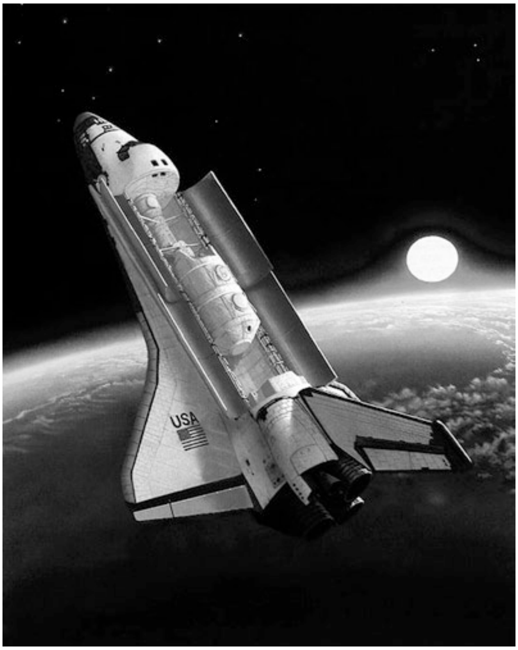

Figure 9.1. View of the Spacelab Module, Which Flew in the Cargo Bay of the Space Shuttle Columbia During 15 Space Missions Ranging from 7 to 16 Days Between 1983 and 1998. The Last Spacelab Missions Paved the Way for ISS Utilization. (Credit NASA).

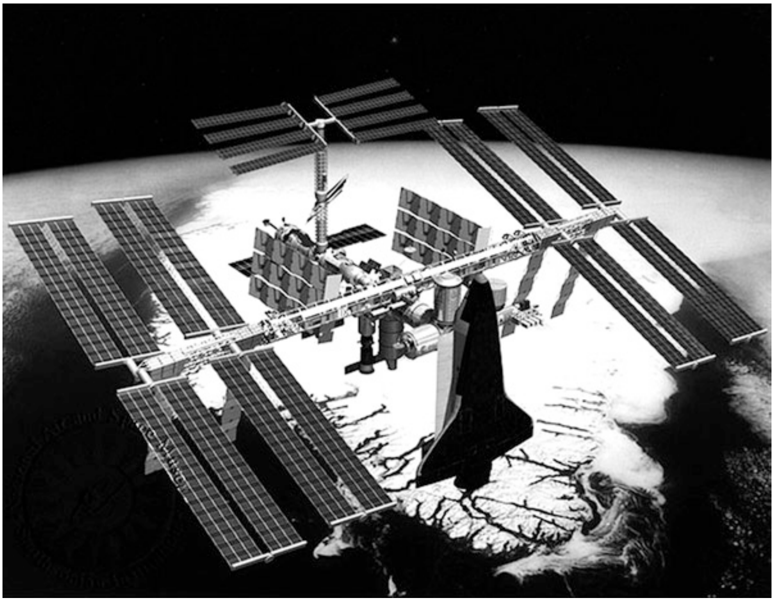

Figure 9.2. Artist View of the ISS During Construction, with the Space Shuttle Docked To It. (Credit NASA).

9.1.1.1. International space station

The first permanent crew on board the ISS arrived on November 2, 2000. It signified the beginning of a continuous human presence in space of at least 20 years, with crew rotations about every 180 days.

During the 10-year construction phase of the ISS, research opportunities were available on a limited basis. Some research was accomplished during space shuttle missions when the shuttle visited the ISS and during the time period between the space shuttle missions when the ISS crew acted as experiment operators and, if necessary, as subjects. It was also possible to conduct a few experiments on board the ISS during this period. However, ISS experiments were severely constrained by limitations on resources such as equipment mass, volume, power, re-supply of consumables, and crew time. Now that assembly is completed, a permanent crew of six astronauts devotes approximately 160 h per week of time to experiments (Table 9.1).

The ISS now has six pressurized laboratory modules, including the U.S. Destiny Laboratory, the Japanese Kibo Experiment Module, the European Columbus laboratory and the three Russian Research Modules. The pressurized logistics elements include the Russian FGB and Service Module, the docking modules, and the *Soyuz* vehicles.

The International Partners involved in ISS operations include NASA in the U.S., Roscosmos in Russia, ESA, JAXA, and the Canadian Space Agency (CSA). NASA provides the overall leadership of the ISS program development and implementation.

Table 9.1. Global ISS Utilization Capabilities. The Variation in Altitude Is a Direct Consequence of the 11-Year Solar Activity Cycle That Causes Earth's Atmospheric Density Profile to Vary (Expanding the Atmosphere at Solar Maximum). Because of the Low Average Altitude of the ISS, Atmospheric Drag Causes a Loss in Altitude of Approximately 200 m Per Day. To Counteract This Altitude Loss, a Periodic Re-boost, Which Occurs Approximately Every 10–45 Days, of the ISS Is Required. Each Re-boost Increases the Altitude Temporarily. (Credit ESA).

Parameters	Characteristics
Truss length	108 m
Total module length	74 m
Mass	450 tonnes
Maximum power output	110 kW (35 kW for payloads)
Total pressurized volume	1,200 m^3
Atmospheric pressure	1,013 mbar (1 atmosphere)
Orbital altitude	350–450 km
Orbital inclination	51.6 deg
Orbital velocity	About 7.7 km/s
Crew	6
Crew time for science activities	160 h/week
Data rate uplink	72 kbits/s
Data rate downlink	150 Mbits/s
Ku-band coverage	70% of time
S-band coverage	70% of time
Anticipated lifetime	Until 2020

Table 9.2. Baseline International Partner Utilization Allocations. Note That as Russia Retains 100% of Its Accommodation, Resources, and Services, It Is Not Shown in the Table.

Utilization Resources, Accommodations and Supporting Services	NASA (%)	ESA (%)	JAXA (%)	CSA (%)
U.S. Destiny Laboratory	97.7			2.3
European Columbus Laboratory	46.7	51.0		2.3
Japanese Experiment Module	46.7		51.0	2.3
Truss Payload Accommodations	97.7			2.3
Resources – power and crew time	76.6	8.3	12.8	2.3
Right to purchase supporting services (upload/download; communications)	76.6	8.3	12.8	2.3

ISS utilization rights are divided among the partners according to the elements and infrastructure they provide. The guiding principle is that each International Partner may use equipment and facilities in or on each other of the Partner's elements in accordance with their respective "utilization rights". Those rights are defined in the Article 9 of the Intergovernmental Agreement and the different Memoranda of Understanding signed by all of the ISS Partners. The baseline usage allocations in terms of percentage of the on-orbit facilities, resources and services for the five International Partners are summarized in Table 9.2.

9.1.1.2. Experiments onboard the Soyuz

The *Soyuz* flights are dedicated to exchange a three-person crew onboard the ISS every 6 months. *Soyuz* vehicles are also used as emergency return vehicles in case of a medical evacuation. There are typically four *Soyuz* flights per year.

The *Soyuz* vehicle has not changed much since its first launch in 1967. After nearly 1,500 launches of the *Soyuz* family, including 120 with humans onboard, it is the most reliable manned spacecraft (Figure 9.3). The *Soyuz* vehicle has undergone a series of upgrades during that period. If not more comfortable, at long last, *Soyuz* is now all digital. The previous *Soyuz* contained five incompatible analog processors for monitoring different spacecraft subsystems, plus the main guidance computer, a ruggedly reliable system that has been in use for more than 30 years. The analog units have all been replaced recently by a single new digital device, but no performance specs have been released. The new system promises to make transmission of spacecraft parameters much more efficient, resulting in significant time savings in prelaunch checkout, which was a necessity with the double launch rate now needed to maintain a crew of six aboard the ISS in the absence of the retiring space shuttle fleet.

Opportunities for flight experiments on board the *Soyuz* are extremely limited. The very few experiments that were carried out onboard *Soyuz* were those that were battery-powered, self-contained with several levels of containment, and with severe size and weight limitations. Typically these experiments were dedicated to cell cultures requiring only a small experiment hardware package.

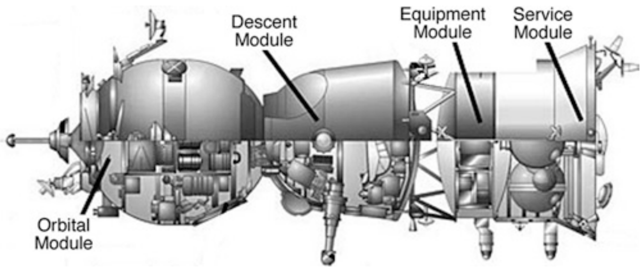

Figure 9.3. ***Soyuz* Spacecraft.** The Equipment Module Contains the Rocket Engines and Power Supplies. The Crew Rides the Descent Module During Launch and Landing. The Orbital Module Contains Additional Living Space and Storage. (Credit Russian Space Agency/James Oberg).

9.1.1.3. Biosatellites (Bion & Foton)

As mentioned in Chapter 1, unmanned biosatellites were once used by the U.S. and Soviet Union to test the effects of spaceflight on animals before the first humans were sent into orbit. These biosatellites are now being used for research. For example, unmanned Bion & Foton capsules are regularly launched from Russia using a *Soyuz* launcher to an orbit of about 280 km for a duration of approximately 15 days. Foton capsules are pressurized and temperature-controlled and can host a payload of 700 kg in a volume of 4.3 m^3. Electrical power at the level of 800 W is provided for the entire duration of the mission, with a battery pack jettisoned before re-entry. Bion capsules are not pressurized.

The re-entry module, a 2.2-m diameter sphere with a mass of around 2.5 tonnes, is the only retrievable part of the satellite. The capsule houses the scientific payload and the landing parachute. The acceleration experienced during the final stages of landing can be as high as 40 g for a very brief period of time. Landing is assisted by parachutes and retro-rockets to cushion the impact with the ground. The internal temperature ranges from 10ºC to 30ºC.

After the flight, the capsule lands along the border of Russia and Kazakhstan (Figure 9.4). The biological specimens are removed from the capsule by a ground team and placed in refrigerated containers. The capsule is then transported back to the *Soyuz* plant in Samaria (Russia). The samples are then dispatched to the participating science teams via Moscow.

These capsules provide a unique opportunity to fly biological specimens (animals, cells, and plants) when no crew activity is needed. Telemetry can be used to activate some procedures, like the fixation of cells or turning a light on or off during the flight. Small onboard centrifuge generating centripetal accelerations of up to 1 g can also be used to provide a comparison with ground controls and ensure that the observed effects of the flight on the specimen are not due to the stress of launch and landing or to atmosphere changes. The samples are loaded in the capsule up to a few hours prior to launch.

Past missions have included studies of the gravity-sensing organs of plants roots (e.g., *Brassica rapa*), the expression of genes that is modified in microgravity in plant

Figure 9.4. Russian Foton Capsule After Landing in the Kazakhstan Desert. (Credit Roscosmos).

cells (e.g., *Arabidopsis*), the influence of gravity on differentiation and tumor formation in cancerous cells (e.g., breast epithelial cells), and on the calcium balance in muscular or bone (osteoblasts) cells [Gasset, 2001].

9.1.1.4. Suborbital flights

The burgeoning private spacecraft industry will provide opportunities not only to spaceflight participants but will also lead to a new generation of platforms for conducting research. Areas of study will include medicine, biology, chemistry, physics, atmospheric science, remote sensing, and technology development. Researchers who want to fly experiments in space will need someone to monitor the payloads, take measurements, and ensure successful operation of the experiment during the flight. They will also need subjects to test engineering designs and systems. The private sector will have a great deal of influence over the types of missions conducted, but much of the research funding will likely come from government grants at first.

Although a few scientists may be able to spend the time and money to get trained to fly themselves, most probably will not. They will need to contract out the work to experienced and trained professionals who can efficiently work in the spacecraft environment, such as those at Astronauts4Hire. As more flights become available and prices decrease, research opportunities will increase and allow for more universities, research institutions, and public and private corporations to participate [Source: http://www.astronauts4hire.org/p/astronauts.html, accessed 15 October 2010].

9.1.1.5. Ground-based investigations

Flight investigations must represent mature studies strongly anchored in previous ground-based research or previous flight research. Ground-based research may, and usually must, represent one component of a flight experiment proposal. Ground-based

Table 9.3. The Various Methods Used to Access to Actual or Simulated Microgravity Condition. Drop Towers Are Usually Evacuated Tubes in Which an Experiment Capsule Is Released and Allowed to Free-Fall. Biosatellites Include the Russian Retrievable Capsules Bion and Foton.

Method	Microgravity	Duration
Bed rest	Simulated	3–12 months
Clinostat	Simulated	Unlimited
Centrifuge	>1 g	2-month (animals)
Drop tower	$<10^{-4}$	2–5 s
Parabolic flight	10^{-1}–10^{-2}	20 s
Sounding rocket	10^{-5}	6–15 min
Biosatellites	10^{-5}–10^{-6}	15 days
Soyuz	10^{-4}	10 days
ISS	10^{-4}	10 years

studies can be performed in reduced gravity, hyper-gravity, or normal gravity environments.

Facilities that provide a reduced gravity for limited duration include drop towers, parabolic flight, and sounding rockets (Table 9.3). Other ground-based laboratory facilities in which the effects of gravity, or hypergravity, can be evaluated consist of clinostats (for cells), animal- or human-rated centrifuges (short- or long-radius), slow rotating rooms, and bed rest clinics.

However, to be supported by a space agency, it is highly recommended that this ground-based research be limited to activities that are essential to the final development of an experiment for flight and for the completion and publication of the scientific results of the experiment. Preparatory ground research designed to define a mature spaceflight experiment can also be proposed separately and in its own right as part of the ground-based program.

9.1.2. Constraints

Life sciences research typically flows in a progression, beginning with challenging problems and questions crucial to our advancement into understanding the relationship between gravity and life; the search for solutions and answers through research in the biological and medical areas; validation and demonstration of crucial concepts in-flight which eventually lead to the knowledge, experiments, and progress which will enable us to meet the challenges of the future (Figure 9.5). The challenge in developing a flight experiment is to package the science objective and the experiment apparatus in ways that satisfy the spacecraft requirements and safety, but also the ethical considerations and the unique constraints of human space missions [International Space Life Sciences Working Group, 2001].

9.1.2.1. Ethical considerations

All use of human subjects for research in conjunction with experiments on the shuttle, the ISS, or pre- and post-mission studies must comply with NASA Policy Directive NPD 7100.8C, Protection of Human Research Subjects. To get approved,

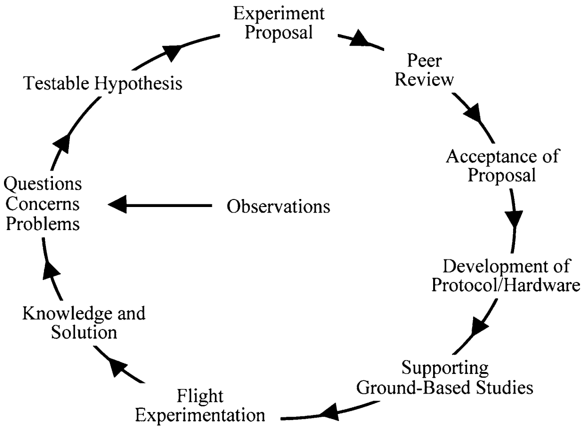

Figure 9.5. Steps of Space Life Sciences Research. (Credit NASA).

all experiments must receive approval from their local ethical committee, from their respective space agency ethical committee, and from NASA ethical committee (also called the Institutional Review Board).

Informed consent of human subjects must be obtained prior to carrying out any study in space, and potential applicants should be aware that obtaining such informed consent involves a uniform process regardless of the country of origin of the applicants. The availability of consenting subjects may impact the probability of achieving experiment objectives within the expected timeframe. Human life sciences experiments generally require at least two crewmembers (experimenter and subject). Although operating most experiments will not pose a problem to astronauts, there is no assurance that all crewmembers will agree to participate as subjects in experiments.

All proposals for the use of vertebrate animals must be accompanied by a certification of approval from the Investigator's institutional Animal Care and Use Committee and a Public Health Service Animal Welfare Assurance number. The use of animal subjects in all NASA ground and flight research is governed by NASA Policy Directive NPD 8910.1, Care and Use of Animals, and NASA Procedures and Guidelines NPG 8910.1, Care and Use of Animals [NASA, 2000, 2001].

9.1.2.2. Other considerations

The major difference between a flight experiment and the same experiment in a standard laboratory on Earth is the smaller number of subjects or specimens and observations in the flight experiment. Experimental sample size has been and will continue to be small.[1] Due to limited space and power, a finite number of animals (including a limited number of species) or specimens is available for in-flight research.

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[1] Overheard at space symposia:

- one case: "In my experience…"
- two cases: "Recent studies showed…"
- three cases: "Case after case after case…"

This limited number often requires the development of elaborate and detailed sharing plans to maximize their use. For example, sharing plans for human blood samples in orbit are a prerequisite since the volume of blood draw is limited.

Also, in Earth laboratories, it is common to repeat experiments. This is in fact the basis for a scientifically sound investigation. Every published scientific manuscript contains or should contain a Methods section detailed enough to allow other scientists to repeat the experiments, to verify and confirm the proposed hypothesis or interpretation of results. For space experiments, it is very rare when the exact same experiment is repeated on a second or a third mission, because of the financial and time constraints. The investigators are doomed to success in the first trial.

To limit the risk of failure in obtaining scientific return from a mission, and to provide more opportunities to investigators, it has become common practice to "integrate" several experiments. In this process, multiple investigators must share the same equipment. The inconvenience is that some common procedures or conditions must be "negotiated" between the investigators (for example, a given centrifuge velocity, or a given temperature for animal habitats), and that a malfunction of the equipment might cancel several experiments.

For a life sciences mission, crew time is the most precious resource. It is also a fact that activities require more time to execute in 0 g. For example, the set-up of complex experimental equipment takes approximately 40% longer in space than on the ground. Other activities may require extra operations, like dissections, or hazardous operations such as the use of a rotating chair. As a result, 4 h of crew time in 0 g corresponds to only 2.4 h on the ground. The availability of the crew for training prior to the mission is also limited. Training requirements depend on the complexity of both the individual instruments and the integrated payload. During the flight, the investigators have limited access to real-time data. In an terrestrial laboratory, a flaw in one experimental protocol is immediately detected and corrected before the experiment continues. During a spaceflight experiment, it is difficult to assess the exact situation remotely, or to suggest changes in an experimental protocol that has been designed over several years. Also, the suggested changes could have an impact on other experiments. Perhaps for these reasons, flight experiments produce mainly unexpected results. In some cases, the results of space investigations have confirmed classical or generally held hypotheses. However, most results have been startling and unexpected, requiring researchers to reexamine their assumptions about the intricate relationship between gravity and life.

Equipments and supplies that have a limited shelf life may be loaded onto the shuttle days or weeks before launch. It is possible to arrange for late preflight installation (approximately launch minus 20 h) and early postflight recovery (landing plus 3 h) of equipment, supplies, and data that have time- or temperature-critical sensitivities. Note that there are periods of time before the flight and after landing when no access to the experiment is possible and maintenance of the equipment integrity must be assured. The availability of shuttle resources for experiments that require animal as subjects is also extremely limited for short-duration experiments [ESA, 2003].

9.1.2.3. International space station constraints

Each ISS increment, also called an Expedition crew, includes six crewmembers for a duration of up to 6 months. All crewmembers participate in life science experiments as operators, or as subjects of research on a voluntary basis. However, there are some flight phases during which crew time is extremely limited, such as just after arrival on board the ISS and just prior to departure, during docking/undocking of other spacecraft, and EVAs. Experiments requiring the least crew-supported in-flight activities are the most likely to be selected, given the limitations on crew training time.

Resupply or crew exchange flights to the ISS occur approximately every 80–120 days. These flights allow the uploading of samples and specimens for experiments, and periodically for returning to Earth samples on board the *Soyuz*. Re-boosts of the ISS to a higher altitude are often performed during these docking maneuvers, which affect the microgravity environment (Figure 9.6).

Depending upon the duration of the active phase of the experiment, onboard sample storage is possible. Most experiments produce data that is stored electronically and transmitted to the ground. Some data can also be stored on board on a temporary basis. After downlink, the flight data is stored in ground control center before being dispatched to the science users. A backup copy of the data is archived at the space agencies.

On average, a total of 160 h of crew time per week are allocated to science activities, including experiment operations and equipment maintenance. A typical on-orbit day on the ISS averaged over a 6-month stay including two EVAs looks approximately as follows: 8 h for sleep; 2 h for pre- and post-sleep activities, including hygiene; 1.5 h for lunch; 2.5 h for exercise; 1 h for exchanges with mission control; 1 h for public relations; and 8 h for payload activities.

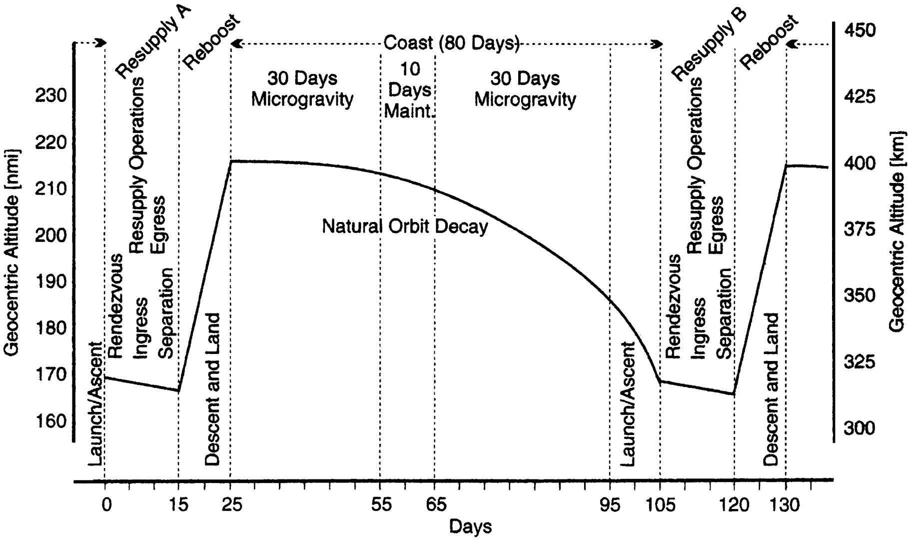

Figure 9.6. ISS Experimental Cycle. A Visiting Vehicle (e.g., Progress or the Shuttle) Rendezvous with the ISS When the Orbit Is Relatively Low, and During the Next 15 Days, the Crew Performs the Necessary Re-supply Operations. During the Following 10 Days the Re-boost Operations Are Performed to Raise the Altitude of the ISS, After Which the ISS Will "Coast" for a Period of 80 Days. This Ensures Two 30-Day Periods of Continuous, Good Quality (Less Than 10^{-6} g) Microgravity. (Credit ESA).

In addition, 1.5 days off is required every week (usually Saturday mornings and Sundays). The first measurements on board the ISS are not performed before mission day 4. EVA preparation by the ISS crewmembers pre-empts the execution of any science payload activities for 1 week. Data and samples are transferred back into the *Soyuz* for a minimum of 2–3 days before undocking.

9.1.2.4. *Soyuz* flight constraints

Transport frequency, power during transportation, and mass of transported items will all be severely constrained following the retirement of the space shuttle. The primary opportunities to transport scientific equipment, supplies, and samples are on the periodic flights of the *Soyuz* (four per year), the Russian *Progress* (four per year), the European Automated Transfer Vehicle (ATV) and the Japanese H-IIB Transfer Vehicle (HTV) (one to two per year) to the ISS. In addition, modest capabilities for research are available on the *Soyuz*. Refrigerated and frozen transport of samples is very limited, and power outages may be experienced during ascent and return.

Time-critical supplies or specimens can be loaded in the *Soyuz* from 40 to 20 h before launch. There is a minimum storage period of 5–6 days before starting an ISS experiment, given that the *Soyuz* must travel for 2 days and reach and dock with the ISS with the experiment finally transferred to its ISS facility. For the return flight, the time between de-orbit and recovery is on the order of a few hours. The *Soyuz* capsule has a pressurized volume of about 4 m^3. The mass of payload that can be uploaded to the ISS is about 100 kg, and the mass that can be downloaded to Earth is about 50 kg for a crew of three. *Soyuz* is also used to carry supplies to the ISS crew, such as spare parts, software updates on CD/DVD, fresh food, and personal items. Therefore, only a limited number and simple experiments can be accommodated. In general, each crewmember is allowed to carry 12 kg of equipment or samples up (volume 0.4 × 0.4 × 0.4 m), and to return 4 kg of equipment (e.g., tapes, films) or samples down to Earth.

Sample return immediately after termination of the mission is extremely limited and without onsite available temperature control capability. Samples and specimens are made available to the scientists after approximately 1–5 h after landing.

9.1.2.5. Constraints on pre- and post-mission studies

Opportunities are available to perform experiments, collect samples, and make physiological measurements on the astronauts both prior to their space mission and following their return to Earth. However, access to all crewmembers immediately before a space mission is extremely limited due to their very busy training schedule. Preflight baseline data collection generally takes place several weeks prior to launch. Preflight measurements can be repeated several times, for example, at 1-month intervals to evaluate the test-retest repeatability and the variance of the responses studied.

Immediate post-flight data collection on the returning crew is even more constrained. One mission rule imposes that the maximum wake time for a crewmember on landing day is 18 h. For the space shuttle, the duration of crew transfer (Figure 9.7) from the runway to the flight clinic took about 2 h, including the "walk-around" on the runway. Typically, the first activities there included a medical exam (0.5 h), a visit with the family, a meal and a shower (1 h). This was followed by 4 h of scientific

Figure 9.7. The Crew Transport Vehicle Is Docked with the Space Shuttle After Landing. Once Access to the Shuttle Is Possible, Physicians Board the Shuttle and Conduct a Brief Preliminary Examination of the Astronauts. They Assist the Crew in Leaving the Vehicle and Removing Their Launch and Re-entry Suits. (Credit NASA).

investigations.[2] By landing on a runway located close to state-of-the-art research laboratories, the space shuttle offered unique opportunities to collect data immediately after return, using measurements that were not possible in-flight, such as MRI, or centrifuging on rotating chairs, for tracking the re-adaptation of body responses to Earth's gravity. Lessons learned from the astronauts' functional re-adaptation were used in several programs of rehabilitation in patients following injuries or surgeries [Clément and Reschke, 2008].

Access to long-duration ISS crews returning on *Soyuz* for a pre- and post-mission study is much more limited. This is because the crew is more fatigued, compared with the space shuttle crew, and because there is no medical infrastructure nearby the landing site. The availability of ISS astronauts for research tests on the day of return to Earth, or the day after, may be as little as 1 h per day total. On a typical *Soyuz* return day, the crew spends up to 10 h in the *Soyuz* until the landing. A medical exam is performed at the landing site, immediately after the crew has egressed the vehicle (see Figure 7.20), or inside of a tent that has been erected to provide protection from the weather and some privacy. When conditions permit, the crew is then transferred by helicopter or all-terrain vehicle (if weather prohibits flying), and then by aircraft to the nearest runway. From here, Russian crewmembers are transferred to the Gagarin Cosmonaut Training Center at Star City near Moscow. U.S. and "foreign national" crewmembers are returned to Houston on board a NASA Gulfstream airplane. This "direct return" was initiated after *Expedition-23* to reduce the need for deployment of

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[2] Another mission rule states that a 1-h break must be observed after data collection during experiments on landing day exceeds 4 h.

personnel to Russia, return the crew back home earlier, and take advantage of the NASA facilities for the rehabilitation program.

During the transfer, which last 6–8 h for the Russian crew and up to 20 h, including two refueling stops, in the case of "direct return", the crew rests and consumes one or more meals. In both cases, the first postflight data collection usually takes place about 24 h after landing. The duration may not exceed 2 h, with the crew remaining in the supine or sitting position.

9.2. How to "fly" an experiment

9.2.1. Flight experiment selection

Space life sciences research is coordinated by the International Space Life Sciences Working Group (ISLSWG), which includes representatives from NASA, ESA, JAXA, CSA, CNES, ASI, and DLR. This worldwide coordination starts with the screening of existing space hardware and the exchange of information on the planning for the development of new hardware. This results in having a common pool of research equipment on the ISS and other platforms. The ISLSWG issues regular joint International Life Sciences Space Research Announcements (ILSRA) for both space and ground-based research opportunities.[3] Proposals to these Announcements of Opportunity (AO) are evaluated by an international peer group agreed upon by the ISLSWG. The ILSRA allows for a worldwide scientific competition and cooperation, by forming the best scientific teams, as well as offering access to an instrument pool from all ISS partners.

Participation in these AO is usually open to all categories of organizations, industry, educational institutions, other non-profit organizations, research laboratories, and government agencies. Proposals from entities among the ISS partner countries are made in response to the solicitation from their corresponding space agency. Present or prior support by any space agency of research or training in any institution or for any investigator is not a prerequisite to submission of a proposal or a competing factor in the selection process. Selections through AO can be for periods of many years, involve budgets of many millions of dollars for the largest programs, and usually are awarded through contracts, even for non-profit organizations, although occasionally grants are also awarded.

Independent internationally recognized experts, so called peers, first evaluate the proposals based on their space relevance and scientific merit. As a result of the peer review, all proposals are ranked according to an absolute scale (from 0 to 100) or a designation of "not recommended for further consideration", based upon the intrinsic scientific or technical merit of the proposal. This score reflects the consensus of the review panel.

A second review is an evaluation of the feasibility of implementing the proposed work using available facilities on a space platform. The flight feasibility review is

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[3] These Research Announcement can be found online at the following URL: http://www.esa.int/SPECIALS/HSF_Research/SEM0TV4KXMF_0.html [Accessed 22 October 2010].

conducted for each flight experiment proposal that receives a scientific merit score greater than a threshold score, which is usually 75, agreed upon by the ISLSWG Steering Committee. This study includes a safety review, an assessment of accommodation possibilities on board ISS, as well as a verification of the availability of the required utilization resources and flight opportunities. An international team of engineers and scientists experienced in the development of spaceflight experiments conducts this review (Figure 9.8).

Once the proposal is recommended by the peer group and its technical assessment confirms feasibility, the next decision layer is based on programmatic aspects, such as funding confirmation for the project realization, confirmation on relevance to the program priorities by the sponsoring space agency, and availability of the resources requested.

The next phase, the implementation of the flight experiment, is actually a multistep process. Following the complete review of flight proposals, successful Principal Investigators (PI) will receive a letter informing them that their experiment has been selected for entry into a definition phase.

During the definition phase, the agency with management responsibility for the experiment will interact with the investigator to determine specific hardware and operational requirements needed to achieve the proposed objectives. Identification of

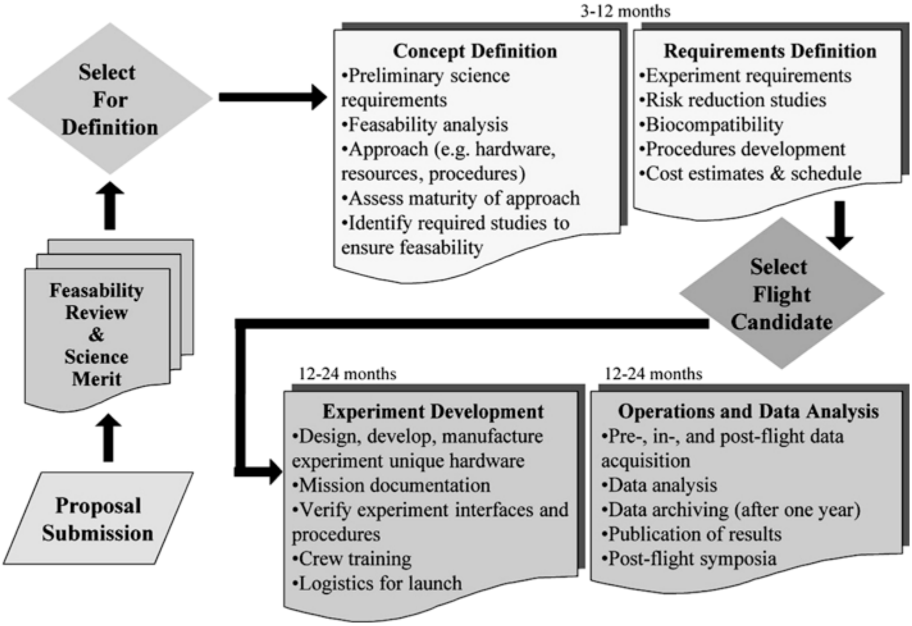

Figure 9.8. Steps of the Experiment Proposal Selection Procedure. The Time from Proposal Submission to Acceptance Is Typically 6 Months. This Period Can Be Shorter for Simple Projects or Longer for More Complicated Projects. The Time from Acceptance to the Actual Launch of an Experiment to the ISS Is Payload-Specific. The Time Period Ranges from 1 to 5 Years, Depending on the Time Needed for Payload Development. (Credit NASA).

issues that will affect implementation of the spaceflight experiment and refinement of the funding requirements are key components of the definition phase.

After successful completion of this phase, the experiment will be selected for flight and enters into a development phase, leading eventually to implementation on a space mission. Proposals are usually funded in 1-year increments until the experiment is completed. Detailed budgets are refined or negotiated for each flight experiment during each phase. The flight experiments selected can be reviewed periodically for technical progress, availability of flight opportunities, implementation feasibility, and to ensure that the science continues to be relevant. This review may result in a decision to deselect a flight experiment prior to its implementation or completion.

9.2.2. Experiment design

The experiment objectives can include applied aspects of space research (e.g., the assessment of operational issues in support of NASA Human Research Program (HRP) or other space agency's programs) or fundamental research.

Biology experiments can use cell cultures, bacteria, small plants, invertebrate animals and amphibian or fish embryos. Conditioned temperature during upload and download of samples ranges from 18°C to 28°C, but is sometimes temporarily unavailable. Therefore, experiments should minimize upload and download mass, volumes and requirements for controlled temperature during transport. Onboard experiment operations generally cannot be started until 3–5 days after launch, due to operational constraints. The period between upload and download of experiment samples is a minimum of 2–4 months, due to the sequence of *Soyuz* and other cargo vehicle rotations to and from the ISS. Only small sample masses and volumes can be downloaded using *Soyuz*, at temperature ranging from 15°C to 30°C. To minimize the need for downloading samples, experiments using on-orbit analysis techniques are encouraged (Figure 9.9).

For human physiology experiments done on volunteers, the number of subjects will obviously be small. The number of subjects is generally 6–12, depending on the variability of the dependent variable and the expected outcome. Therefore, flight experiments require control studies for a small N data set. In particular, (a) the dependent variable needs to be well defined (i.e., valid, reliable, relevant, practical); (b) the astronauts' preflight data must be compared with those of control groups on Earth; (c) preflight tests must be repeated several times for variance analysis; and (d) multiple postflight tests are required to establish the return of the variable to baseline. Indeed, only then can the changes observed during the flight be attributed to the adaptation to the new environment.

As a general rule, flight experiment proposals must clearly define the actual experiment duration and all requirements and conditions required to successfully complete the experiment. Be sure to explain succinctly all experiment requirements and procedures in terms that a layperson can understand. The investigator should allow for flexibility in the selection of the best hardware to be used to accomplish the experimental goals. The functional capabilities of hardware available to support human and non-human experiments are described in the AO. This information should be used to develop an understanding of the available capabilities. Investigators should use this information as a guide for developing experiment requirements and procedures rather than selecting specific hardware items.

Figure 9.9. Astronauts Use a Laptop-Based Simulator on Board the ISS to Prepare for a Soyuz Relocation Maneuver. Note That They Still Make Heavy Use of Hard Copy Procedure Documents. (Credit NASA).

A statement from the PI's institution is required asserting that the proposed work meets all local requirements concerning research on animal or human subjects. Safety assessments, including a description of possible hazardous situations for the test subjects and the foreseen countermeasures, must be provided. In addition to this statement, a letter signed by the chairperson of the Institutional Review Board (IRB) or ethics committee regarding approval of the experimental protocol that includes animal or human subjects, is required.

9.2.3. Hardware selection

Not every experiment requires new hardware development. Space agencies have a growing inventory of flight hardware that is available for use by investigators [Wilson, 2003]. Some investigators may wish to develop their own special experiment hardware to work in conjunction with the facilities and functional capabilities of existing hardware. Design, construction, and flight of major experiment-unique equipment hardware items or facilities usually require the commitment of large quantities of resources, including power, crew time, volume, and budget. Below are some tips for the design or selection of flight experimental hardware:

Mass and volume must be as small and compact as possible. It must be simple and intuitive to use because crew training time will be limited.

Power and data management requirements add immensely to complexity. It is preferable to use non-powered or battery-operated equipment when possible, and to store the data in the instrument. Although it is possible to store the data on board the shuttle or ISS, or to use the downlink capability, providing for data recording within the instrument reduces the interface count, the chance for failure, and competition for spacecraft capability. This option does not provide a data quick-look capability, but quick-look data are of benefit only if one can act on the information.

Data management should use identified standards and meet laboratory data analysis capability (e.g., provides useful information). Because experiments can take years to fly, non-standard ground-support equipment might not be available by the time the experiment is performed. There is no dedicated data storage facility on board the ISS. Therefore, if on-board data storage is required, this feature must be implemented within the instrument payload.

A long shelf life using "bullet-proof" technology is desired. The useful lifetime of the ISS should cover a period of more than 10 years,[4] and some of the equipment like the racks, freezers, and treadmills will stay on board for all that period.

Hardware must be modular and should be build such as it is easy to replace and upgrade components. At over $50,000 per kilogram, the cost of returning failed equipment to the ground for repair and returning it again to space becomes prohibitive. In addition, the disruption of the associated research program, use of limited crewtime, and impact on the restricted upload/download transportation capability would be significant. A well-balanced reliability and maintainability approach is therefore necessary.

Last but not least, think zero-g! Things people hardly notice can be big problems in space. A broken test tube, spilled liquid, or a dropped screw can float through the cabin instead of falling harmlessly to the floor, creating a potential hazard for the crew. As we seldom are exposed to gravity levels other than 1-g for any length of time, we have developed a "1-g mentality". We use gravity in our daily life without even thinking about it and have difficulty comprehending the appropriate design of space hardware or human-machine interfaces in reduced gravity. To design space hardware, engineers must develop a microgravity mentality, rather than solely a 1-g mentality.[5]

In addition, equipment that is carried on manned vehicles must meet the requirements for structural integrity, safety, flammability, odor, and toxicity. Usage of materials that produce toxic outgassing is avoided in habitable areas, except in controlled enclosures, such as the "glove boxes" for the manipulation of biological samples (Figure 9.10).

9.2.4. Feasibility

Of particular concern regarding the evaluation of the feasibility of a proposal is the identification of risk factors that could impact the implementation of an otherwise meritorious proposal. For example, the feasibility of implementing a scientific experiment and associated risks will be evaluated using the following technical criteria:

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[4] The Russians abide by the philosophy of "if it is not broken, don't fix it!" The *Mir* space station was originally planned to stay 8 years in orbit, and was actually used for more than 15 years.

[5] According to NASA, approximately 40% of equipment flown in space for the first time does not work, often due to heat build-up from lack of convection, lack of dissipation of air bubbles, or designs more appropriate to normal gravity than microgravity.

Figure 9.10. An ISS Crewmember Manipulates Hazardous Biological Samples in One of the Gloveboxes of the Russian Research Module. (Credit NASA).

Functional Requirements – Will the planned flight and ground hardware meet the requirements of the experiment? What experiment-unique hardware will be required, and can it be developed in time for projected flight opportunities? Are the numbers of subjects or specimens required attainable within a reasonable period of time (1–2 years) considering projected flight opportunities and other competition for those flight opportunities?

Operational Feasibility – How complex are the experiment procedures? Will the crew have sufficient time to be trained to perform the experiment? Will they have sufficient time in space to perform the experiment? Are the requirements for launch vehicle loading and unloading of the experiment specimens compatible with the capabilities of these vehicles? Can requirements for data collection on human subjects be accommodated in the preflight and postflight schedules for the astronauts? Has the experiment protocol taken into account the unavoidable period of time between the launch of an experiment and the actual initiation of the experiment? Will the experiment requirements for crew time, experiment volume, mass, power, or other features of on-orbit operations (such as temperature-controlled storage) affect the completion of this or other experiments? What other impacts will the experiment have on activities or experiments planned for the same mission?

Environmental Health and Safety – Are there elements of the proposed ground or flight activities that pose concerns for the health and safety of personnel or the environment? For experiments that use the crew as research subjects, could the implementation of these experiments, even if considered safe, lead to a negative impact on the performance of the human subjects with respect to their other crew duties? Is it possible that specific restrictions on the human subjects (such as diet, exercise, etc.) will interfere with their other activities?

Using the risk factors identified in the evaluation of the feasibility of a proposal, a score is assigned to indicate this level of uncertainty. The proposals are scored "low risk", "medium risk", or "high risk" when the risk to the successful achievement of objectives is considered minimal, moderate, or extreme, respectively.

9.2.5. Experiment integration

The primary goal of the integration process is to assemble a group of space experiments in such a way that maximizes the scientific return of the mission while effectively using the resources of the space vehicle. During this process, the PI is responsible for providing the mission managers with a complete description of the experiment, its equipment, and the interfaces with the space vehicle. Before the final decision to build the equipment, and during its construction, the PI also participates in a number of technical reviews. When the equipment is ready and "integrated" in the space vehicle, the PI is also asked to participate in the functional evaluation of the equipment and its utilization procedures.

9.2.5.1. Key documentation

When a proposal is selected for the Definition Phase, a nominated space agency Project Scientist will initiate the development of a detailed Experiment Scientific Requirements (ESR) document together with the PI and the science team. This process will also involve an instrument developer and an ISS operations manager.

The ESR document describes: (a) the science objectives in a summary format; (b) the experiment equipment mass, size, power, thermal control, and interfaces; (c) whether the equipment is to be used before, during, or after the flight; and (d) how it will be used, including command, data management, software, man-machine interfaces, and data analysis. Once approved by the space agency and signed by the science team, the ESR will become one of the contract documents for the experiment development and implementation. The ESR may evolve over the course of the project realization to keep track of all of the changes agreed to and include progressively more details of relevance to the following phases of the project.

These phases are typically the following: (a) study; (b) manufacture; (c) testing; (d) launch; (e) on-orbit operations; and (f) exploitation. The first phase includes a definition phase that is based on the early requirements defined above, followed by a Phase A/B where a preliminary design is proposed. This is followed by a Phase C/D, which includes detailed design, production (manufacture), and flight qualification and verification (testing). During this process, the Project Manager tracks the changes in the requirements, manages the risks, makes cost estimates, and organizes project reviews on a regular basis.

The PI is in regular contact with the space agency, the Payload Manager, and the Payload Experiment Developer (PED). In the case of flight or programmatic delays, the PI should inform the agency at least annually as to whether the project is still relevant from the scientific point of view, given the recent advances of research in his area of expertise. All selected projects are subject of regular reviews by scientific advisory committees.

9.2.5.2. Reviews

For most research projects, a series of formal program reviews play an important role in coordinating the experiment integration process. Each review occurs at a natural transition point in the development and integration activities and has a specific purpose associated with it.

The Experiment Requirement Review (ERR) – The experiment requirements defined by several Principal Investigators are combined into an integrated requirements document. As a result of this review, the available space resources on board the space vehicle are allocated to the experiment instruments and subsystems elements.

The Experiment Preliminary Design Review (PDR) – The purpose of this review is to finalize the mission requirements (resources, crew time), baseline the equipment design interfaces, finalize the safety verification methods and begin their implementation, initiate the planning for physical integration and flight support, and finalize the planning for crew science training.

The Experiment Critical Design Review (CDR) – The purpose of this review is to provide an in-depth review of the final design and compare it with the requirements to verify compatibility with the space vehicle and the other experiment equipment, as well as to verify overall system safety.

After the equipment has been delivered, the PI is expected to support the integration of their hardware into the space vehicle and its preparation for flight. Documents such as procedures for interface tests, calibration, special tests, servicing, and maintenance are provided. The PI is also expected to participate in science verification testing of their equipment, both before integration in the space vehicle using a high fidelity mock-up, as well as after the integration is completed.

Integration in the *Soyuz* or *Progress* vehicle typically occurs 3 months before flight, but the equipment should be delivered to Russia not less than 6 months prior to launch. Experimenter activity in the *Soyuz* is very limited during integration, but there may be provisions for hands-on work if needed (i.e., loading samples or specimens) and if the requirement is identified early enough. Small experiments and equipment can be installed in the *Soyuz* modules up to 12 h before launch.

9.2.6. Crew science training

While the flight equipment is being integrated in the space vehicle, exact copies of this equipment, called “training models”, are used for crew training. Training is aimed at ensuring that the ground personnel and flight crew involved in performing an experiment do so both safely and effectively under nominal and off-nominal conditions.

The first step is to inform the crewmembers selected for the given mission about the rationale of the research and the associated hazards. Once the crewmembers have agreed to participate in an experiment and signed the Informed Consent Form, they are then briefed in more depth about the scientific rationale for the experiment. This phase is important should the astronauts discover new research approaches during the flight, which were not foreseen by the investigators. With a complete understanding of the scientific background and rationale for the experiment, the astronauts could then suggest, in agreement with the investigators, appropriate changes to the flight protocol to maximize scientific return.

The second step is to train the participating on a copy of the flight equipment to refine the experiment operations flow. The activities related to an experiment are described in sequences of operations or Functional Objectives (FO) that satisfy a specific engineering or scientific goal. A FO typically consists of a number of functional steps, such as activation, calibration, various steps of the experiment operations, standby, and deactivation. The experiment operations flow is a basis for developing step-by-step procedures that will be used by the crew, and followed from the ground, during the actual mission. Procedures for both nominal operations and contingencies, like trouble-shooting the equipment, are developed. These procedures and the reference material for each experiment are assembled into a Payload Flight Data File (PFDF). This document is stowed on board for use by the science crew during the mission (Figures 9.9, 9.11, and 9.12).

The third step is to evaluate the time required to perform the operations (proficiency) on the ground. This time is multiplied by a factor of 1.4 to take into account the microgravity factor. Once each experiment has been through the same evaluation process, the mission management can decide if and when several experiments can be executed in parallel. These evaluations allow assembly of the operations flows during the mission, which will lead to the crew timeline. At this point the crew is trained as a team to use the experiment procedures according to the timeline. Occasionally, integrated simulations are conducted with the support of ground controllers in the same configuration as during the actual mission.

Science briefing and familiarization courses are conducted approximately 1 year before launch. Hands-on familiarization using a copy of the flight model occurs

Figure 9.11. Two Astronauts Support an Extravehicular Activity from Inside the ISS. Even With so Many Laptops on Board, Paper Documents Are Abundant. (Credit NASA).

Figure 9.12. Even the EVA Checklists Are Still Provided on Paper! (Credit NASA).

3–6 months before launch. Simulations of on-orbit operations are conducted in the final months before launch.

9.2.7. In-flight science operations

9.2.7.1. Organization

As with all space missions, the crew in orbit receives instructions during flight from a mission control center on the ground. The ISS flight operations are performed in a decentralized manner, under the overall responsibility of the Mission Control Center in Houston (MCC-H) for U.S. system operations, the Mission Control Center in Moscow (MCC-M) for Russian system operations, the Payload Operations and Integration Center in Huntsville (POIC) for U.S. payload operations. Other control centers have responsibility for operations of certain modules and their associated payloads, interfacing with the MCC-H and POCC, respectively. For example the Columbus Control Center (Col-CC) in Munich is responsible for payload operations on the *Columbus* module.

Scientists can control their experiments and payload operations from a User Space Operation Center (USOC). More commonly, the scientists remain in their laboratory during the periods their ISS experiments are performed. On rare occasions, some science teams are allowed to remotely control their instruments, sending uplink commands directly from the MCC or from their USOC via the POIC.

9.2.7.2. Communications

The NASA Tracking and Data Relay Satellite (TDRS) system is the primary communications link between the space shuttle and ISS with the ground. The link is made to the ground station at White Sands in New Mexico. The data is then routed to various locations around the world, including Europe, Russia, and Japan.

Communication between the space shuttle and the ISS and the ground is performed via S-band (bi-directional, i.e., uplink and downlink, or to and from the ISS, respectively) and Ku-band (downlink data only):

S-Band – The uplink capability (maximum 72 kbps) is used to uplink payload and system commands, files, and audio data to the ISS. The downlink capability (maximum 192 kbps) is used to downlink audio, caution and warning data, command confirmations, recorder dumps and telemetry, i.e., system data and limited payload "housekeeping" data but not payload research data. The average S-band coverage is approximately 70% per orbit. During loss of signal (LOS) periods, the downlink data is recorded on board for later downlink on request during acquisition of signal (AOS) periods.

Ku-Band – The downlink capability (maximum 100 Mbps, rates may vary from 1.8 to 95 Mbps) is distributed over eight data channels. It is used to downlink video and high-rate research data. The average Ku-band coverage is approximately 70% per orbit. For LOS periods, the Ku-band data are stored in one high rate communication recorder on board ISS (Figure 9.13).

The data downlink must be scheduled in advance. All instrument payloads need to have autonomous capacity for storage of data and potentially employ data compression. Typically, preliminary planning is started 12–18 months prior to the initial operation of

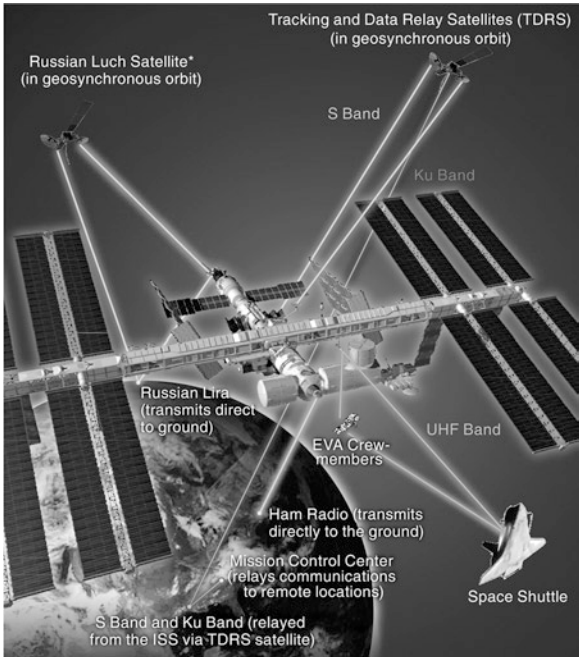

Figure 9.13. The Communication Pattern Between the ISS, Shuttle, and Both the U.S. and Russian Ground Segments. Note That the Luch Satellite (*) Is Not Currently in Use. (Credit Wikipedia).

the instrument or payload, with definition of requirements in the ESR (i.e., desired data rates, frequency of transmission, and total volume of data to be transmitted).

For crews in orbit, the voice at the other end of the radio link can be unfamiliar, making smooth communication a challenge. It's beneficial, therefore, for the astronauts and mission personnel on the ground to meet in person before launch, to put a live, human face to a name and a picture. Usually, voice communications from ground to spacecraft are relayed though an astronaut. From NASA MCC-H in Houston, the individual fitting this role of CAPCOM (for capsule communicator) has extensive and personal knowledge of the onboard activities and of the potential for miscommunication issues. From the other mission control centers, the crew interface communicator (CIC) is either an astronaut (he/she is called EUROCOM for ESA) or a third party who relays instructions from the science teams to the crew in space.

Investigators find that their ability to collaborate with crewmembers-operators is significantly impaired by this multiple-step process. Only on rare occasions does the PI talk personally to the crewmember experimenters in orbit to congratulate them for their good work, discuss an unexpected result, or to determine together the best methods for modifying a failed experiment. Alternately, if many individuals were to have access to the air-to-ground communication system, the aggregated messages could become overly burdensome and interfere with effective communication and scientific return.

By analogy with the amateur radio communication "étiquette", there is a code for communication to and from orbit, with the first word pronounced being the organization or the person to be called. For example, the CAPCOM in Houston will use "Alpha" (the nickname for the ISS, by analogy with the Star Trek series) or "MS1" (for Mission Specialist 1) as a call sign from the ground. Similarly, the crew in orbit will use "Houston" as the call sign from orbit.[6] Other codes are used for acknowledging good reception ("Roger") or for answering positively ("Affirmative") or negatively ("Negative") to a question.

9.2.7.3. Planning

Planning is a process used to build timelines of activities on board the ISS to optimize the use of crew, power, and other resources. Planning is performed prior to the start of the increment and during the increment. Planning involves the International Partners, including NASA, Roscosmos, ESA, JAXA, and CSA. NASA is the overall integrator of ISS plans and schedules; POIC integrates payload plans and schedules; MCC-H integrates system plans and schedules,[7] and combines system and payload plans and schedules. Figure 9.14 shows the organization and who is involved in planning activity.

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[6] A popular poster in Houston claims "Houston, first word from the Moon". Indeed, just after the Lunar Exploration Module had landed on the Moon in July 1969, the first communication between Astronaut Neil Armstrong and Earth began with those words: "Houston…Tranquility Base here… The Eagle has landed."

[7] A plan is a high-level timeline, with activities tied to a particular day. A schedule is a detailed timeline, with activities tied to a particular time of day.

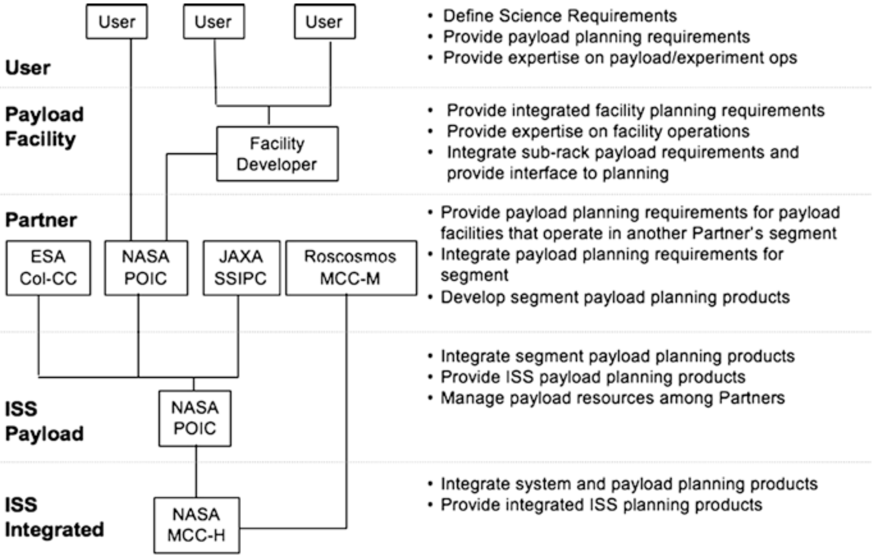

Figure 9.14. The Pre-increment Planning Process Starts When the Users Submit Their Payload Planning Requirements at About 8 Months Prior to the Increment. The Process Ends About 2 Weeks Prior to the Increment When the Final On-Board Operation Summary (OOS) Is Signed. (Source NASA POIC).

Prior to flight, an operations timeline will have been developed and practiced during the flight simulations. The schedule for activities on board the ISS is densely packed. The lessons learned over more than 15 years of Spacelab flights laid the foundation for the planning used for the ISS increments.

Before each increment, two ISS payload planning products are produced: (a) the payload On-board Operations Summary (OOS) is a high-level plan of the increment, with payload activities (attended and unattended) and sequences tied to a particular day; and (b) the payload Increment-specific Execute Planning Ground rules and Constraints (Gr&C) is a compilation of payload planning constraints that are high-visibility and affect the operations of all the modules. These products are built by MCC-H based on the inputs from the planners of all the International Partners. These products are posted on web pages with username and password access for everyone who needs to consult them.

The Increment Planning is the process to build detailed schedules of activities during the increment and update them as required. Increment planning is performed on-console in the POIC. During the increment operations, three planning products are produced each week: (a) the Weekly Look-ahead Plan (WLP) is a 7-day detailed schedule of crew and unattended operations, which begins on the Monday 2 weeks prior to execution and completed on that Friday; (b) the Short Term Plan (STP) is a 1-day detailed schedule of crew and unattended operations, completed 6 days prior to the day of execution; and (c) the On-board STP (OSTP) is the on-board version of the

STP, viewable in OSTP Viewer (OSTPV) (Figure 9.13). The OSTP is maintained for the execution day and 5 days in advance for the crew and flight control teams to view the current and upcoming daily timelines. After the STP is finalized at execution minus 6 days (E-6), it is uplinked as part of the OSTP.

During the flight, Control team members make sure that in-flight activities are on schedule and everything is operating properly, and determine the impact of mission events on the science timeline. The USOCs are responsible for monitoring specific experiments and informing the Mission Scientist and PIs about deviations from the planned activities. Some minor changes can be made during the planned operations, but most changes, such as those due to failure of equipment, will usually be accomplished by re-planning the timeline of the next in-flight session (Figure 9.15).

Any modification of the planned timeline requires consideration of the impact on spacecraft operations, science operations, and crew activities. This re-planning usually requires several days to accomplish. The Mission Scientist informs the PI during the mission to review progress and make schedule adjustments for the next in-flight session. Any changes to payload planning requirements or the timeline are submitted using an Operations Change Request (OCR). If the change results in an update to the final WLP or STP (incorporated in OSTPV), a Planning Product Change Request (PPCR) is submitted to MCC-H and all the International Partners. Only critical science changes are allowed within 2 days of execution.

The mission scientist will meet with the experimenters to assess the impact on each experiment and reach a consensus on the modifications that should be made.

Figure 9.15. Astronaut Koichi Wakata and OSTPV Showing on Laptop. The OSTP Is a Rolling Timeline That Can Be Updated in Real Time. The Crew Annotates the OSTP After Experiment Execution. These Messages Are Reviewed by the Ground Controllers and the Science Teams. (Credit NASA).

The mission control management team will then implement the changes. Major changes to the timeline usually take the form of substitution of one experiment for another within the timeline resource allocations. Experimenters can request changes in the operation of their own equipment in response to preliminary results from the flight. Such changes should not impact crew time or other experiments, though.

9.2.8. Data analysis

Following completion of on-orbit and postflight operations, the investigators process the data for later publication in peer-reviewed scientific journals. In general, the space agencies grant the PI an exclusive right of prior access to the raw and calibrated data. The duration of the exclusive right (also called "Period of Prior Access") is 1 year from the provision by the agency of the data to the PI in a form suitable for analysis. The exclusive right of prior access is granted to the PI under the condition that the PI analyzes and publishes the results. After this 1-year period, the data belong to the public domain.

After 1 year following the mission, the PI must give a debriefing on the experiment status and preliminary results to the crewmembers who have participated as test subjects. 1 year after the completion of the experiments by all crewmember-subjects, the PI must deliver a Final Report and file the information required for the mission databases.

Databases exist at space agencies, which provide access to information regarding space life sciences experiments carried out since the 1960s. Generally, an experiment description in the database, submitted by the investigators themselves, provides information about the Principal Investigator, the flight or mission on which the experiment was performed, the experiment equipment, and an extended abstract that includes the objectives, procedures, and results of the experiment.

The Life Sciences Data Archive (LSDA) at the NASA Johnson Space Center is an online database containing descriptions and results of completed NASA-sponsored flight experiments. This database includes descriptions of the experimental objectives and protocols, hardware, biospecimens or data collected, personnel, and documents. For a limited number of experiments, the final reports and spreadsheet data suitable for downloading are posted at the URL address http://lsda.jsc.nasa.gov. Data from human subjects are unavailable online for privacy reasons. The Erasmus Experiment Archive (EAA) is a database of ESA funded or co-funded experiments covering a wide range of scientific discoveries, which were performed during missions and campaigns incorporating various space platforms and microgravity ground-based facilities over the past 30 years. It contains information collected into experiment records. The website is http://eea.spaceflight.esa .int/.

Further information on the Russian and Japanese central repository for space life sciences mission data can be obtained at http://www.rssi.ru/ and http://www.jaxa.jp/guide/researcher_e.html, respectively. The ESA, NASA, and JAXA archives are all part of the International Distributed Experiment Archives (IDEA), and can be searched as if they were a local archive. A well-established Interoperability Document rules the exchanges of records.

9.3. Benefits to life on Earth

Research aboard the ISS is preceded by years of related research, supported by ongoing research on the ground, and may continue for years after data are downlinked or the experimental samples or hardware are returned from the ISS. Along the way, the science that falls under the ISS research umbrella has spawned many innovations, patents, and real-world applications of techniques or findings.

It is difficult to capture all of the science, applications, and innovations that have been spun-off from research aboard the ISS. In the best examples, data from the ISS have provided critical insight or results, perhaps ancillary to the actual hypothesis that is being tested, and have influenced the trajectory of subsequent research on the ground. In almost all cases, experiments on the ISS are a small part of an overall research program. Even highly targeted research demonstrations stem from a broad base of prior investigations and findings.

Many experiments have direct applications to Earth-based processes. A recent NASA publication on the ISS scientific accomplishments from 2000 to 2008 provides a few examples of some of the success stories from ISS research [Evans et al., 2009]. NASA anticipates that chapter will grow in the coming years as results from ISS experiments feed new innovations in scientific and technical circles.

Since the early days of the space program, NASA's research has provided obvious benefits back on Earth, mostly in the form of commercial products and services. Even without manufacturing, marketing, or selling commercial products, NASA's technology has been transferred and effectively used in many commercial products adapted by private industry for non-space applications. NASA estimates that since 1958, the number of successfully implemented spin-offs for commercial uses is on the order of 30,000 [Peeters, 2000]. NASA's spin-off portfolio includes many distinctive economic and industrial sectors, such as transportation, environment and agriculture, public safety, home and recreation goods, computer technologies, and industrial performance and productivity [NASA, 2008].

Recently, Miguel Brito, a student of the International Space University, compiled a list 271 space life sciences spin-offs in the area of biotechnology, pharmaceuticals, biomedical technologies, nutrition and pharmaceuticals, fitness and rehabilitation, food processing, biomedical devices, cosmetic, patient monitoring, telemetry, and telemedicine. Biomedical devices involve the highest number of successful spin-off cases. In fact 61.5% of the space life sciences spin-offs considered in this study are related to medical devices that are beneficial for human health and welfare. Biomedical technology spin-offs come in second place with 21.4%. In third and fourth positions appear, respectively, biotechnology with 6% and patient monitoring, telemetry and telemedicine with 4%, significantly less than the previous two categories.

The transfer of space technologies has particular relevance today and it is included in the major space agencies management programs. This process allows companies to make profits by designing new technology and selling new products or services, or simply enhancing their efficiency by introducing new production or management processes. These positive effects spread throughout the economy via sales of goods and services, intellectual property licenses, technical or scientific documents. They are the

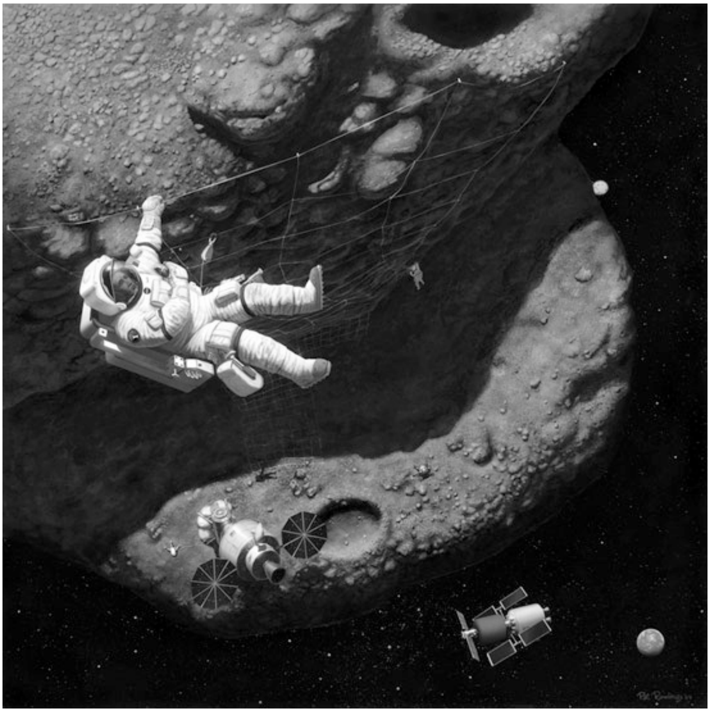

Figure 9.16. Artist Concept of a Human Mission to a Near-Earth Asteroid. Even Though Such a Mission Is Fraught with Risks and Challenges, Human Judgment and Dexterity Are Key for Assessing and Successfully Extracting Valuable Minerals from an Asteroid. (Credit NASA/Pat Rawlings).

basis of the long-term economic effects of space programs, a "passage obligé" for the future of human space exploration, and one of the fundamentals of space medicine (Figure 9.16).

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