Human Health and Performance Risks of Space Exploration Missions

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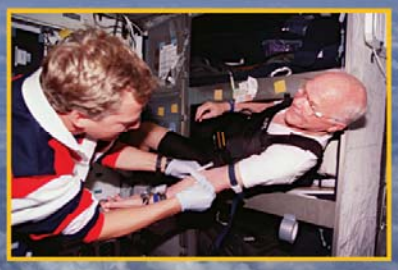

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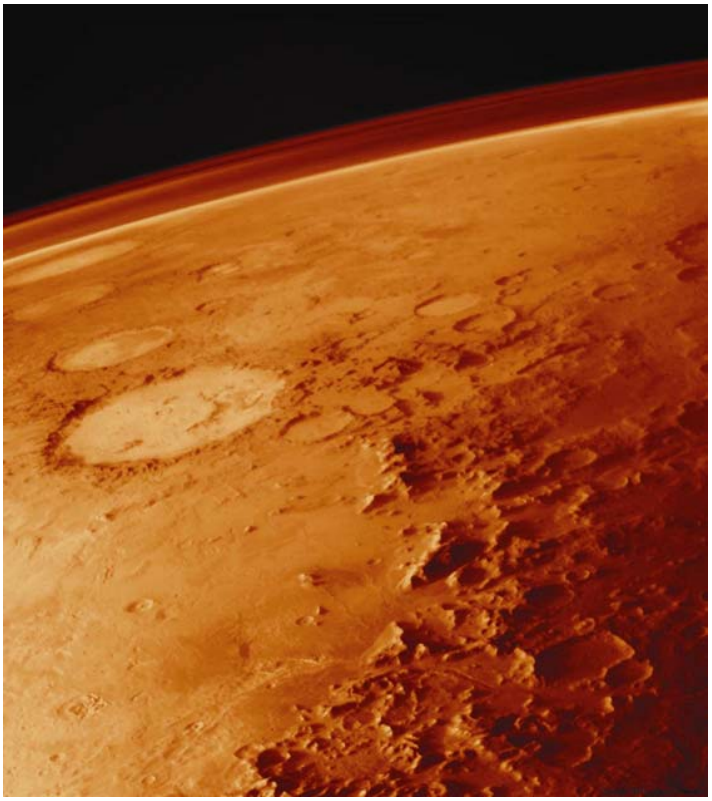
Evidence reviewed by the NASA Human Research Program



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Introduction

The Human Research Program (HRP), which is within the NASA Exploration Systems Mission Directorate, is a directed and applied research program that addresses agency needs for human health and performance risk mitigation strategies in support of space exploration as described in the Vision for Space Exploration[1], the U.S. National Space Policy[2], and the NASA Strategic Plan[3]. These exploration undertakings include missions to the moon and Mars. Although all of them will involve some of the same human health and performance challenges, each mission also will include specific challenges that depend on the nature of the exact undertaking and the development schedule. Accordingly, HRP research and technology development are focused on the highest-priority risks to crew health and safety, with the goal of ensuring mission success and maintaining long-term crew health.

Three core documents describe the HRP. The first is the Program Requirements Document (PRD)[4], which defines, documents, and allocates high-level requirements to different organizational arms of the program; these requirements include responsibility for specific human system risks listed in the PRD. Previously, the Bioastronautics Roadmap[5] documented the health and performance risks and areas of concerns of a wide cross-section of the professional space life sciences community, but it did not have the level of detail that is necessary to prioritize risks across physiological disciplines or to compare strategies for how to manage a given risk across mission operational architectures. The HRP 2009 PRD risk list thus identifies a narrowed and more operationally-focused series of risks.

The second HRP document is the Integrated Research Plan[6] (IRP), which describes what implementation activities are necessary to fill the knowledge and mitigation gaps that are associated with each risk that is listed in the PRD. It also details when those activities will be accomplished, where they will be accomplished (e.g., the International Space Station (ISS) or a ground analog), who will accomplish them (investigators within a specific project or organization within the HRP), and what is being produced (risk uncertainty reduction, candidate health or performance standard, countermeasure strategy, etc.).

The third HRP document is the Evidence Book[7], which is a collection of evidence-based risk reports and journal articles for each individual risk that is contained within the HRP PRD and for which implementation activities are listed in the Integrated Research Plan. Thus, the collection provides the current state of knowledge for each of the defined human health and performance risks for future NASA exploration missions. All three of these documents, which are updated as evidence or events dictate, provide relevant information that can be used to manage the HRP.

The initial 2008 Evidence Book was a collection of written evidence reports that was created from both published and unpublished information reviewed by the HRP in 2006. From April to August 2008, the 2008 Evidence Book was reviewed by members of the Committee on NASA's Research on Human Health Risks, established by the Institute of Medicine (IOM), which is the arm of the U.S. National Academy of Sciences that is charged with examining public health policy. The resulting thorough *Review of NASA's Human Research Program Evidence Books: A Letter Report (2008)* provides guidance for both a revision of the current risk reports and for the development of future versions. It is publicly available via the National Academies Press Website.[8]

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[1]See http://www.nasa.gov/missions/solarsystem/explore_main_old.html.
[2]See http://www.ostp.gov/galleries/press_release_files/Unclassified%20National%20Space%20Policy%20--%20FINAL.pdf.
[3]See http://nodis3.gsfc.nasa.gov/npg_img/N_PD_1001_000_/N_PD_1001_000_.pdf.
[4]See http://humanresearch.jsc.nasa.gov/files/hrp-47052_revc_PRD.pdf.
[5]See http://bioastroroadmap.nasa.gov/index.jsp.
[6]See http://humanresearch.jsc.nasa.gov/files/hrp-47065_reva_IRP.pdf.
[7]See http://humanresearch.jsc.nasa.gov/elements/smo/hrp_evidence_book.asp.
[8]See http://books.nap.edu/openbook.php?record_id=12261.

The IOM strongly recommended that the 2008 and future Evidence Book risk report information be made publicly available. For more than half of the HRP risk reports, therefore, single reports were revised to incorporate as much as possible the recommendations from the IOM Review and are presented as a collection in this NASA Special Publication, *Human Health and Performance Risks of Space Exploration Missions*; these reports are also available on the HRP Evidence Book Website. For the remaining risks, report information is currently being revised and reviewed as per the specifications of the specialized, subject-specific journals in which the authors have requested to publish the work. Citations for these journal publications, as they become available, will also be listed on the HRP Evidence Book Website. In the future, updated risk report information for all of the HRP risks will be maintained on the HRP Evidence Book Website in an electronic and rapidly updatable text format.

To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

The NASA categories are comparable to more familiar versions of Levels of Evidence scales (e.g., Silagy C, Haines A. *Evidence Based Practice in Primary Care, 2nd Ed.*, London: BMJ Books, 2001). The use of a coordinated data categorization system is new to many NASA life scientists, but authors were encouraged to use such a system to help clarify the type of evidence that was presented and thus provide additional information about the strength of interpretations that were derived from those data; however, scientists were not required to use the categorization system hierarchically if they determined that this system would obscure or otherwise interfere with the clarity of the evidence that they were presenting.

The HRP, which recognizes the limitations of the distribution of the current risk report information, is evaluating even more thorough distribution possibilities for future editions of the risk evidence information. Through these initial actions, however, the HRP has made a good-faith attempt to fulfill the recommendation of the IOM and the requirement in the Space Act of 1958 (as amended) to disseminate to the widest possible audience the knowledge that is acquired during the course of NASA publicly funded activities.

Jancy C. McPhee and John B. Charles
May 2009

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Chapter 1:
Risk of Behavioral and Psychiatric Conditions

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Behavioral issues are inevitable among groups of people, no matter how well selected and trained. Spaceflight demands can heighten these issues. The Institute of Medicine [(IOM)] report, Safe Passage [Ball & Evans (eds.), 2001], notes that Earth analog studies show an incidence rate of behavioral problems ranging from 3-13 percent per person per year. The report transposes these figures to 6-7 person crews on a 3-year mission to determine that there is a significant likelihood of behavioral conditions and psychiatric disorders emerging. Impacts of behavioral issues are minimized if they are identified and addressed early. The HRP must provide the best measures and tools to monitor and assess mood and to predict risk for and management of behavioral and psychiatric conditions prior, during and following spaceflight. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

An iconic photograph of Russian cosmonaut Valery Poliakov, who has clearly demonstrated his capacity for long-duration space flights, having completed two tours of duty on the Russian space station* Mir*, including one that lasted 438 days, thus setting a record that remains unbroken to this day. Current International Space Station missions involve crew stays of up to 6 months, with provision of an effective set of psychosocial countermeasures to aid crew morale and team cohesion.

Executive Summary

Space flight, whether of long or short duration, occurs in an extreme environment that has unique stressors. Even with excellent selection methods, behavioral problems among space flight crews remain a threat to mission success. Assessment of factors that are related to behavioral health can help minimize the chances of distress and, thus, reduce the likelihood of behavioral conditions and psychiatric disorders arising within a crew. Similarly, countermeasures that focus on prevention and treatment can mitigate the behavioral conditions and psychiatric disorders that, should they arise, would impact mission success.

Risk, which within the context of this report is assessed with respect to behavioral health, is addressed in terms of occurrence in space flight and analog populations, and of predictors and other contributing factors. Based on space flight and analog evidence, the average incidence rate of an adverse behavioral health event occurring during a space mission is relatively low. While mood and anxiety disturbances have occurred, no behavioral emergencies have been reported to date in space flight. Anecdotal and empirical evidence indicates that the likelihood of a behavioral condition or psychiatric disorder occurring increases with the length of a mission. Further, while behavioral conditions or psychiatric disorders might not immediately and directly threaten mission success, such conditions can, and do, adversely impact individual and crew health, welfare, and performance, thus indirectly affecting mission success.

Identification of predictors and other factors that can contribute to the risk of behavioral conditions and psychiatric disorders at all stages of a mission increases the efficacy of prevention and the treatment of those conditions. Many factors predict or otherwise play a role in the occurrence of a behavioral condition or psychiatric disorder. These include: sleep and circadian disruption, personality, negative emotions, physiological changes that occur when adapting to microgravity, lack of autonomy, daily personal irritants, physical conditions of life in space, workload, fatigue, monotony, cultural and organizational factors, family and interpersonal issues, and environmental factors. Positive or salutary aspects of space flight also contribute to behavioral health outcomes. Some factors have both detrimental and salutary aspects; teamwork, giving and receiving social support, and leadership responsibilities are a few examples of these.

The current approaches to prevent behavioral conditions and psychiatric disorders begin during selection and continue post-flight. The goal of the behavioral health component of the astronaut selection system is to identify individuals who, at the time of application, have diagnoses that are incompatible with the demands of space flight, and also to identify those who are believed to be best suited psychologically to be astronauts. Countermeasures are a second line of defense to prevent behavioral conditions and psychiatric disorders from occurring pre-flight, during flight, and post-flight. For example, psychological support services are provided to crew members and their families before, during, and after missions.

Approaches that prevent or mitigate behavioral conditions and psychiatric disorders often can be used to treat the occurrence of behavioral problems. Private psychological conferences, for example, can provide both prevention and treatment. While anecdotal evidence suggests that current practices may be sufficient, the efficacy of these practices has not yet been assessed systematically.

In sum, evidence indicates that development of behavioral conditions and psychiatric disorders is a risk for human space flight, and that this risk increases as mission length increases. Multiple methods are employed to prevent and treat behavioral problems and appear to have some effect, although the extent to which prevention and treatment are effective has not been quantified.

Introduction

The NASA commitment to long-duration space flight includes astronauts who will be returning to the moon as well as those who will take part in human missions to Mars. Successful exploration will require a better understanding of the effects that extended missions pose for the behavioral health of astronauts, not just during flight but also pre- and post-flight. As space flight missions lengthen, astronauts will spend longer periods away from families and friends. The absence of Earthly conveniences and daily routines will also intensify their feelings of isolation (Ball and Evans, 2001) (Category III[9]) because the astronauts will be spending more time confined in the spacecraft and living in an environment that is fraught with potential danger. On their return to Earth, they will have to reintegrate into a world that has adapted and changed without them. Consequently, predicting the effect that extended periods of isolation will have on astronaut performance and psychological well-being becomes increasingly important (Kanas and Manzey, 2008). Further, the potential for psychiatric disorders developing in long-duration crews during or after missions requires that consideration be given to prevention and treatment (Kanas and Manzey, 2003; Palinkas, 1986) (Category IV).

During astronaut selection, applicants who have been identified with a psychiatric disorder that would impede on-the-job success are removed from further consideration. However, important aspects of an individual's mental health history – e.g., exposure to a traumatic event, family history of mental health struggles such as depression or schizophrenia – may not have been disclosed to NASA at the time of astronaut selection. Not only may potential astronauts be hesitant to share information that would prohibit selection, but some current astronauts have also demonstrated a reluctance to share information if they perceive such information could jeopardize their flight status.

Disorders such as anxiety, post-traumatic stress, sleep loss/insomnia, adjustment, and depression can also develop unexpectedly in otherwise healthy individuals. A recent study by Tozzi et al. (2008) indicates that the average age of onset of depression for persons who have no family history of depression is 41 years (standard deviation (SD)=13.67); therefore, even astronauts who have never experienced depression are not immune from its development. The age of astronaut candidates when selected for the Astronaut Corps has ranged between 26 and 46 years (NASA, 2008b). Between 1989 and 2003, the average age of the astronauts who were selected was 36.5 years. It is important to note that depression could occur at any phase of an astronaut's career. Furthermore, as reviewed by Collins (1985), behavioral problems that occur during space flight often do not terminate when the mission ends, but can linger with notable aftereffects (Category IV).

Although the incidence of reported psychiatric disorders on shuttle missions has not been significant (Billica, 2000) (Category III), as the length of space missions increases the incidence of behavioral conditions and psychiatric disorders is also expected to increase (Ball and Evans, 2001; Otto, 2007; Stuster, 2008) (Category IV). Additionally, the ramifications of a disorder developing in flight are severe if that disorder is left unresolved. Anecdotal and empirical evidence from space flight and behavioral health incidence rates from

[9]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
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space analogs suggest that assessing, preventing, and treating behavioral health problems are essential to protecting the health of crew members and, consequently, the success of a mission.

The NASA Human Research Program (HRP) is organized into topical areas called Elements; the Behavioral Health and Performance (BHP) Element is tasked with the responsibility of managing three risks: (1) risk of performance errors due to sleep loss, circadian desynchronization, fatigue, and work overload; (2) risk of performance errors due to poor team cohesion and performance, inadequate selection/team composition, inadequate training, and poor psychosocial adaptation; and (3) risk of behavioral and psychiatric conditions. While each of these risks is addressed in a separate chapter of this book, they should not be construed to exist independently of one another but, rather, should be evaluated in conjunction with one another. Furthermore, BHP risks overlap with risks in other HRP Elements and, as such, must also be considered in conjunction with one another. Refer to figure 1-1 for an example of these possible overlaps.

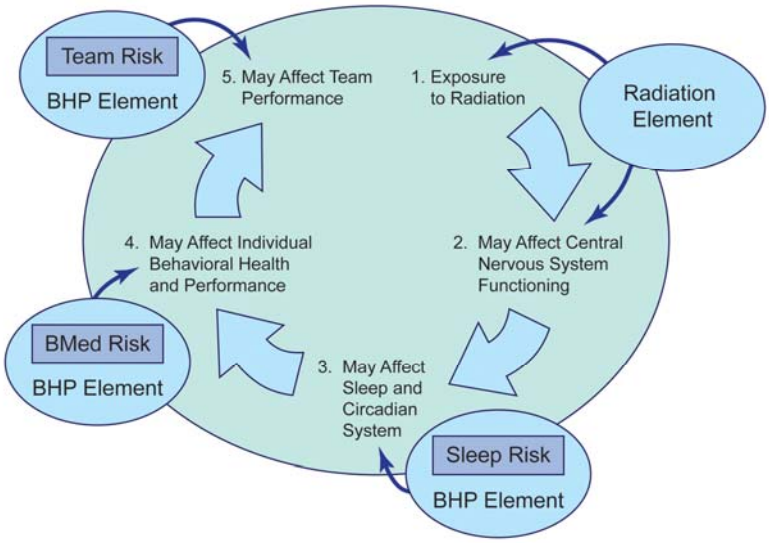

Figure 1-1. ***Example of possible BHP risks overlapped with risks in other HRP Elements.***

The relationships of the BHP Element with other HRP Elements are further outlined in the HRP Integrated Research Plan (IRP)[10]. The nature of the IRP implies that the BHP Element is continually reviewing and updating integration points with other elements. While research is designed to address identified gaps, it will be necessary to update and revise each of the BHP evidence reports and the IRP as the element gaps are closed and new gaps emerge.

[10]See http://humanresearch.jsc.nasa.gov/about.asp.

Evidence

Assessment of behavioral conditions and psychiatric disorders

An assessment of behavioral conditions and psychiatric disorders improves our understanding of the factors that contribute to the development of these conditions, and the treatment options that are best to manage this risk. Assessments occur within a framework, or a theoretical approach, of assessing behavioral conditions and psychiatric disorders. This theoretical approach, which is taught by NASA BHP to astronauts and flight surgeons, is described below. Evidence of the occurrence of behavioral and psychiatric problems in space flight and space analogs is then presented. Predictors and other factors that contribute to the occurrence of a behavioral condition and psychiatric disorder are then discussed. Lastly, current countermeasures and treatments are described.

The majority of the evidence that is cited is Category III. Please note that from this point on, only categories other than Category III are noted within the text.

Theoretical approach

Behavioral and psychiatric problems can be classified in several ways. NASA relies heavily on the classification system that is used by the American Psychiatric Association (APA) in the *Diagnostic and Statistical Manual Fourth Edition* Text Revision (*DSM-IV-TR*) (APA, 2000). In a slight departure from the DSM-IV-TR classifications, behavioral medicine training that is taught by a NASA psychiatrist also incorporates the *International Classification of Diseases-10* (*ICD-10*) (World Health Organization (WHO), 1996) standard diagnostic classification system. The *ICD-10*, which is used worldwide, is a more comprehensive system than the *DSM-IV-TR*; it is used to classify physical and mental diseases as well as conditions for all general epidemiological and many health management purposes. Mental and Behavioural Disorders is only one chapter in this much broader tome. In contrast, the *DSM-IV-TR*, which focuses on mental and behavioral disorders, assigns the following classifications:

- Axis I – clinical disorders
- Axis II – personality disorders and mental retardation
- Axis III – general medical conditions
- Axis IV – psychosocial and environmental problems
- Axis V – global assessment of functioning

When using the *DSM-IV-TR*, general medical conditions, psychosocial and environmental problems, and global assessment of functioning are relevant only to the extent that they contribute to or exacerbate psychiatric diagnoses.

Behavioral medicine training for the International Space Station (ISS) teaches NASA flight surgeons, crew medical officers (CMOs), and astronauts that there are three main types of significant mental disorders that might be encountered in a long-duration mission (NASA, 2008a): (1) *delirium*, which is a severe behavioral and cognitive response to physical injury or illness; (2) *adjustment disorder*, which is a severe and negative emotional response to a tragedy; and (3) *asthenia*, which is a progressive negative psychological response to the isolation and rigors of a long-duration mission. The Russian Space Agency, even more so than NASA, recognizes asthenia as a condition that occurs during long-duration missions (Kanas, 1991). NASA behavioral medical training also instructs astronauts to be vigilant for other possible psychiatric or behavioral conditions. These other conditions fall under the rubric of *any other psychiatric disorders*, which is the first indication of a preexisting or latent mental disorder that is, perhaps, worsened or triggered by the stress of long-duration space flight.

Occurrences of behavioral conditions and psychiatric disorders

NASA differentiates between a behavioral condition and a psychiatric disorder in the following manner: a behavioral condition is any decrement in mood, cognition, morale, or interpersonal interaction that adversely affects operational readiness or performance; whereas a psychiatric disorder is one that meets the diagnoses criteria as outlined in the *DSM-IV-TR*. In other words, a behavioral condition is a sub-clinical, off-nominal set of behavioral and psychological circumstances or symptoms that, if left unchecked or unmitigated, may lead to the development of a psychiatric disorder that will, at that time, be considered an illness that requires a specific medical and psychiatric treatment plan. In the future, the title of the risk that is described in this chapter is expected to change to more clearly reflect these distinct definitions.

Space Flight

The flight surgeon is usually the confidant if, and when, an astronaut reports behavioral signs and symptoms. Thirty-four behavioral signs and symptoms were reported among the 208 crew members who flew on 89 shuttle missions between 1981 and 1989, spending a total of 4,442.8 person-days in space. This is an incidence rate of 0.11 for a 14-day mission; in other words, behavioral signs and symptoms, regardless of the type of sign or symptom, occurred at the rate of approximately one per every 2.86 person-year (Billica, 2000). The behavioral symptoms that were most commonly reported in these 89 missions were anxiety and annoyance (Billica, 2000). Between March 1995 and June 1998, seven astronauts flew on the Russian space station *Mir*; during this time, psychiatric events were reported twice for an incidence rate for astronauts of 0.77 per person-year (Marshburn, 2000). The actual incidence rate for both shuttle and *Mir* is likely to be understated, however, because of astronaut reluctance to report such symptoms (Ball and Evans, 2001; Shepanek, 2005). The actual reported behavioral events and recurrences can be reviewed in the U.S. Medical Events Tables found in the chapter appendix.

Behavioral and psychiatric emergencies

NASA considers any behavioral condition or psychiatric disorder that causes serious behavioral or cognitive symptoms leading to incapacitation and severe mission impact as a behavioral emergency. Examples include the development of delirium due to a head injury, or a brief psychotic disorder following a tragic event such as the death of a family member or an international catastrophe. To date, no behavioral emergencies have occurred before or during any U.S. space flight. As previously mentioned, however, as the length of space missions increases, the probability of a behavioral and psychiatric emergency occurring also increases (Ball and Evans, 2001; Stuster, 2008) (Category IV).

Not a lot of data are available from which to assess the many types of behavioral conditions and psychiatric disorders that could occur during a long-duration mission. This is due, in part, to the relatively few numbers of long-duration flyers, and to the fact that the consistent length of a mission for most of these flyers is approximately 6 months. Based on past NASA experience, one estimate of the possible rate of a behavioral or a psychiatric emergency occurring in flight as the result of depression or anxiety ranges from 0.000087 to 0.000324 cases per person-year (NASA, 2007b). The likelihood of such an emergency occurring would further increase as mission length exceeds 1 year. Calculation of this estimate, which is based on NASA space flight data, is discussed more fully in the Mood and Mood Disorders section below.

Some Russian space flight missions in the 1970s and 1980s were terminated early due to psychological factors (Cooper, 1976). In 1976, during the Soyuz- 21 mission to the Salyut-5 space station, the crew was brought home early after the cosmonauts complained of a pungent odor. No source for this odor was ever found, nor did other crews smell it. Since the crew had not been getting along, the odor may have been a hallucination. In 1985, the crew of the Soyuz T-14 mission to Salyut-7 was brought home after 65 days be-

cause cosmonaut Vladimir Vasyutin complained that he had a prostate infection (Clark, 2007). Doctors later believed that the problem was partly psychological. The Soyuz TM-2 mission in 1987 was similarly cut short because of some apparent psychosocial factors (Clark, 2007). The early termination of these missions may have prevented escalation of behavioral and psychiatric occurrences.

The stress of space flight does not end at landing. In early 2007, an astronaut who had recently returned from a space mission allegedly engaged in actions that might be considered indicative of a behavioral and psychiatric emergency (c.f., Editorial, 2007). Space flight is not necessarily the sole or even the primary cause of post-flight behavioral conditions and psychiatric disorders. Other stressors in life, such as marital distress (Aldrin, 1973; Kanas, 1987) or the death of a family member (Clark, 2007), also may contribute to similar behavioral conditions and psychiatric disorders. Nevertheless, space flight and its associated factors – e.g., isolation, confinement, workload – can become significant triggers or sources of stress. These space flight stressors, when they are paired with traditional life stressors, will likely have an exponential impact on behavioral health for long-duration astronauts (Kanas and Manzey, 2008).

Mood and mood disorders

Mood states can be dichotomized into positive and negative moods (Watson and Tellegen, 1985). Positive moods have been linked to increased helping behavior toward others (e.g., Fisher, 2002; George, 1991; Isen and Levin, 1972). A positive mood may result in better performance through interpersonal processes such as helping others (Tsai et al., 2007). Further, employees in positive moods may perform better through a motivational process such as higher self-efficacy and task persistence (Tsai et al., 2007). George and Brief (1996) found that people who were in positive moods were more likely to view their progress toward task goals positively and engage in increased task diligence.

Like positive moods, negative moods can be functional. They can cause individuals to better identify problems by focusing on their current situation rather than on their underlying assumptions, attending to shortfalls in the status quo, identifying opportunities, and exerting high levels of effort to improve a situation (George and Zhou, 2002; George and Zhou, 2007; Kaufmann, 2003; Martin and Stoner, 1996; Schwarz, 2002; Schwarz and Skurnik, 2003). Additionally, negative moods promote creativity under certain conditions (e.g., Gasper, 2003; George and Zhou, 2002; Kaufmann, 2003; Kaufmann and Vosburg, 1997), which can facilitate problem-solving.

The effects of positive mood are discussed in later sections of this chapter and address salutogenesis in space flight and analogs, respectively. Space-flight-related research, albeit quite limited, has focused on the displacement of negative mood from crew members to Mission Control personnel, and from Mission Control personnel to management (Kanas, 2005; Kanas et al., 2007).

Mood disorders, which are categorized in the NASA integrated medical model (IMM) as depression and anxiety, have occurred during space flight. Data that were collected for 28.84 person-years of NASA space flight reveal that 24 cases of anxiety occurred in space flight for an incidence rate of .832 cases per person-year (NASA, 2007a). Over the same 28.84 person-years, four astronauts experienced signs and symptoms of depression during space flight for an incidence rate of .139 per person-year (NASA, 2007a). In other words, signs and symptoms of anxiety during space flight occurred once every 1.2 years, and signs and symptoms of depression occurred once every 7.2 years.

According to a National Institute of Mental Health (NIMH) (1999) pamphlet (Category III), approximately one in 10 adults during a given year will suffer from some form of depression. Despite careful selection, a depression-free past does not guarantee a depression-free future.

The data that were collected in the general population as well as in NASA are not definitive enough at this time to accurately predict the likelihood of an astronaut becoming depressed or suffering from a mood disorder while in flight. Rather, it emphasizes that the risk is real and should not be ignored. Therefore, NASA is continuing to gather the data that are needed to define and mitigate the risk of an astronaut developing an anxiety or a depressive disorder.

Asthenia

Russian medical personnel view asthenia as one of the greatest problems affecting the emotional well-being of cosmonauts (Kanas, 1991). This syndrome, which is also called neurasthenia and asthenization, has been defined as "a nervous or mental weakness manifesting itself in tiredness…and quick loss of strength, low sensation threshold, extremely unstable moods, and sleep disturbance" (Kanas and Manzey, 2003, p. 115). It can be caused by excessive mental or physical strain, prolonged negative emotional experience or conflict, as well as somatic illness (Petrosvsky and Yaroshevsky, 1987). The diagnostic criteria for asthenia and neurasthenia are listed in the *ICD-10* (WHO, 1996). However, this diagnosis is not recognized in the *DSM-IV-TR* (APA, 2000). Other diagnoses with similar symptoms that are listed in *DSM-IV-TR* are adjustment disorder, dysthymia, major depressive disorder, and chronic fatigue syndrome.

Examination of cosmonauts suggests that asthenia is particularly likely to occur when space flights last longer than 4 months (Myasnikov and Zamaletdinov, 1996). Symptoms and signs of asthenia have been reported anecdotally by U.S. astronauts who flew during *Mir* and Skylab (Burrough, 1998; Freeman, 2000; Harris, 1996). Kanas et al. (2001), however, failed to find empirical support for the occurrence of asthenia during *Mir* missions. This failure to find support could be due to the method that was used to operationalize asthenia. Only the psychological component of asthenia was examined; furthermore, the study used an instrument that was not specifically designed to measure asthenia.

At present, the occurrence of asthenia in space flight crews does not require medications; this may be due in part to the current space flight parameters (e.g., length of flight, contact with the ground, Progress and shuttle flights, etc.). Furthermore, this is likely due in part to stringent selection methods that select out those with psychiatric problems, and to diligent monitoring and application of countermeasures when symptoms first appear (Myasnikov et al., 2000, as cited in Kanas et al., 2001). Longer-duration missions may demonstrate a need for asthenia medications.

Psychosomatic reactions

Psychosomatic reactions occasionally have been reported during space flight. Psychosomatic is defined as "pertaining to a physical disorder that is caused by or notably influenced by emotional factors" (Dictionary, 2008). These health struggles are not imaginary; in fact, more than half of all individuals who are seeking medical attention are suffering from psychosomatically induced or exacerbated illnesses (Goldensen, 1970; Birley, 1977; Fava and Sonino, 2000). For example, an otherwise healthy cosmonaut experienced a cardiac arrhythmia that required medication after being exposed to sustained stressors related to on-board equipment failure (Carpenter, 1997; Cowings et al., 2000; Kornilova et al., 1998, 2000).

There are direct self-reports of somatizing by cosmonaut Valentin Lebedev during the record-breaking length of his Salyut 7 mission. Other psychosomatic reactions include complaints of toothaches after dreams of tooth infections (Chaikin, 1985) and fears of impotence due to perceived prostatitis (Harris, 1996).

Salutogenesis

Not all of the effects of long-duration space flight are expected to be negative. Antonovsky, in 1979 (Category IV), coined "salutogenesis" as the opposite of pathogenesis. Salutogenic experiences are those that promote a sense of health. The key factor of salutogenesis, according to Antonovsky (1979), is a person's sense of coherence. He defined this sense of coherence as "a global orientation that expresses the extent to which one has a pervasive, enduring though dynamic feeling of confidence that one's internal and external environments are predictable and that there is a high probability that things will work out as well as can reasonably be expected." Kobasa et al. (1979) described individuals who stay healthy, even when they find themselves in challenging circumstances, as having the following characteristics: believing that they exert control over their environment; embracing life as meaningful; and experiencing changes in life as normal and beneficial. Factors contributing to salutogenesis are comprehensibility, manageability, meaningfulness, social support, spirituality, happiness, humor, and love (Kent, 2002; Smith, 2002). Smith (2002) commented that "an organism with a salutogenic brain would experience the world as manageable and coherent ... with a self-perpetuating cycle for enhancing self-confidence and well-being."

Suedfeld (2005) differentiates between positive environmental aspects and the positive personal and social aspects of space flight. Environmental aspects concern the external environment (e.g., mystery; beauty of space; views of Earth) and the capsule environment (e.g., safe haven; familiarity; free time). The positive personal and social aspects of space flight were likewise dichotomized into astronaut group dynamics (e.g., membership in an elite group; superordinate goals) and post-mission consequences (e.g., self-confidence; respect; new skills and values).

Preliminary results suggest that a salutogenic response to space flight is common across astronauts and endures for some time post-flight. Astronauts and cosmonauts have reported experiencing transcendental, religious experiences or a sense of the unity of humankind while in space (Connors et al., 1985; Ihle et al., 2006; Kanas, 1990). Analysis of the memoirs of four astronauts reveals that all four reported post-flight feelings of increased spirituality, defined as "meaning and inner harmony through transcendence" (Suedfeld and Weiszbeck, 2004, p. C7). Ihle et al. (2006) examined the positive psychological outcomes of space flight. All 39 astronauts and cosmonauts who responded to the survey reported a positive reaction to being in space. The most frequently endorsed benefit of space flight related to the perception of the Earth; i.e., its beauty and fragility. Analysis of photographic images taken from ISS during Expeditions 4 through 11 indicates that most images taken by crew members were self-initiated (84.5% of 144,180 photographs) and that photography was considered a leisure activity (Robinson et al., in press). During missions to Mars, however, the Earth will not always be visible. The effects of not being able to see Earth could have a detrimental effect on the psychological well-being of crew members (Kanas and Manzey, 2003; 2008).

Psychosocial adaptation and disorders

Anecdotal evidence from crew members illuminates the distress that some individuals encounter during long-duration space flight missions. Psychosocial adjustment is, by definition, the psychological and social process of adapting or conforming to new conditions (Merriam-Webster, 2008). Unsuccessful psychosocial adaptation can lead to adjustment disorders that are characterized by decrements in performance (APA, 2000).

In-flight diaries of cosmonauts and astronauts recount periods of psychological distress experienced during extended periods in space (Ball and Evans, 2001). Even crew members with otherwise cheerful dispositions may demonstrate changes in temperament when meeting the challenges of space flight adaptation. Lebedev wrote in his journal, "[M]y nerves were always on edge, I get jumpy at any minor irritation" (Lebedev, 1988, p. 291). One astronaut described his inability to fully prepare for long-duration space flight challenges, "I was astounded at how much I had underestimated the strain of living cut off from the world in an other-worldly environment" (Linenger, 2000, p. 151).

Ineffective adjustment to life in space can take many forms. Withdrawal from fellow crew members or ground support crew is one form of ineffective adjustment. Discord or tense relations with fellow crew members is another form of ineffective adjustment.

A third form of ineffective adjustment is deviant behavior. One expert of isolated and confined environments has identified two categories of deviant behavior in U.S. Antarctic winter-over crews: (1) individuals who fail to conform to group norms/expectations; and (2) individuals who act as the station class jester, whose behavior is outside of the mainstream yet not outrageously disruptive or threatening (Palinkas, 1989, 1992). Deviant types of behavior in space may fall into these same two categories. For example, Lebedev admitted that he disregarded safety procedures when he became frustrated. In his haste to access new letters from home, he did not wear safety goggles because "they fogged up, but if metal dust had entered my eye the flight would have ended" (Lebedev, 1988, p. 304). Illustrating the second category of deviant behavior is Linenger's coping behavior: "I also made my own diversions … Playing the space version of 'sneaking up' … Flying silently down the length of a module, I would approach one of my crewmates and, still undetected by him, move very close. I would then hover patiently until he turned around. I knew that I had gotten him whenever he would gasp and flail his arms backward" (Linenger, 2000, p. 159). Anecdotal evidence from space flight suggests that astronauts and cosmonauts at times engage in disruptive coping behaviors that could presage larger behavioral issues.

Crew size may be another factor contributing to different behavioral outcomes. In examining rates of deviance in seven polar and three space flight missions (Salyut 7; Apollo 11; and Apollo 13), Nolan and Dudley-Rowley (2005) determined that deviance rates were highest for crews of three. These researchers classified deviant behavior in three general categories: (1) bizarre or puzzling behavior, such as withdrawal; (2) acts of violence, either verbal or physical; and (3) acts of deliberation, such as hoarding resources. They found that when crew size increases to four, there is an apparent significant decrease in the amount of deviant behavior exhibited.

Summary

Based on our past space flight experiences, various types of behavioral conditions and psychiatric disorders are expected to be a risk for future Exploration missions (Table 1-1). While current selection and countermeasure strategies have prevented the occurrence of any behavioral health emergencies during space flight that could have jeopardized mission success, the uniquely long durations and distances of future Exploration missions necessitate comparisons with analog environments that might indicate the other types of occurrences that could be expected.

Analog Populations

Ground-based analogs, such as those in the Arctic and Antarctica or undersea habitats, are frequently used as a comparison to space flight because they are more accessible than space flight and provide an Earth environment in which to test and validate the feasibility of BHP countermeasures, tools, and procedures. Analogs, however, are

also frequently criticized. It has been suggested that their fidelity, especially in laboratory simulation studies, is not always high. Natural analogs, such as those found in Antarctica and on submarines, frequently depart from actual space flight conditions. Most frequently, there are more individuals in analog settings than the two to six crew members that are common to current, and expected in future, long-duration space flight operations. Regardless of their limitations, however, some of the higher-fidelity mission analogs are the best, and often the only, method that is available for gathering the data that are necessary to successfully prepare for Exploration missions. Presenting data from his Antarctic mission, Astronaut Donald Pettit succinctly summed up the value of analogs when he stated that "analog physics might be wrong, but the mindset is right" (Pettit, 2007).

Table 1-1. ***Behavioral Conditions and Psychiatric Disorders Occurring During Space Flight***

Condition	Occurred During Space Flight	
	YES	NO
Behavioral/Psychiatric Emergency		√
Mood and Mood Disorders	√	
Anxiety	√	
Depression – Signs and Symptoms	√	
Asthenia – Signs and Symptoms	√	
Psychosomatic Reactions	√	
Salutogenic Responses	√	
Poor Psychosocial Adaptation and Disorders	√	

Behavioral and psychiatric emergencies

Examining actual occurrences in Antarctica between 1994 and 1997, Palinkas et al. (2004) found that 12.5% of the crew members at two Antarctic stations, McMurdo and South Pole, presented to the clinic with symptoms that met the *DSM-IV-TR* criteria for one or more disorders. This translates to an overall incidence rate of 5.2% over an 8.5-month austral winter. Age, gender, year, level of education, and prior winter experience were not statistically correlated to the DSM-IV-TR diagnoses. (It is important to note that an individual may have symptoms without qualifying for a diagnosis or a disorder in the *DSM-IV-TR*.)

Another analog environment for space flight is submarines, with their typical mission lengths of 3 months. As with space missions, submarine missions occur in a physically confined, socially and physically isolated, and extreme environment. For submariners, the incidence of psychiatric disorders that were severe enough to result in either the loss of a workday or the need to be medically evacuated ranged between 0.44 and 2.8 per person-year (Wilken, 1969; Tansey et al., 1979; Dlugos et al., 1995; Thomas et al., 2000).

Mood and mood disorders

Palinkas et al. (2004) found that the most common category of disorders for individuals who were wintering-over in Antarctica was mood disorders; these accounted for 30.2% of all diagnoses. Depressive symptoms were significantly related to gender (females were at greater risk), military occupation (rather than civilian), station (all diagnosed individuals were stationed at McMurdo; none were stationed at South Pole), year of expedition, and having a DSM-IV diagnosis.

Otto (2007) based his research on 12 years of data from the South Pole Station. At the South Pole Station, between 1994 and 2005, the overall incidence rate for depression that required pharmacological intervention was 2.03%. This means that one case of depression can be expected every 1.1 winter seasons. The incidence

rate for diagnoses of overall mental disorders, including depression, was 4.5% at the three Australian stations according to the Australian National Antarctic Research Expeditions (ANARE) and 6.4% at McMurdo Station (Otto, 2007). These incidence rates appear to be lower than those for the general public, which average 9.5% (Kessler, et al., 2005). Antarctic incidence rates could be artificially lower, however, due to a selection process that disqualifies individuals with existing diagnoses from wintering-over. Alternatively, the lower rate in Antarctica could be a result of self-selection, whereby individuals who apply to serve in winter-over crews tend to have better behavioral health than the general population.

Winter-over syndrome

Winter-over syndrome consists of a cluster of symptoms that includes interpersonal tension and conflict, cognitive impairment, sleep disturbance, and negative affect (Palinkas and Suedfeld, 2008; Strange and Youngman, 1971). This syndrome usually is not severe enough to warrant a DSM-IV diagnosis. Rather, it might more accurately be considered a subclinical condition (Judd et al., 2002). Some research has shown that symptoms peak shortly after the mid-point of an expedition (Palinkas and Suedfeld, 2008). This effect, which is called the third-quarter effect, is independent of the length of the expedition. It is believed to occur as a result of individuals realizing that their expedition is only half over. Evidence regarding this third-quarter effect is inconclusive, however, and researchers continue to debate its existence (e.g., Kanas and Manzey, 2008; Stuster, 2008).

Winter-over syndrome shares many similarities with asthenia (Palinkas and Suedfeld, 2008; Otto, 2007). Perhaps the most telling similarity is that they both reflect de-adaptation to a stressful situation (Myasnikov et al., 2000, as cited in Kanas and Manzey, 2008).

Salutogenesis

Palinkas and Suedfeld (2008) (Category IV) dichotomize the salutary effects of polar expeditions as being: (1) the enjoyable characteristics inherent in the situation, and (2) the positive reactions that come from having successfully met and overcome the challenges of the environment. The former are positive effects that are felt during the mission. These effects can require coping and resilience. The latter are positive effects that are more long-term in nature, and they are met through post-return growth (Palinkas and Suedfeld, 2008) (Category IV).

The isolated, confined, and extreme (ICE) environment, for some individuals, provides personally rewarding experiences (Palinkas et al., 1995). For example, the number of people requesting repeated winter-over assignments in Antarctica is evidence of the positive benefits that are associated with the ICE experience (Steel, 2000; Wood et al., 2000).

These kinds of effects are also seen in simulation studies. For example, three crew members were isolated in the *Mir* space station simulator for 135 days. They reported more expressiveness and self-discovery and less tension than during their pre-isolation training session (Kanas et al., 1996).

Cognitive changes

Some evidence from Antarctic research suggests that clinical cognitive changes may occur in individuals who are exposed to ICE environments, such as space, for long periods of time. Investigators studying animal research have further speculated that behavioral changes in such environments may even be attributable to the effects of chronic stress on the hippocampus (Otto, 2007).

Physical aspects of the environment can also produce cognitive changes. Exposure to high levels of radiation, for example, can damage the subcortical basal ganglia and hippocampus that are critical to cognitive functioning (Madsen et al., 2003; Vasquez et al., 2003, as cited in Lieberman et al., 2005). For specifics regarding the risks of space radiation, please refer to Chapters 4 through 7 in this book.

Analog mission duration of 2 or more years

Available evidence from assignments in any analog lasting 2 or more years, as will occur for a Mars mission, is scant. In Biosphere 2, an eight-member team was isolated on a 3.15-acre artificial, closed ecological system in Arizona for 2 years (September 1991 to September 1993). Although they were in a relatively lush and diverse environment – with access to television and radio, and daily contact via an observation window – the inhabitants of Biosphere 2 nevertheless experienced psychological stress (MacCallum and Poynter, 1995). The team split into two factions within 6 months; stolen food was hoarded; and daily tasks were reported as monotonous. One month after the midpoint, some crew members reported experiencing depression that was severe enough to interfere with their ability to complete daily tasks (Poynter, 2006). The severity of these behavioral and psychiatric responses was most likely due, in part, to a need for more rigorous psychological evaluation when selecting those who were best suited for this study. Problems that were experienced with Biosphere 2, in comparison to those of space flight, include poor selection of participants and lack of adequate preparation and training. Extensive publicity also may have influenced the experiences of the Biosphere 2 team by sensationalizing them. Although the reader is cautioned about over-interpreting data as well as misapplication of the study to space flight, the Biosphere 2 experience is included in this report because it is one of the few examples of very long-duration isolation and confinement.

Two-year assignments, which are common at the Russian Antarctic Station of Vostok, provide additional evidence that lengthier periods spent in isolation and confinement increase behavioral and psychiatric problems (Otto, 2007). Alcohol consumption contributed to the main power-generating building burning down as well as to the death of a station physician due to alcoholic liver failure. The depth of psychological stress that was experienced by some at the Vostok station is vividly illustrated by the example of a wintering-over Russian male who, after losing a game of chess, murdered his opponent with an axe (Anthony, 2006).

These examples most likely do not generalize to astronauts and space travel due to the differences between analog and astronaut populations as well as the differences in mission characteristics. However, these examples are alarming and have been included to emphasize the increased risk of behavioral health and psychiatric problems that is associated with extended stays in highly isolated, confined, and extreme environments; such long durations are clearly at the outside boundary of our experience and evidence base.

Predictors and contributing factors

Precursors of behavioral health distress serve as warning signals, and many factors contribute to an individual's behavioral health. Monitoring the presence of predictors and contributing factors will allow for the development of better screening methods to prevent behavioral conditions and psychiatric disorders from emerging and the implementation of countermeasures more quickly and, thus, more effectively.

As noted previously, numerous factors contribute to an individual's behavioral health status. Certain factors such as crew member personality together with the quality and quantity of sleep predict the likelihood that behavioral and psychiatric distress will develop. These factors, which can be viewed as "stressors," are discussed in the following section. Note that not all "stressors" are negative in terms of their impact on the behavioral health of an individual.

The Space Studies Board of the U.S. National Academy of Sciences (NAS) differentiates between physical and psychosocial environmental stressors (National Research Council (NRC), 2000) as factors that contribute to changes in behavioral health. Physical environmental stressors include microgravity and the inherent hazards of space flight. Psychosocial environmental stressors include the isolation, confinement, and monotony of life in space.

Personality

The results of personality tests have been used to predict job performance for many years. As mission length and distances from Earth increase, selecting astronauts and, latterly, composing entire crews/space flight teams based on personality traits becomes increasingly critical.

Some personality evidence that is specific to astronauts exists. Generally speaking, the following types of personality comparisons are found. These are comparing: (1) astronauts or astronaut applicants to a normative group; (2) astronauts to another occupational group; and (3) astronauts to peer/supervisor performance ratings or selection decision. No research has been undertaken that examines the relationship between personality and objective job performance. This lack of objective job performance limits any true attempt to identify the "right stuff." Further, no known research has examined astronaut personality with respect to successful reintegration post-flight.

To date, the published research that is related to space flight has focused on two approaches of personality. One examines instrumentality and expressivity, while the other delineates personality in terms of the "Big Five" factors (i.e., openness, conscientiousness, agreeableness, extroversion, and neuroticism). The findings of each approach are discussed below.

Instrumentality and expressivity

Personality can be examined in terms of the broad categories of instrumentality and expressivity. The first of these, instrumentality, describes the degree of goal-seeking and achievement orientation. Individuals who rate highly in instrumentality are highly goal-oriented and have an elevated need for achievement. Those who are low in instrumentality tend to be considered egotistical, dictatorial, and arrogant. Expressivity, which is the second of the broad categories, is defined as social competence or how an individual behaves in interpersonal relationships. High expressivity is reflected as kindness, emotionality, and warmth. Those who are low in expressivity demonstrate negative communion (e.g., submissiveness, servility, gullibility) and are verbally aggressive (Kanas and Manzey, 2008).

Viewing personality in terms of instrumentality and expressivity has been found to be predictive in flight crews as well as in other aviation and space populations (Chidester and Foushee, 1991; Chidester et al., 1991; McFadden et al., 1994; Musson et al., 2004; Musson and Helmreich, 2005) and in the analog environments of submarines, hyperbaric chambers, polar expeditions, and the military (Sandal et al., 1996, 1998, 1999).

Categorizing personality in terms of instrumentality and expressivity has led to three groups that have been informally termed the "right stuff," the "wrong stuff," and "no stuff" (Gregorich et al., 1989). The right stuff, which is characterized as high on instrumentality and on expressivity, is related to higher peer evaluations of job and interpersonal competence (McFadden et al., 1994). Having the right stuff in settings that involve complex group interaction is related to superior performance (Musson and Helmreich, 2005). In contrast, those who have the wrong stuff are high on instrumentality and low on expressivity. Individuals that are low on both instrumentality and expressivity are considered to have "no stuff."

Males and females who make it to the final round of astronaut selection are generally high on instrumentality compared to normative (student) scores; no differences are apparent on expressivity. Those who are astronauts demonstrate the same pattern as that of final-round astronaut applicants (Musson, 2003) suggesting that personality between the groups is homogenous enough to warrant the use of other attributes to further distinguish the best applicants for the job.

The Big Five

As stated earlier, neuroticism, extroversion, openness to experience, agreeableness, and conscientiousness comprise the Big Five. Individuals who are highly neurotic are prone to psychological distress. Those who are highly extroverted direct a significant amount of energy toward others. Persons who are highly open to experience actively seek that which is new. Agreeable individuals prefer interactions that are compassionate rather than tough-minded. Those who are highly conscientious show a level of goal-directed behavior that is organized, motivated, controlled, and persistent (Costa and McCrae, 1992). While agreeableness is closely related to aspects of positive expressivity, the other four factors (i.e., neuroticism, extroversion, openness to experience, and conscientiousness) do not easily map onto the instrumentality/expressivity approach (Musson et al., 2004).

A 1991 meta-analysis suggests that conscientiousness is positively related to job performance (defined as job proficiency, training proficiency, and personnel data) across occupations as varied as professionals, managers, sales, police, and skilled/semi-skilled (Mount and Barrick, 1991). Whether this holds true in Antarctica and possibly other ICE environments such as space flight is uncertain. Palinkas et al. (2000) found the opposite to be true in Antarctica, namely that better job performance was related to lower conscientiousness. These results could be artifacts of the sample or a function of how job performance was operationalized, however.

Musson (2003), in his examination of human performance data that were collected by the Human Factors Research Project at the University of Texas, found that males who made it to the final round of astronaut selection were high on agreeableness and conscientiousness and low on neuroticism. As with males, female applicants were high on agreeableness and conscientiousness and low on neuroticism. Female applicants were also high on extroversion.

Regarding astronauts rather than astronaut applicants, Musson (2003) found that male astronauts follow the same pattern as male astronaut applicants; i.e., they are high on agreeableness and conscientiousness and low on neuroticism. Female astronauts, on the other hand, appeared much different from their female applicant counterparts. This may be an artifact of the small sample size for female astronauts (N=10); interpretation of the apparent differences is not recommended.

Tying personality to performance, Rose et al. (1994) found that agreeableness is positively related to four ratings of performance (i.e., peer-rated interpersonal, technical, and leadership competence as well as supervisor-rated job performance) for U.S. astronauts. Openness to experience was negatively related to peer-rated technical and leadership competencies and to supervisor-rated job performance. No other significant correlations were found between these performance ratings and the Big Five. It is possible that a lack of significant correlations concerning conscientiousness could lend credence to the finding that conscientiousness is not a positive predictor of performance in ICE environments (Palinkas et al., 2000). Alternatively and perhaps more likely, the lack of additional significant relationships could be due to the fact that subjective rather than objective job performance ratings were used.

Antarctica research suggests that ideal candidates for wintering-over in such an isolated and confined environment are relatively low in neuroticism but also relatively low in extroversion and conscientiousness (Palinkas et al., 2000). Rosnet et al. (2000) confirm that ideal individuals would be low on extroversion. In a third study, polar workers were found to place more highly than the normative group in all factors except neuroticism. Breaking these findings down by occupation reveals that scientists are lower than military personnel on extroversion and lower than technical/support staff on both agreeableness and conscientiousness. Differentiating by South vs. North Pole, Antarctic workers are higher than those in the Arctic in terms of extroversion, agreeableness, and conscientiousness (Steel et al., 1997).

Personality as a predictor of adjustment

Individuals who are wintering-over in Antarctica tend to adapt better when they are low in extroversion and assertiveness (Rosnet et al., 2000). Gunderson (1966a) found that "achievement needs, needs for activity, needs for social relationships and affection, aesthetic needs, needs for dominance or leadership, a sense of usefulness in one's job, and control of aggressive impulses [are] particularly important for adjustment in Antarctic small groups" (p. 4). Three individual characteristics that are related to adaptation in isolated and confined conditions in Antarctica are: high social compatibility, high emotional stability, and high task motivation (Gunderson, 1966; Stuster, 1996).

Emotional Reactions

Emotional reactions, according to the NRC report by the Committee on Space Biology and Medicine (1998), have three primary response systems: language, behavioral acts, and the physiological response of alterations to the hypothalamic-pituitary-adrenal (HPA) axis. Language can be used to voice reactions to stress through reports of feelings and other communications. Behavioral reactions to emotions are more physical in nature, however, and include acts of avoidance or attack. Negative emotions are associated with decreased performance and motivation; disruptions to short-term memory, attention, and other cognitive processes; increased interpersonal conflict; isolation from others; and various psychosomatic and psychophysiological symptoms (NRC, 1998). HPA activation can be affected by or cause inadequately regulated emotions, thereby suppressing the immune system and leaving the individual at greater risk for disease (Charles and Mavandadi, 2004). HPA is a major component of the stress system that regulates the secretion of corticosteroids. Activation of HPA during depression is common, although whether HPA activation causes or results from a depressed mood is not known (NRC, 1998). Alterations of the HPA axis are known to be associated with negative emotion in ICE environments (Connors et al., 1986; Palinkas, 1991; Palinkas et al., 1989). Thus, during long-duration missions, it is possible that changes may take place in the HPA axis that might also affect mood and memory and the immune system (Baum et al., 1982; NRC, 1998; Otto, 2007).

Sleep and Circadian Rhythm

While it is difficult to predict who will or will not develop depression, sleep disruption is one early warning sign. Sleep disturbances are common diagnostic criteria for many psychiatric disorders (Colton and Altevogt, 2006). Comorbidity of a sleep disorder with a psychiatric disorder is also common; e.g., 40% of individuals who are diagnosed with insomnia also have a psychiatric disorder. This comorbidity is higher for hypersomnia, where 46.5% of individuals also have a psychiatric disorder (Ford and Kamerow, 1989). Insomnia is both a risk factor for and a manifestation of major depression (Livingston et al., 1993; Ohayon and Roth, 2003; Cole and Dendukuri, 2003). Research indicates that 15% to 20% of individuals who are diagnosed with insomnia also suffer from major depression (Ford and Kamerow, 1989; Breslau et al., 1996).

The circadian rhythm of the human body is linked to patterns of biological activities such as brain wave activity, hormone production, and cell regeneration. Circadian rhythms can be affected by environmental

factors; e.g., the amount of ambient light (Czeisler et al., 1986) (Category I). Humans require 2,500 lux to entrain their circadian cycles; however, the illumination that is available on ISS at this time is limited to between 108 and 538 lux. Sleep is a large component of the daily circadian cycle and, as such, is affected by changes that influence the underlying circadian rhythm (NCR, 1998). Recent Category III unpublished data (Barger and Czeisler, 2008) from the ISS and shuttle confirm the findings of previous assessments of sleep quantity and quality on orbit; i.e., sleep in flight is indeed reduced in comparison to terrestrial sleep. Changes in work schedule also can adversely affect a crew member's circadian rhythm. During the Russian Soyuz program, sleep schedules were occasionally set counter to the local time of the launch site. This change in sleep schedules was associated with decreased quantities of sleep and decrements in performance among the cosmonaut crews (NASA, 1991). Indeed, the Space Studies Board states that a lack of sleep leads to increased stress and decreased cognitive and psychomotor functioning (NRC, 1998).

Current ISS operations often require slam shifting (i.e., sudden shifts in sleep/wake schedule), which can result in sleep loss and fatigue for the astronauts. Such schedule changes force critical mission operations to occur against the natural circadian rhythm of the body. The commander of Expedition 3, Frank L. Culbertson, Jr., did not consider slam shifting to be a problem for the flight crew as long as they had "adequate recovery time following the sleep shift and ensuing activities." He advised that sleep/slam shifting did have some physiological effects on the crew with respect to insufficient rest time (Safety Review Panel, 2002). Slam shifting also impacts the ground teams that support the ISS during critical operations as well as the ground teams that work overnight against the homeostatic drive to sleep. For detailed information on the performance risk that is associated with sleep loss and circadian rhythm disturbances, please refer to Chapter 3 in this book.

Monotony and Boredom

Monotony is a frequent complaint of individuals in ICE environments such as space flight (Kanas, 1998; Otto, 2007). In particular, it is the combination of monotonous work with requirements for high degrees of alertness and penalties for errors that is seen as especially stressful (Thackray, 1981). Even in the face of monotony, however, performance remains high enough for mission success, provided that the motivation is high (Kanas and Fedderson, 1971). The lack of variety in social interactions and the physical environment can lead to boredom, interpersonal conflict, and loss of energy and concentration (Otto, 2007; NRC, 1998). Members of Biosphere 2 reported that finding sources of stress relief was a major part of working in the Biosphere (MacCallum and Poyntner, 1995). Of major concern during long-duration missions is the possibility of too much monotonous free time. Boredom has long been known to be the worst enemy of polar explorers (Stuster, 1996). As missions become longer, the focus on the amount of work that humans can safely perform changes from how much to how little (Weiner, 1977).

Environment and Job Design

In an environment in which an individual floats freely, distinctions between up and down are no longer meaningful. Environmental design, or habitability, is thus no longer confined to the Earthly distinctions among floors, walls, and ceilings; this is an asset when the size of the ship or the station is limited. How readily a crew member adapts to this truly three-dimensional world varies by individual (Connors et al., 1986).

The lack of privacy, which has been associated with impaired individual well-being in analog studies, is a major psychosocial stressor in space flight (Connors et al., 1985). Individuals who are in confined spaces tend to withdraw from one another during leisure time. Further, the leisure time is characteristically spent in more passive activities (Seeman et al., 1971). Having private crew quarters in which a crew member can be alone thus becomes extremely important on long-duration missions (Santy, 1983; Kanas and Manzey, 2008).

Anecdotal evidence suggests that interior décor can affect well-being (Stuster, 1996). Use of many different colors and the wide use of darker colors are contraindicated (Kanas and Manzey, 2008). Colors can also be used to orient crew members since gravitational cues, which are missing in space, no longer provide navigational aids (Raybeck, 1991). Windows promote well-being in ICE environments by decreasing the sense of confinement and monotony of the environment (Haines, 1991). Anecdotal evidence from the earliest space flights supports the importance of being able to look outside (Haines, 1991; Lebedev, 1988). Kelly and Kanas (1992) provide empirical evidence that "watching" activities became more important.

In addition to designing the environment to promote well-being, jobs can be designed in such a way as to promote well-being and performance. To the extent possible, crew members should have autonomy in planning their work schedules, managing their workloads, and deciding when to perform nonessential tasks (Kanas and Manzey, 2008). Further, the appropriate amount of work that is to be performed daily must be determined. Overworking can result in performance errors as physical and mental exhaustion occur (Nechaev, 2001). At the same time, a lack of sufficient meaningful work can adversely affect mental well-being. Quoting the first U.S. astronaut on *Mir*, Norman E. Thagard: "[T]he single most important psychological factor on a long-duration flight is to be meaningfully busy. And, if you are, a lot of the other things sort of take care of themselves" (Herring, 1997, p. 44).

For greater detail, please refer to Chapter 10 in this book.

Daily Hassles and Major Life Events

Although some stressors that are found in space are a result of the fact that space is an ICE environment, other stressors are unique to space itself. The number and extent of daily hassles of life, i.e., those "irritating, frustrating demands that occur during everyday transactions with the environment" (Holm and Holroyd, 1992, p. 465), are significant predictors of health (DeLongis et al., 1982; Lazarus and DeLongis, 1983; Rowlison and Felner, 1988) since increased stress can lead to diminished health. Daily hassles that are associated with the physical environment that is unique to space include: a growing accumulation of garbage, limited facilities for sanitation, the need for constant vigilance, and a relative lack of privacy. The noise and vibration of ISS are acoustic stressors that can affect sleep quality and quantity, the low level of illumination on ISS is a photic stressor, and the physical space on ISS or in any space vehicle is limited. Social density is thus an added stressor (NCR, 1998).

Cultural and Organizational Factors

Cultural and organizational factors can contribute to the stress of space flight. Both organizational and national cultural differences between the Russian Space Agency and NASA can influence crew dynamics (NRC, 1998). Perceived stress can be aggravated by cultural differences in interpersonal distance. An "us vs. them" attitude can develop between the crew and its off-site support, as well as feelings of animosity toward the same off-site support. This dynamic is sometimes termed "displacement" because the team is displacing the intra-group tension onto safer, more remote individuals (Kanas and Feddersen, 1971). Although displacement is not an uncommon occurrence between remote teams and their support centers, it nevertheless becomes more critical for space flight as the missions grow longer and the conditions of isolation expand.

In 1974, friction between crew members and Mission Control during a Skylab mission resulted in a work stoppage in which crew members insisted on taking a scheduled day off after weeks of work without a day of rest. Russian crews have also experienced conflict with their ground support teams. The crew of one Salyut space station shut down communications with Mission Control for 24 hours. Lebedev (1988) and crew members failed to report a fire to the ground because "it would have just caused more panic" (p. 309). In addition,

Antarctic winter-over crews report having avoided communicating with their administrative support or deliberately misleading their administrative support (Otto, 2007).

Family and Social Support

According to the NASA Family Support Office, astronauts have reported feeling more relaxed and able to concentrate on tasks at hand when they believe that someone is taking care of their families (Category IV). Worrying about family and family events that might occur at home while the crew member is away can be extremely stressful. Psychiatric intervention was required post-flight for an Apollo 11 astronaut due to his marital distress and depression (Aldrin, 1973; Kanas, 1987). The death of his mother caused cosmonaut Vladimir Nikolaevich Dezhurov to withdraw for 1 week during his mission (Clark, 2007).

Astronaut Daniel M. Tani experienced an unexpected personal loss during his ISS mission when his mother died in an accident in her hometown. A fuel gauge problem required that a shuttle mission be postponed for 2 months. This resulted in Tani's duties as a space station flight engineer being extended by 4 months. It was during this extension period that Tani's mother died. At his return home ceremony, which was held in Houston on February 21, 2008, Tani commented on the importance of psychological support: "We so rightfully thank every technical trainer we have, but when you go and live on the station, there is a whole aspect of living that we have to think about and anticipate." He expressed his gratitude for flight surgeons and psychologists as well as the implication for future missions: "That was invaluable to me. This is something we will have to learn how to really support and develop for long-duration flights to the moon and Mars" (Carreau, 2008). Such tragedies affect all crew members, including those who are on the ground crews, and they can be especially challenging for mission commanders who seek to lend support to a grieving crew member.

World Events

In addition to family events, world events viewed from space, can be stressful. In 1991, the *Mir* space station crew launched as Soviet Union cosmonauts yet later returned to Earth as Russian Federation cosmonauts (Russian Spaceweb, 2008). On board ISS, Astronaut Frank L. Culbertson, Jr., used video and still cameras to document the aftermath of the Twin Towers attack on September 11, 2001. On being told of the attacks, he writes that he "zipped around the station" (Culbertson, 2001) until he found a window that would give him a view of New York City. Culbertson states, "It was pretty difficult to think about work after that, though we had some to do, but on the next orbit we crossed the U.S. farther south. All three of us were working one or two cameras to try to get views of New York or Washington" (Culbertson, 2001). Although far from home, astronauts and cosmonauts are not untouched by political turbulence.

Prevention and treatment countermeasures

Psychological support is provided to prevent or mitigate the impact of potential stressors and to minimize the risk of occurrence of behavioral conditions and psychiatric disorders for all current long-duration space flight missions. If conditions do arise, a psychological support system allows for early detection of the condition and timely application of countermeasures. If necessary, more aggressive treatment methods can be applied. Countermeasures can be dichotomized into those that prevent the occurrence of a risk or mitigate the potential severity of the risk and those that monitor or treat the risk if it does occur (Strangman, 2008).

Prevention Countermeasures

Seyle's model of the General Adaptation Syndrome states that as a stressor appears and continues, an individual's coping resources are first mobilized, deployed, and depleted if not resolved. Seyle (1978) termed these

stages alarm, resistance, and exhaustion. One of the goals of prevention is to avoid distress by providing crew members with the wherewithal to minimize or negate a stressor.

The lack of behavioral and psychiatric emergencies during flight is evidence of the efficacy of current countermeasures, given current mission lengths of approximately 6 months. The current practices and services that are offered by the BHP Operational Psychology Group at NASA include: pre-flight, in-flight, and post-flight preparation; training and support; resources from the Family Support Office; in-flight monitoring; clinical care for astronauts and their families; and expertise in the workload and work/rest scheduling of crews on ISS (Sipes and Vander Ark, 2005). These services are shaped in part by a crew member's personal preferences, family requests, and specific events during the missions, as well as by programmatic requirements and other lessons learned.

Pre-flight

Prevention begins with selection. Those individuals with the greatest likelihood of having a behavioral and psychiatric emergency in flight are eliminated during the selection process; i.e., they never become astronauts. This facet of the selection process is commonly called "select-out." The NASA select-out system is thorough, but the predictive ability of all selection systems diminishes over time. Individuals and circumstances change as time passes so that a test that was administered during selection 10 years before an individual is assigned to a mission has a limited ability to predict in-flight and post-flight behavior. Not only are the individuals who are most likely to have a behavioral and psychiatric emergency selected-out, but the individuals who are best suited to being astronauts are identified. This aspect of selection is typically termed "select-in." In the current NASA selection system rather than being "selected-in," this aspect of selection is more accurately considered "suitability."

A suitability score, which is given to each interviewee, is a clinical judgment of the degree to which that interviewee would make a good astronaut. Factors that are considered when determining suitability include: personality, emotional stability, and family demands. Again, as with select-out tests, select-in suitability scores are less predictive over time. To counteract the deterioration of the selection data, annual psychological assessments were recommended in the "NASA astronaut health care system review committee: report to the administrator (February – June, 2007)" (Bachmann et al., 2007). Annual BHP assessment interviews, which are performed by an experienced flight surgeon who is also board-certified in psychiatry, started in October 2008. This assessment is comprised of a 30-minute interview in the NASA Johnson Space Center (JSC) Flight Medicine Clinic and covers broad areas of occupational relevance, including space flight experience, workload, fatigue, sleep, peer relationships, family, challenges, goals, and future plans. These annual assessments are not intended to be comprehensive psychological screenings for mental disorders or psychiatric illness, however. Such an assessment would be very time-consuming and produce an extremely low yield of any useful data. Of greater importance operationally are the ISS pre-flight assessments that begin 1 year prior to an astronaut being given a backup assignment. These interviews are longer (90 minutes) and far more intensive in terms of content.

Despite the annual and pre-flight BHP assessments, there is a risk of unpredicted in-flight behavioral degradation due to unforeseen circumstances such as mishap, personal tragedy, interpersonal conflict, or the development of symptoms of a mental disorder that was latent before flight. In this regard, there remains a risk of mission-impacting mental distress and performance degradation that cannot be ignored, one that requires further review, improved assessment techniques, and autonomous intervention methods.

The Operational Psychology (Op Psy) component of BHP provides psychological support to ISS crew members (Sipes and Vander Ark, 2005) (Category IV). While the majority of Op Psy support occurs in flight,

preparations begin pre-flight as astronauts express their preferences for support options such as crew member Website content, movies, games, and food. These decisions allow crew members to take some of the familiarity and comfort of home with them.

"Lessons learned" are shared both formally and informally among astronauts and family members. Formal Astronaut Office briefings are scheduled following each short- and long-duration mission as well as between the assigned crew members of adjacent missions. These lessons learned are documented and distributed among astronauts and their families. Formal briefings and training sessions are also scheduled with crew and family members before each mission. Informal briefings occur between experienced and inexperienced astronauts, as well as between their spouses or significant others. Other opportunities to share information are provided by the Astronaut Spouses Group (ASG) during social and educational events. General advice that is not targeted to a specific individual or family is available from a variety of resources such as the ASG newsletter, Astronaut Office documents, and Flight Medicine Clinic handouts.

The JSC Family Support Office (FSO) acts for astronauts and their family members by liaising with the Astronaut Office, the ASG, BHP, JSC security, the Flight Medicine Clinic, the Military Liaison Office, the Public Affairs Office (PAO), and others. An organizational FSO is needed when employee tasks include lengthy deployments or hazardous duties that affect employee families. Personnel in the FSO assist with all issues or concerns in a confidential manner. They also connect and communicate with families so that these families are informed and ready in the event of an emergency. To support families in their readiness preparations, the FSO provides publications, newsletters, email notices, training and educational classes, and specialized seminars. The FSO was created to address the unique challenges that face astronauts and their families during astronaut training cycles and flight assignments (Sipes and Vander Ark, 2005). As several astronauts have noted, the FSO provides the support that enables them to more easily concentrate on their work in space because they believe that their family needs are being met by FSO personnel in their absence.

One method for providing crew members with additional coping mechanisms is to teach them specific coping skills. BHP Op Psy provides classes to astronauts and, in some cases, their families. These classes are discussed below:

In-flight Resource Plans 1 and 2 provide astronauts with an overview of the support that BHP provides to ISS astronauts. This course familiarizes astronauts with BHP and its functions, and provides them with a first look at some of the coping mechanisms that are available.

Self-care/self-management refers to keeping oneself satisfied and productive under demanding circumstances and managing one's own stress. This class teaches astronauts to apply strategies of self-care/self-management as they encounter the stressors that are common to long-duration missions.

Psychological Factors 1 exposes crew members to the psychological effects of long-duration space flight. The manifestations of various psychological factors are discussed, as well as the procedures that are used to manage any contingencies.

Psychological Factors 2 continues the discussion of the support resources that are available during a mission for the crews and their families. It also identifies the principle environmental, interpersonal, and programmatic factors that can impair psychological health and performance during extended confinement.

Psychological Support Planning 1, Psychological Support Planning 2, and ISS Crew/Family Psychological Support Familiarization classes brief crew members on the psychological support program that is established to assist crew members and their families during the pre-flight, in-flight, and post-flight phases of the mission. Each crew member begins to identify his or her desired in-flight support resources, based on the options that are currently available. At the crew member's discretion, family and/or primary support individuals will be invited to the meeting.

Practical Planning for Long-duration Missions encourages crews and family members to consider important personal arrangements before long-duration missions. This class stresses critical actions (e.g., wills, emergency contact information), reviews "lessons learned," and provides tools and checklists to help simplify the personal preparation process. The FSO offers this class in conjunction with BHP and the Astronaut Office. Spouses, significant others, and other key family members may attend this event at crew member discretion.

Conflict Management is a discussion-oriented lesson that introduces a three-point cycle that drives, escalates, and de-escalates conflict. The course reviews methods for breaking the cycle at each of the three points so that conflicts are resolved in ways that preserve relationships with colleagues, friends, and family. Techniques include "rules" for fair fighting, checking the accuracy of interpreted meanings, and recognizing and managing emotions that can perpetuate conflict. This training was based on materials that were developed in a National Space Biomedical Research Institute (NSBRI)-supported study (Carter et al., 2005).

Cross-cultural Training exposes U.S. astronauts to special circumstances that can arise from working with crew members and ground control personnel from the International Partners of NASA. The course addresses cultural factors, communication and negotiation styles, and work and social factors. Potential positive and negative effects of cultural differences are identified. Methods, strategies, and resources that can be used to handle cross-cultural challenges are described and practiced within the context of case-situations that occurred previously. This course was devised in answer to the interview requests of astronauts who flew on ISS and Mir for more and better cross-cultural training (Cartreine, 2009).

ISS Behavioral Medicine Training is provided to CMOs and flight surgeons. This training provides an overview of the psychiatric symptoms and disorders that might be seen during a mission. Discussion includes the therapeutic clinical response and resources that are available on ISS should a crew member exhibit seriously disordered behavior. The focus of this training is on serious psychiatric symptoms or illness as opposed to behaviors that fall within the norm for persons who are living in stressful circumstances.

Behavioral medicine psychiatric interviews begin 12 months before launch and at 30 days post-return. These interviews are the mainstay of pre-flight detection and prevention of in-flight psychological or psychiatric problems (NASA, 2008). Interviews focus on mission training issues, crew-crew interaction, family issues, sleep and fatigue, workload, crew-ground communication, mood, cognition, ground re-adaptation, and family reintegration.

Another behavioral medicine requirement on the ISS is the WinSCAT (space flight cognitive assessment tool for Windows), which is an 11- to 15-minute computer-based cognitive screening test. Baseline testing begins 6 months before launch, and the astronaut is requested to take it once a month while in orbit. WinSCAT is an operational medical requirement that will be used after an astronaut has suffered any unexpected medical

event (e.g., head trauma, decompression sickness (DCS), exposure to toxic gases, medication side effects); it will serve as a data point for crew surgeon medical assessment/disposition (Kane et al., 2005). Off-nominal WinSCAT scores are evaluated in context before adjusting the work-rest schedule or taking another course of action.

These extensive ISS pre-flight behavioral medicine interviews and assessments, along with the BHP training classes and other support that are provided, help to prepare crews for long-duration space flight and act as another behavioral health-screening aid.

In-flight

Currently, provision of psychological support is at its most intensive when the astronauts are in flight as opposed to during the pre- or post-flight periods. This support system, which is provided by BHP Op Psy, includes crew care packages, contact with family and friends, communication technologies, and leisure/recreation activities. Crew care packages are either sent with the crew to be opened later or via resupply to ISS. They consist of items that are selected by crew members and their families and friends, such as favorite foods. In a *Mir* simulator study, researchers found that after a resupply event, crew anxiety, total mood disturbance, and overall crew tension significantly lessened (Stuster, 1996) (Category II).

Providing crew members with the opportunity to keep up regular contact with their families is important for maintaining crew member behavioral health. Private family conferences are conducted via video between crew member and family from within the privacy and comfort of the family home. The internet protocol (IP) telephone is an additional link between a crew member and that crew member's family. The crew member can call home when Ku-band coverage is available. The NASA tracking and data relay satellite uses Ku-band to communicate with both the shuttle and the ISS.

Other social contact with the ground that is not necessarily family-specific helps to broaden the social support networks of crew members and acts to lessen crew member feelings of being objectified and separated. According to BHP Op Psy, Expedition crew members received approximately 20 greetings during one Christmas season. A greeting is a short message, usually in the form of a video that is recorded by family, friends, or coworkers, that is sent to a crew member.

The crew Webpage, the IP telephone, and email can help crew members feel more connected to events on Earth. The crew Webpage, which is updated twice weekly for each crew member, is specifically tailored to a crew member and, thus, provides that crew member with a gateway to personal news selections, videos, MP3s, and photographs.

Providing choices of leisure activities for crew members is another tool that can prevent behavioral health distress. Before flight, crew members request movies, music, and electronic books that will be uploaded to them. Even equipment can be requested; for example, in response to the request of various ISS crew members, several musical instruments are now on board the station. Astronauts have stated that they use movies and music to accompany their required daily exercise regimes. In addition to its physical benefits, exercise also is an effective countermeasure for maintaining positive mood.

Regular private psychological conferences begin once an astronaut is in flight and continue throughout the duration of the mission. Private psychological conferences, which are held between a psychologist or a psychiatrist and a crew member, are normally conducted every 2 weeks for at least 15 minutes. These con-

ferences enable the psychologist or psychiatrist to assess the behavioral health of the astronaut and provide that astronaut a venue for venting and voicing concerns.

The WinSCAT, which, as mentioned earlier, assesses cognitive functioning, is scheduled to be taken once a month by crew members while they are in orbit. The WinSCAT scores that are recorded after an astronaut has sustained any unexpected medical event are compared to that astronaut's baseline and other pre-insult scores. The WinSCAT, along with other data, allows the crew surgeon to make an evaluation regarding the severity of an event (Kane et al., 2005).

Post-flight

Prevention and treatment of post-flight behavioral conditions and psychiatric disorders rely primarily on behavioral medicine interviews after a crew member returns to Earth. These post-flight interviews may not be of sufficient length to be of benefit, since time is required to allow astronauts to feel comfortable and open up. Before astronauts will speak candidly, they must also trust the individual who is conducting the interview and believe that the contents of the interview will not adversely affect their future flight status.

Other post-flight prevention and treatment methods could be incorporated. For instance, the annual psychological exams for current astronauts that are recommended in the Bachmann report (2007) would provide post-flight support for flown astronauts. A similar psychological exam could be implemented for retired astronauts. As all of the effects of flight and return might not be present immediately, continuing the behavioral medicine interviews for a longer period of time would provide astronauts with opportunities to discuss issues that might arise post-flight. If necessary, pharmacological aids can be prescribed.

In addition to providing the best measures and tools to monitor and assess mood and predict risk for and management of behavioral conditions and psychiatric disorders before and during space flight, the HRP BHP Element is required to continue this provision after an astronaut's return from space flight (NASA, 2007). When astronauts return to Earth, reintegration back into the family is not easy. It takes time and will require adjustment from all family members. A class for astronauts and their families that specifically targets the challenges of reintegration could be developed or an existing class could be modified. Education of astronauts and their families regarding reintegration is especially important for those who have no deployment experience.

Treatment

Pre-flight

Astronauts and their families have pre-flight access to counseling. There might be some hesitancy to use these services, however, given the NASA culture and astronaut concern that flight status might be negatively impacted (Shepanek, 2005).

In-flight

Medical kits that are aboard space shuttle and ISS missions contain supplies to help crew members cope with a variety of possible medical emergencies. These kits include medications that can be used in the treatment of space motion sickness, sleep problems, illnesses, injuries, and behavioral health problems. For example, space shuttle medical kits have included medications that can help to counter anxiety, pain, insomnia, fatigue (Caldwell et al., 2003), depression, psychosis, and space motion sickness (Graybiel and Lackner, 1987; Savin et al., 1997; Bagian and Ward, 1994; Davis et al., 1993; Harm et al., 1999; Hughes and Forney, 1964; Parrott and Wesnes, 1987; Cowings et al., 2000; Rice and Synder, 1993; Wood et al., 1985, 1992). Putcha et al. (1999) evaluated the in-flight use of medications from astronaut debriefings

that were conducted after 79 U.S. shuttle missions. The results show that 94% of the records indicated that medication was used during flight.

Space motion sickness accounted for 47% of the medications that were used, while sleep disturbances accounted for 45%. The remainder of the medications was reportedly taken for headache, backache, and sinus congestion. These findings are an increase from the findings of Santy (1990), who reported that 78% of crew members took medications in space, primarily for space motion sickness (30%), headache (20%), insomnia (15%), and back pain (10%). Currently, the ISS medicine kit contains two anxiolytics, two antidepressants, and two antipsychotics. While the use of these medicines would be unexpected and unlikely, their inclusion is necessary in the event of an actual emergency, just as flying a defibrillator is a medical requirement, although no cardiac arrests have occurred to date. In extreme situations, a physical restraint system is available. Sedatives are also included in the medical kit if a crew member requires sedation to ensure the crew member's or fellow crew members' safety.

As described above, several non-pharmacological tools are available to monitor behavioral issues on U.S. spacecraft. The first, and perhaps most important, is the private psychological conference that is held between a psychologist or a psychiatrist and a crew member. Private psychological conferences are useful both as a monitoring tool and in cases in which an intervention is required. They also can be used to counsel or treat astronauts. Initial statistical data that were compiled by BHP experts representing European, Russian, and U.S. space agencies indicate that private psychological conferences are accepted by crew members (Manzey et al., 2007). During private psychological conference debriefings, astronauts have praised the preflight briefings as well as the psychological services that are provided by operational psychology during flight (e.g., private family conferences, crew discretionary events, crew care packages, recreational items) and the behavioral medicine support (pre-flight briefings and private psychological conferences). Astronauts have told BHP in debriefings that they did not realize how important "that psych stuff" was until after they were on the ISS.

The flight surgeon is also an important line of defense for reducing the likelihood of a behavioral condition or psychiatric disorder occurring or developing. The role of the flight surgeon is to monitor the physical health and well-being of the astronaut. To ensure this, the flight surgeon conducts a 15-minute private medical conference once a week with the astronaut. As with the psychologist or psychiatrist, the flight surgeon may be able to recognize early signs of behavioral health distress in an on-orbit crew member. Lebedev describes his crew doctor intervening during his Salyut 7 flight: "I kept myself under control but I was irritated. Our crew doctor, Eugeny Kobzeb, sensed it, and during the evening period of communication said, 'Wait a minute.' Suddenly I heard a very familiar Ukrainian melody. I couldn't understand where it came from. Finally it dawned on me: it was my son playing the piano. It was so wonderful and unexpected that tears ran from my eyes" (Lebedev, 1988, p. 77).

Post-flight

Several of the methods that are used to prevent the occurrence of post-flight behavioral conditions and psychiatric disorders can also be used to treat these conditions if they occur post-flight. Annual psychological exams for current and retired astronauts can be used as a springboard for targeting treatment options; e.g., continued counseling or pharmacological aids. As not all effects of space flight and reintegration are immediately present at the time at which an astronaut returns, post-flight behavioral medicine interviews could be continued at additional intervals beyond those intervals that currently occur post-flight. To the extent that a family is experiencing difficulty with an astronaut reintegrating, family counseling is another treatment option that is available post-flight.

Summary

The operational set of activities that was described in the previous sections consists of specific medical requirements that are determined to be necessary by an international group of behavioral health specialists. If flight surgeons as well as astronauts had seen no value in these activities, they would have been waived or removed. Instead, astronauts have communicated their appreciation of and desire for these services. According to the lead NASA psychiatrist (personal communication), every ISS astronaut has stated that these training measures and countermeasures of behavioral medicine and operational psychology support are both valued and beneficial. Areas of enhancements that were cited by these astronauts include: crew morale, mood, motivation, crew cohesion, and family ties during the mission.

Astronaut use of many BHP operational services is voluntary. They are presented to the crew member and family from the first meeting as a "buffet" from which they can choose all, some, or none, and they have an opportunity to request their own services. The fact that crew members and their families consistently have requested more operational psychology support as the program has developed and continue to request specific services that are already offered are indicators that these services are needed and should be continued. The internationally publicized death of a crew member's family member during Expedition 16 tested the value and benefit of the services that are currently offered by BHP.

This type of tragedy is addressed in pre-flight behavioral medicine training with all crews. As humans continue to explore space, it will surely not be the last time that this type of event occurs. The response to such a tragedy requires the implementation of all facets of operational psychology and behavioral medicine countermeasures. Lastly, the high number of Silver Snoopy awards[11] that have been awarded by the astronauts to the BHP Op Psy Behavioral Specialists who have directly supported these services demonstrates astronaut appreciation of BHP training, treatment, and prevention services.

Risk in Context of Exploration Mission Operational Scenarios

Depression is becoming more common in the general population. The WHO (2001), in its annual report, predicts that depression will become the second-largest cause of disability worldwide by the year 2020. It is already the leading cause of disability in the U.S. according to the NIMH (2000). In a given year, approximately 20.9 million U.S. adults, or about 9.5% of the population who are age 18 or older, will develop a mood disorder (Kessler et al, 2005; NIMH, 1999).

To assess and quantify the risk of behavioral conditions and psychiatric disorders in the context of future Exploration missions, it is important to consider the crew member's nationality and age. Annual rates of depression differ from one region to another. In the U.S., depression is the third-most-frequent psychiatric diagnosis (NIMH, 2000). In other countries, however, the rate of depression is considerably lower. The likelihood of a mood disorder developing also varies by age group. Close to one-half of the psychiatric disorders that led to U.S. Naval aviation personnel waivers were for persons who were older than age 30 (Bailey et al., 1995). Major depression along with manic depressive disorder and obsessive compulsive disorder are highly likely to develop for the first time in North American and Western European astronauts' age groups (Burke et al., 1990; Flynn, 2005).

[11]The Silver Snoopy is the most prestigious award given by the members of the NASA Astronaut Corps. The award consists of a sterling-silver Snoopy lapel pin that has flown on a space shuttle mission, plus a certificate of appreciation and commendation letter.

The total incidence rate for the general adult population is a summation of the incidence rates for each subgroup based on age and gender. The incidence rates for the subgroups are therefore lower than the total adult population incidence rate. More specifically, tailoring the incidence of depression in the general population to the age range of the astronaut population will yield a considerably lower rate than the 9.5% that is estimated for the general U.S. population. The NASA IMM uses an incidence rate of depression and anxiety (for males 0.00029 cases per person-year and females 0.0036 cases per person-year) that is extrapolated from the Longitudinal Study for Astronaut Health, whose incidence rate is limited to the average age range of the astronauts (i.e., 40 to 49 years). Behavioral emergencies in the general population occur in 3% to 9% of depression cases (Murphy et al., 1988; Ramadan, 2007). Extrapolating from these rates, the overall incidence rate of behavioral emergencies due to depression for astronauts can be estimated as 0.000087 to 0.000324 cases per person-year (NASA, 2007b). However, it is important to note that the rates that were used in these calculations were based on reported symptoms only and were not derived from a confirmed diagnosis. Therefore, the incidence of depression and anxiety may or may not be higher in crew members in space flight than in the age-adjusted general population due to the high workload and stressors that are associated with some aspects of space flight missions (NASA, 2007a).

Rather than basing his estimate on the incidence rate of depression in the general population, Stuster (2008) predicted that the incidence rate of behavioral problems that could be expected on long-duration Exploration missions is based on known incidence rates in analog environments. Reporting physicians defined behavioral problems as symptoms that normally would warrant hospitalization. Stuster's analyses show that as the length of a mission increases, so will the incidences of psychiatric disorders (see Table 1-2). Stuster's (2008) assumptions are as follows:

Table 1-2. ***Calculation of Expedition Risk of a Behavioral Problem Occurring Based on Incidence and Probabilities in Analog Environments***

		Long-stay Option				
	Incidence Per 365 Days	Outbound	Surface	Return	Total Long-stay Risk	Expected in a Crew of Six
		180 days	545 days	180 days	905 days	
Behavioral Problem	0.060	0.030	0.090	0.030	0.149	0.893
Differential	0.020	0.030	0.030	0.030	0.089	0.534
		Short-stay Option				
	Incidence Per 365 Days	Outbound	Surface	Return	Total Short-stay Risk	Expected in a Crew of Six
		313 days	40 days	308 days	661 days	
Behavioral Problem	0.060	0.051	0.007	0.051	0.109	0.652
Differential	0.020	0.051	0.002	0.051	0.104	0.626

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The figures in the row labeled *Behavioral Problem* assume a 6% per year incidence rate of serious behavioral problems throughout the durations of the two mission options considered (i.e., Mars Long Stay, 905 days total; and Mars Short Stay, 661 days total). This predicted incidence rate is based on incidence rates of behavioral problems reported from Antarctic experience (i.e., Matusov, 1968; Gunderson, 1968; Lugg, 1977; Rivolier and Bachelard, 1988; ANARE; Otto, 2007). The row labeled *Differential* assumes a 6% incidence rate per person-year during the interplanetary transit phases and a 2% rate per person-year while on the surface of Mars, when confinement would probably be less of a factor and other stressors might be offset by the novelty of task performance. The expected oc-

currence of a behavioral problem serious enough to require hospitalization on Earth in a crew of six is estimated to be .534 for the long-stay option and .626 for the short-stay option. Using the differential values, these translate to a 53.4% probability that a serious behavioral problem will occur during the long-stay option and a 62.6% probability during the short-stay option. Stuster asserts the probability of a serious problem occurring to be greater for the short-stay option [on Mars], due to the substantially longer time that must be spent by the crew confined to the space craft than in the long-stay option. However, the long-stay option will always generate a higher probability if the incidence rate were to remain constant throughout the mission. A uniform 6% incidence rate per person-year would increase the estimated probability of a serious behavioral problem to 65.2% for the short-stay option and 89.3% for the long-stay option.

The two approaches (IMM and Stuster's analog-based) to estimating the incidence rate of behavioral conditions and psychiatric disorders yield very different predictions. Further investigation of the discrepancies between the two estimates is warranted. What is noteworthy in both approaches is the predicted occurrence of a behavioral problem during a long-duration mission.

Conclusion

Evidence that was gathered from long-duration stays in ground analogs demonstrates that, despite the focus on screening and selection for suitability, behavioral conditions and psychiatric disorders such as depression develop. Of greater relevance, anecdotal reports from the earlier long-duration space missions (i.e., *Mir* and Skylab) and evidence from current long-duration missions on the ISS reveal that the signs and symptoms of depression and other behavioral disorders also have occurred in flight. The relevance of the risk of behavioral conditions and psychiatric disorders is supported further by the implementation by NASA of the Family Support Office as well as by the psychiatric support that is made available to the ISS crews and their families.

Exploration missions will require crews to live in ICE environments for as many as 3 years. This is a significant leap from the 6-month duration of lower Earth orbit missions. To date, only five individuals have lived and worked in space for longer than 1 year.[12] The incidence of behavioral and psychiatric disorders is expected to increase as the length of the mission increases (Ball and Evans, 2001; Otto, 2007; Stuster, 2008) (Category IV). The additional, unique stressors of radiation exposure, remote distances, and unknown dangers that will be experienced during long-term Exploration missions to the moon and Mars also may contribute to an increased likelihood of this risk.

If a behavioral condition or psychiatric disorder should develop on an Exploration mission, the consequences could jeopardize mission objectives. Therefore, future research addressing the prevention of behavioral problems, as well as the early detection and treatment of problems that do occur, is recommended.

The current rigorous astronaut selection system prevents some behavioral problems from manifesting themselves. Refining and updating the system could prevent the onset of additional problems. Recommended improvements to the selection system include: validation of the current system and implementation of a true select-in system (i.e., one that identifies the interviewees who are most likely to succeed as astronauts). Periodic psychological reassessment also could possibly detect early signs of a behavioral condition or psychiatric disorder. Further, if those who assign astronauts to crews and missions were to employ psychological selection methodology,

[12]To date, three Russian cosmonauts (Sergei Krikalev, Sergei Avdeyev, and Alexander Kaleri) and two U.S. astronauts (C. Michael Foale and E. Michael Finke) have spent more than 1 year in space.

they might increase the likelihood that those astronauts who are selected for a crew would be unlikely to experience an in-flight behavioral medicine emergency.

Early detection is important in deterring and treating behavioral and psychiatric problems. Research that investigates the best assessment measures to detect behavioral and psychiatric disorders is warranted. Thus, one example of a possible future research topic is which personality measures best predict astronaut psychosocial adjustment to space flight.

NASA has many countermeasures in place and will need to develop additional countermeasures that are tailored to long-term lunar and Mars missions. The efficacy of the current countermeasures for future Exploration mission scenarios needs to be formally assessed. The astronauts who will be venturing out on long-duration space flight missions beyond low-Earth orbit (LEO) will face unique challenges, including the need to manage behavioral health problems autonomously. Research is needed to address appropriate countermeasures that are specific to the Exploration mission environment. A better understanding of factors affecting positive emotional reactions also will be important when developing countermeasures for use during long-duration Exploration missions.

Early, quick, and effective treatment of any behavioral problems that do occur is essential. Future research should include investigation of other treatment options and an assessment of the efficacy of those treatment options.

This review of the evidence to date reveals that much work has been done to identify, prevent, and treat the behavioral conditions and psychiatric disorders that might affect astronauts and their performance during all phases of a mission. Given the relative lack of behavioral conditions and psychiatric disorders that have occurred within the astronaut population, the lack of behavioral and psychiatric emergencies in flight, and the number of long-duration mission successes, the current system for mitigating the risk of behavioral conditions and psychiatric disorders appears to be effective. As missions return to the moon and then look toward Mars, changes to behavioral medicine will be required. Our view of the "right stuff" will need to be adjusted. Factors such as personality might play a greater role, while other factors, such as pilot experience, might play a lesser role than they do at present. The selection system will therefore need to reflect those changes. Countermeasures will need to evolve. Some current countermeasures will not be relevant for longer flights, while other, new ones will need to be developed (e.g., alternative to seeing Earth). Effective countermeasures will help to protect and ensure astronaut behavioral health and performance, and, in turn, help NASA achieve mission success on the most challenging Exploration missions that humankind has dared to undertake to date.

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Appendix: Incidence of Physical and Behavioral Medical Events during Space Flight

In-flight medical events for U.S. astronauts during the Space Shuttle Program (STS-1 through STS-89, Apr 1981 to Jan 1998)

Medical Event or System by ICD-9[a] Category	Number of Events	Percent	Incidence/ 14 days	Incidence/ year
Space adaptation syndrome	788	42.2	2.48	64.66
Nervous system and sense organs	318	17.0	1.00	26.07
Digestive system	163	8.7	0.52	13.56
Skin and subcutaneous tissue	151	8.1	0.48	12.51
Injuries or trauma	141	7.6	0.44	11.47
Musculoskeletal system and connective tissue	132	7.1	0.42	10.95
Respiratory system	83	4.4	0.26	6.78
Behavioral signs and symptoms	**34**	**1.8**	**0.11**	**2.87**
Infectious disease	26	1.4	0.08	2.09
Genitourinary system	23	1.2	0.07	1.83
Circulatory system	6	0.3	0.02	0.52
Endocrine, nutritional, metabolic, and immunity disorders	2	0.1	0.01	0.26

[a]*International Statistical Classification of Diseases and Related Health Problems, 9th Ed.*
Source: Billica (2000)

Medical events among seven NASA astronauts on* Mir*, Mar 14, 1995 through Jun 12, 1998

Event	Number of Events	Incidence/100 days	Incidence/year
Musculoskeletal	7	0.74	2.70
Skin	6	0.63	2.30
Nasal congestion, irritation	4	0.42	1.53
Bruise	2	0.21	0.77
Eyes	2	0.21	0.77
Gastrointestinal (GI)	2	0.21	0.77
Psychiatric	**2**	**0.21**	**0.77**
Hemorrhoids	1	0.11	0.40
Headaches	1	0.11	0.40
Sleep disorders	1	0.11	0.40

Note: Data from the Russian Space Agency report that there were 304 in-flight medical events on board the *Mir* from Feb 7, 1987 through Feb 28, 1998. The numbers of astronauts at risk or the incidence per 100 days was not reported.
Source: Marshburn (2000)

Chapter 2: Risk of Performance Errors due to Poor Team Cohesion and Performance, Inadequate Selection/Team Composition, Inadequate Training, and Poor Psychosocial Adaptation

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Human performance errors may occur due to problems associated with working in the space environment and incidents of failure of crews to cooperate and work effectively with each other or with flight controllers have been observed. Interpersonal conflict, misunderstanding and impaired communication will impact performance and mission success. The history of spaceflight crews regarding team cohesion, training and performance has not been systematically documented. Tools, training and support methods should be provided to reduce the likelihood of this risk and improve crew performance. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

Shared diversions on the International Space Station, including musical performances and movie nights, provide rest and relaxation while promoting team cohesion.

Executive Summary

Evidence from space flight and ground-based studies supports the idea that performance and health are both influenced by several interpersonal factors that are related to teamwork, including: team cohesion, team selection and composition, team training, and psychosocial adaptation. Space flight evidence regarding performance and the effect of these psychosocial factors is more limited than evidence that is available from ground-based research. However, numerous NASA-funded and -supported reviews and reports (regarding space flight and space analogs) emphasize the need to consider the team as well as the psychosocial factors affecting the team (Ball and Evans, 2001; Hackman, 1996; Helmreich, 1985; NASA, 1987; Paletz and Kaiser, 2007; Vinograd, 1974). To date, no systematic attempt has been undertaken to measure the performance effects of team cohesion, team composition, team training, or psychosocial adaptation during space flight. As a result, evidence does not help us to identify specifically what team composition, level of training, amount of cohesion, or quality of psychosocial adaptation is necessary to reduce the risk of performance errors in space. Ground-based evidence demonstrates, however, that decrements in individual and team performance are related to the psychosocial characteristics of teamwork, and there are reasons to believe that ground support personnel and crew members experience many of the same basic issues regarding teamwork and performance (Hackman, 1996; Lautman and Gallimore, 1987; Vinograd, 1974).

Although evidence does not identify specific factors or how these factors are important, evidence that was reviewed in this report demonstrates that addressing the psychosocial characteristics of teamwork will promote crew health and performance. Before this knowledge can be effectively applied to long-duration missions, however, more research must be done to determine what practices (e.g., selection, training, coaching, psychological support) best address the psychosocial characteristics of teamwork in space flight. The BHP Element has identified the gaps in the knowledge that is related to these issues, and a review of these gaps is included in this report.

Introduction

Evidence that links crew selection/composition, training, cohesion, or psychosocial adaptation to performance errors is uncertain. This is mainly due to the fact that the research on performance errors is itself ambiguous. The study of performance errors implies that human actions may be simplified into a dichotomy of "correct" or "incorrect" responses, where incorrect responses or errors are always undesirable. Some researchers have argued that this dichotomy is a harmful oversimplification, and that it would be more productive to focus on the variability of human performance and how organizations can manage that variability (Hollnagel et al., 2006) (Category III[13]).

Two particular problems occur when focusing on performance errors: (1) the errors are infrequent and, therefore, are difficult to observe and record; and (2) the errors do not directly correspond to failure. Research reveals that humans are fairly adept at correcting or compensating for performance errors before such errors result in

[13]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

recognizable or recordable failures (Hollnagel et al., 2006) (Category III). Most failures are recorded only when multiple errors occur and humans are unable to recognize and correct or compensate for these errors in time to prevent a failure (Dismukes et al., 2007) (Category III).

More commonly, observers record variability in levels of performance. Some teams commit no observable errors but fail to achieve performance objectives or perform only adequately, while other teams commit some errors but still manage to perform spectacularly. Successful performance, therefore, cannot be viewed as simply the absence of errors or the avoidance of failure (JSC Joint Leadership Team, 2008). While failure is commonly attributed to making a fatal error, focusing solely on the elimination of error(s) does not significantly reduce the risk of failure. Failure may also occur when performance is simply insufficient or an effort is incapable of adjusting sufficiently to a contextual change. The surest way to reduce the risk of failure is to achieve optimal performance. If NASA is to spend the same amount of money launching one of two crews and both crews have an equal risk of committing performance errors but one crew is more likely to perform more of the mission objectives (or otherwise perform better), it follows that the most desirable crew remains the highest-performing crew. From this point of view, the more critical question is: how can we optimize human performance during long-duration missions?

Fortunately, the evidence that links crew selection/composition, training, cohesion, or psychosocial adaptation to performance differences is more conclusive and more relevant to future human space exploration operations than is the evidence regarding performance errors. The list of what is known from existing research (ground-based, space analog, and space flight) is considerable. In light of the positive influences of team performance, we know that

- We can select individuals who are more capable of performing well in a team (Barrick et al., 1998) (Category III).
- Different team compositions better facilitate different types of performance (Mannix and Neale, 2005) (Category III).
- Training individual team skills and training teams together encourages better individual and team performance (Hirschfeld et al., 2006; Paris et al., 2000; Salas et al. Bowers, 2000) (Category II and Category III).
- Teams that are more cohesive demonstrate better performance than less cohesive teams (Grice and Katz, 2005) (Category II).
- Better teamwork increases the likelihood of recovery and survival in the event of a malfunction or error (Baker et al., 2006; Shapiro et al., 2004) (Category III).
- Members of more cohesive teams demonstrate better individual performance and report more physical and psychological resilience under duress (Kidwell et al., 1997; Palinkas, 1991; Podsakoff et al., 1997; Vallacher et al., 1974) (Category II and Category III).
- Individuals and teams perform better and maintain high performance and good health longer when they adapt more quickly and effectively to the stressors that are inherent in a psychosocial environment (Burke et al., 2006; Gunderson, 1966a; Lugg, 1977; Riggio et al., 1993) (Category III).
- Psychosocial factors that influence teamwork and performance in traditional work environments appear in the space exploration work environment (Kanas et al., 2000) (Category III).

Negative influences of team performance have also been researched. From the perspective of these, we know that

- Negative consequences (e.g., incomplete objectives; lost time) that are related to interpersonal stressors such as isolation, confinement, danger, monotony, inappropriate workload, lack of control,

group composition-related tensions, personality conflicts, and leadership issues have been observed on previous long-duration missions (Kanas and Manzey, 2003) (Category III).

- Interpersonal stressors, which are cumulative over time, pose a greater threat to performance and team success as work duration increases (Cropanzano, 2003; Halbesleben and Bowler, 2007; Rasmussen and Jeppesen, 2006; Staal, 2004; You et al., 1998) (Category II and Category III).

Selection, training, cohesion, and psychosocial adaptation influence performance and, as such, are relevant factors to consider as we prepare for costly, long-duration missions in which the performance objectives will be demanding, endurance will be tested, and success will be critical. During the selection of crew members, throughout their training, and during their psychosocial adaptation to the mission environment, we will have several opportunities to encourage optimal performance and, in turn, minimize the risk of failure. Researchers, who are faced with the very real prospect of needing to promote successful human explorations of the moon and Mars within the next 15 to 20 years, should not spend limited time and resources in attempts to quantify risks of failure or performance errors due to inadequate selection, training, cohesion, or psychosocial adaptation. Instead, these researchers should focus on how they can most efficiently optimize and support performance through selection, training, team building, and psychosocial adaptation. Human performance professionals currently possess the knowledge to be able to make this kind of research productive and operationally relevant within the projected time until launch. The evidence that is detailed in the following sections supports this argument.

The NASA HRP BHP Element is responsible for managing three risks: (1) risk of performance errors due to sleep loss, circadian desynchronization, fatigue, and work overload; (2) risk of performance errors due to poor team cohesion and performance, inadequate selection/team composition, inadequate training, and poor psychosocial adaptation; and (3) risk of behavioral and psychiatric conditions. While each of these is addressed in a separate chapter in this report, they should not be construed to exist independent of one another; they instead should be evaluated in conjunction with one another. Moreover, as the BHP Risks overlap with the Risks in other HRP Elements, they must also be considered in conjunction with these Elements as well. Refer to figure 2-1 for an example of possible overlaps.

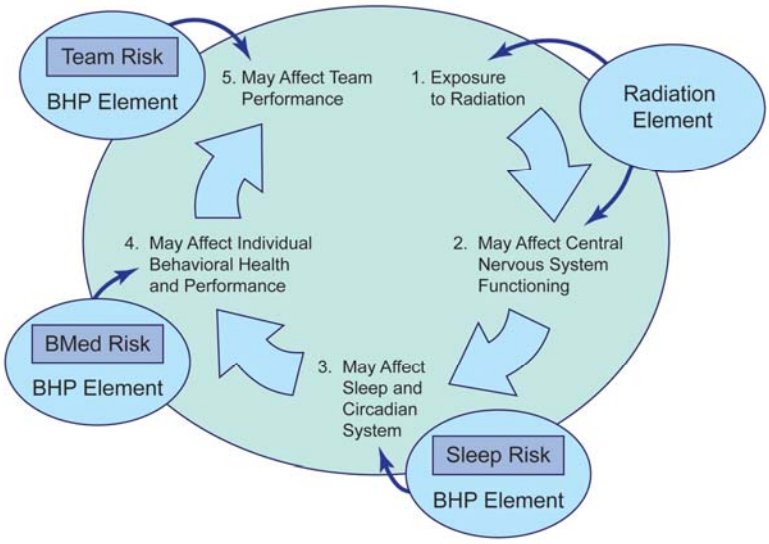

Figure 2-1. ***Example of possible BHP Risks overlapped with Risks in other HRP Elements.***

The BHP relationships with other Elements are further outlined in the HRP IRP (2008). The nature of the IRP implies that BHP is continually reviewing and updating integration points with other Elements. While research is designed to address identified gaps, it will be necessary to update and revise each of the BHP Evidence Reports that constitute this document and the IRP as the element gaps are closed and new gaps emerge.

Evidence

Individual selection and crew composition

Selecting Individuals to Perform in a Team

A team is defined as: "two or more individuals who interact socially and adaptively, have shared or common goals, and hold meaningful task interdependences; it is hierarchically structured and has a limited life span; in it expertise and roles are distributed; and it is embedded within an organization/environmental context that influences and is influenced by ongoing processes and performance outcomes" (Salas et al., 2007a, p. 189). From the NASA perspective, a team is commonly understood to be a collection of individuals that is assigned to support and achieve a particular mission. Thus, depending on context, this definition can encompass both the crew and the individuals who are assigned to support that crew during a mission. Regardless of the extent to which the term is used, the selection of a team can be both complex and difficult when considering individual differences that may influence the functioning of a team.

One way of selecting for teams is to identify those individuals who are best suited to work in teams, ensuring that each individual team member possesses the qualities and skills that lend themselves to optimal teamwork. For example, many organizations use competency frameworks to select individuals (e.g., IBM, GE, Verizon, Waste Management, Hanover, Shell, 3M, the United States Office of Personnel Management) (Rodriguez et al., 2002). Within these frameworks, a "team-working" competency may be found that measures how an individual supports other team members, shares knowledge with them, etc. Both space flight (Category III) and ground-based (Category I and Category II) evidence suggests that "teamwork" competencies help predict individual performance in teams.

Several efforts have been made, within space flight operations, to identify factors that are important for selecting individual crew members for long-duration space flight (Caldwell, 2005; Galarza and Holland, 1999; Hackman, 1996; Holland, 2000; NASA, 1987; Nicholas and Fouchee, 1990; Vinograd, 1974) (Category III and Category IV). Galarza and Holland (1999) conducted a preliminary job analysis to identify the skills that would be necessary for long- vs. short-duration missions to inform the initial astronaut candidate selection process (Category III).

Twenty experts (including astronauts) rated 47 relevant skills on criticality and rated an additional 42 environmental and work demands on their probability of occurrence. The environmental and work demands for long-duration space missions included group dynamics within a heterogeneous crew and with external groups such as ground control. The experts' ratings resulted in 10 broad factors that were deemed important for long-duration missions, including performance under stressful conditions, mental/emotional stability, judgment/decision-making, teamwork skills, conscientiousness, family issues, group living skills, motivation, communication skills, and leadership capabilities. These 10 factors overlap somewhat with those that were identified in previous peer-rating studies, which suggests both a job competence and an interpersonal dimension for astronaut performance (McFadden et al., 1994; Santy, 1994) (Category III).

In 1990, a European astronaut working group reevaluated selection criteria for the selection of European astronauts. Although astronauts had not been historically screened for interpersonal skills, this group included social capabilities as criteria for selection (Sandal, 1999) (Category III). Selection research within space flight is severely limited by a lack of job performance data that are available to researchers. This lack of performance data is due, in part, to the fact that such a limited number of astronauts is actually selected (around 340 U.S. astronauts over the life of the program), and that there is so much evolution in job duties and selection practices (from Project Mercury to the International Space Station Program). This issue is also related to the difficulty in identifying different levels of performance. Quantifying different levels of performance (i.e., optimal vs. adequate vs. inadequate) in relation to optimal selection methods or predictors is unrealistic with such small sample sizes. In such cases, it is unlikely that there are enough observable variances in performance to accurately quantify levels, and the levels thus quantified cannot be validated.

These issues are also relevant for other international space agencies, which also suffer from a lack of performance data and small sample sizes. For example, Russian researchers have long collected personality data on cosmonauts (Kanas and Manzey, 2008), but the empirical linking of personality factors to specific performance levels that are necessary to provide cut-scores or norms for selection still eludes these researchers, perhaps because of small samples or inadequate performance data. Typically, space agencies have not provided objective performance data on enough astronauts to create a reasonably sized sample on which to perform an analysis. This lack of data also obfuscates the ability to identify optimal selection criteria and methods for teams. Thus, we do not have a good idea of the specific individual skills and characteristics that would best predict successful astronaut teamwork. Future researchers who are evaluating crew selection for space flight will thus have to resort to more creative tactics when quantifying performance and validating predictors. For example, space agencies should, at a minimum, conduct studies that generalize and validate predictors among samples of teams whose work approximates some portion of the work that will be performed by astronauts.

In the meantime, 50 years of ground-based research on individual selection for work that is performed in teams, including small group research that is conducted in analog and/or extreme environments, informs astronaut selection for teamwork. Ground-based studies have identified many individual teamwork-related skills and characteristics. For new teams, picking individuals who are skilled at training and articulating their roles to others, compromising, and helping other team members take on their tasks as well as those who also understand effective team processes resulted in better-performing teams than when these individual skills were ignored at selection (Jones et al., 2000) (Category III). Individual values also make a difference, as teams that consist of members who value being on a team perform better than teams that consist of members who do not value being on a team (Bell, 2007; Salas et al., 2005) (Category II and Category III). Members who do not value being on the team are less likely to be motivated to learn team skills (Salas et al., 2005) (Category III). Evidence suggests that individual characteristics (in addition to individual skills and values) influence performance in a teamwork setting. Researchers who conducted a recent meta-analysis found that, in lab-based team studies, team performance was significantly positively related to average team general mental ability and average team task-relevant expertise (Bell, 2007) (Category I).

In the field studies that were considered, the Big Five personality factors (i.e., openness, conscientiousness, extroversion, agreeableness, and neuroticism) were also all significantly correlated with team performance (Bell, 2007). In a traditional work environment, Barrick et al. (1998) found that a team member who had a very low score on conscientiousness (as measured by the NEO PI-R[14]) impacted team performance by acting

[14]Refers to revised the NEO (neuroticism, extroversion, and openness to experience) personality inventory.

as the "weakest link," thus constraining team performance (Category II). In assembly and maintenance work teams, team averages on three personality factors (i.e., emotional stability, conscientiousness, and agreeableness) and general mental ability were positively correlated with supervisor ratings of team effectiveness. Team average general mental ability and two personality factors (i.e., extroversion, emotional stability) were also positively related to supervisor ratings of the ability of the team to maintain itself over time (Barrick et al., 1998). Another review suggests that in team environments, agreeableness and emotional stability are the personality characteristics that are most strongly associated with job performance (Stewart and Barrick, 2000) (Category III). A meta-analysis that was conducted across a range of occupations found that interpersonal facilitation was significantly predicted by three personality factors: conscientiousness, emotional stability, and agreeableness (Hurtz and Donovan, 2000) (Category II). All of these studies provide evidence that individual factors, such as personality and general mental ability, help predict the quality of performance in a teamwork setting. (Note that although the authors of this chapter reviewed the Russian personality literature, findings from these studies were not included in this report due to sample size issues and the fact that the conceptualization of variables (e.g., certain personality factors) were not similar, and were thus not comparable.)

Research on pilots offers further evidence that individual personality factors are relevant to selecting an individual who is capable of teamwork. In regards to interpersonal characteristics, a "right stuff" cluster that is based on the Personality Characteristics Inventory (PCI) is composed of high levels of expressivity (i.e., warmth, sensitivity), and low levels of negative instrumentality (i.e., arrogance/hostility) and verbal aggressiveness (i.e., complaining, nagging, passive-aggressive) (Chidester et al., 1991; Gregorich and Helmreich, 1990; Musson and Helmreich, 2005). A "wrong stuff" cluster, in regards to interpersonal characteristics, includes high levels of verbal aggressiveness and a low level of positive expressivity; whereas, a "no stuff" cluster includes low scores on expressiveness, instrumentality, mastery, etc. The "right stuff" cluster pilots were considered more effective by observers in a 1.5-day simulated trip with a crew than were the "low stuff" and "no stuff" pilots (Chidester et al., 1990). The results of U.S. Navy research in Antarctica suggest that while technical competence is necessary, it is also important to select individuals who exhibit "social compatibility or likeability, emotional control, patience, tolerance of others, self-confidence without egotism, the capacity to subordinate routinely one's own interests to work harmoniously as a member of a team, a sense of humor, and the ability to be easily entertained" as well as those who are practical and hard working (Stuster, 1996, p. 268) (Category III).

In summary, evidence suggests that individual factors should be considered when selecting astronauts for long-duration missions, but more research within the space flight context must be done to determine those factors that are most likely to support optimal performance and minimize errors that are related to astronaut teamwork (refer to Table 2-1 for a summary of presented evidence). More research must also be conducted in the analog context using arduous environments or simulation chambers that may resemble situations that are closer to those that are experienced by astronauts. By using both analog and space flight contexts to conduct this research, we may collect sufficient objective performance data so that the selection methods that are used may be examined within a team.

Table 2-1. *Summary of Findings Presented for Selection*

Source	Predictor	Outcome	Context	Evidence Type
Sandal, 1999	Teamwork competencies	Improved individual performance in teams	Space flight	Category III
McFadden et al., 1994	Teamwork competencies	Improved individual performance in teams	Ground-based	Category III
Jones et al., 2000	Factors: Skilled at training and articulating their roles to others, at compromising, and at helping other team members as well as at understanding effective team processes	Higher team performance	Ground-based	Category III
Bell, 2007	Average team general mental ability	Higher team performance	Ground-based	Category I
Bell, 2007	Big Five personality factors	Higher team performance	Ground-based	Category I
Barrick et al., 1998	Team average general mental ability, and extroversion and emotional stability	Higher team effectiveness	Ground-based	Category II
Chidester et al., 1991	"Right stuff" personality cluster	Increased teamwork ability	Ground-based	Category II
Stuster, 1996	Personality characteristics (e.g., social compatibility, emotional control, patience, etc.)	Increased teamwork ability	Analog	Category III

Composing Teams to Perform

The selection process by which individuals are chosen for their good "teamwork" or interpersonal skills does not take into account several additional factors that meaningfully impact team performance. For example, many researchers suggest that the composition of a team has a major impact on how successful that team is likely to be. Kanas et al. (2001), who based their findings on the shuttle/*Mir* missions, contend that composing an interpersonally compatible crew is an important countermeasure for potential psychosocial problems. Although selecting a crew for interpersonal compatibleness is preferred, operational constraints have severely limited space flight research opportunities. Furthermore, there is no empirical evidence from either U.S. space flights or international space flights that indicates how best to compose crews that have both the right technical competencies and the right interpersonal mix to achieve optimal performance.

While literature on selecting individuals for team work abounds, there is little research literature on the composition of entire teams (Paletz, 2006). Most ground-based studies deal with teams that are already assembled and compare team-level features that are associated with high or low levels of team performance. For example, the teams that did not have any members who were particularly low in agreeableness or extroversion (personality factors) were found to be high-performing teams (Allen and West, 2005) (Category II). Likewise, high-performing teams had more moderate proportions of members who were more extroverted (Barry and Stewart, 1997) (Category II).

Although little empirical evidence exists that would inform the composition of teams, evidence suggests that team composition is a key differentiating factor between high- and low-success teams. One measure of team composition is the heterogeneity or diversity of team members. In one study, Harrison et al. (1998) studied two types of diversity in teams – surface-level (i.e., gender, age, ethnicity, tenure) and deep-level (attitudes, values, beliefs, cultural norms) diversity – and the effects of these two types of diversity on team cohesion. Their findings suggest that the effects of surface-level diversity weakens as group members spend more time together while the effects of deep-level diversity strengthens. Surface-level diversity includes heterogeneity in age, sex, race, and, to a lesser extent, how long the individual has been a part of an organization (i.e., tenure).

Heterogeneity, at a deep level, includes differences among members' attitudes, values, beliefs, and cultural norms. Information concerning deep-level factors is communicated through both verbal and nonverbal behavior patterns and is only learned through extended, individualized interaction (Harrison et al., 1998). Attitudinal similarity may facilitate communication as well as reduce role conflict as communication on the job increases and team members realize that they share similar conceptualizations of their organizations and jobs (Tsui et al., 1992). Although we do not know to what extent future Exploration missions will be based on international partnerships, it is important to remember that deep-level diversity is associated with differing cultural norms.

Several studies have reported that deep-level similarity is one of the most important predictors of team cohesion (Byrne, 1971; McGrath, 1984) and long-term performance (Edwards et al., 2006; Hirschfeld et al., 2006). In contrast, studies generally do not find support that surface-level diversity affects long-term performance; rather surface-level diversity affects short-term performance until team members have enough time to get to know each other, and the focus shifts away from surface-level differences. For example, Schmidt et al. (2004) found that perceptions of leadership effectiveness were significantly related to the general satisfaction of team members with their work, performance, and each other; but the authors of the study did not find any evidence that diversity in demographic composition variables (i.e., age, gender, tenure) was related to the satisfaction of team members (Category III). While some studies indicate that surface-level diversity affects performance and decision-making, these studies focus on short-term performance and decisions that require greater creativity (e.g. advertising decisions) (Bell, 2007; Harrison et al., 2003). The effects of surface-level diversity dissipate over time and are not likely to enhance the ability of a team to avoid "group think" or to continue creative problem solving; whereas the effects of deep-level diversity have little impact on short-term performance but become more salient the longer that a team exists (Harrison et al., 1998).

Research in identifying the right "mix" of team members indicates that different kinds of diversity have different consequences on team conflict and, in turn, on team performance (Pelled and Xin, 2000). An important distinction in team conflict literature is the distinction between interpersonal and task conflict (De Dreu and Weingart, 2003). Interpersonal conflict is generally found to be destructive of team performance, while task conflict, in moderate amounts, is generally found to promote task performance because team members may correct each other's misperceptions or argue out better alternatives (Pelled et al., 1999; Porter and Lilly, 1996). In a review of the literature, Mannix and Neale (2005) conclude that surface-level differences (e.g., demographics) negatively impact the short-term performance of teams as these teams initially experience more interpersonal conflict, but these differences have less impact on performance the longer that the teams are together. Deep-level diversity negatively impacts long-term performance only when teams are not provided with the training and incentives to manage interpersonal conflicts. When training and incentives for managing diversity are provided, deep-level diversity helps teams to maintain moderate amounts of the positive task conflict that supports team performance. Mannix and Neale (2005) suggest that giving teams ample time in which to train together and instructions on how to take advantage of multiple perspectives reduces the odds of interpersonal conflict stemming from either surface or deep-level diversity and increases the ability of teams to leverage the task conflict (Category III). Realistically, if future Exploration missions involve international partnerships, it may be difficult to schedule sufficient time for crew members to train together and learn to leverage their differing cultural norms. Future research should help to determine whether there are other viable means of training team members together (e.g., virtual training connections) that might also enable teams to take advantage of multiple perspectives and, at the same time, minimize interpersonal conflicts.

In summary, the relationship between deep-level diversity, conflict, leadership, and team performance is of more interest for long-duration missions than for surface-level diversity (refer to Table 2-2 for a summary of the evidence). However, the lack of extensive empirical research in these areas demonstrates the little that

is known about team composition and how the makeup of a crew may impact crew performance. Furthermore, the lack of empirical research conducted in a space flight or similar analog setting also brings into question the suitability of applying these findings of team composition to space flight. Thus, a further examination of crew composition, as it relates to optimal team performance, must be conducted (when in a space or similar analog setting) to help determine what deep-level diversity actually exists among crews, what deep-level characteristics impact astronaut performance, and what kinds of operational interventions (e.g., composition considering interpersonal compatibility, time spent training together, etc.) and leadership behaviors will promote optimal team performance.

Table 2-2. ***Summary of Findings Presented for Crew Composition***

Source	Predictor	Outcome	Context	Evidence Type
Allen and West, 2005	Lack of members low in agreeableness or extroversion	Higher-performing teams	Ground-based	Category II
Barry and Stewart, 1997	High proportion of members who were extroverted	Higher-performing teams	Ground-based	Category II
Harrison et al., 1998; McGrath, 1984	Deep-level similarity	Increased team cohesion	Ground-based	Category II
Edwards et al., 2006	Deep-level similarity	Higher long-term performance	Ground-based	Category II
Schmidt et al., 2004	Perceptions of leadership effectiveness	Improved general satisfaction of team with work, performance, and each other	Ground-based	Category III

Team skills training for the individual and the collective team

Long-duration space flights (i.e., flights that are in excess of 3 months), such as ISS missions, are so physically, mentally, and emotionally demanding that simply selecting individual crew members who have the "right stuff" is insufficient (Flynn, 2005). Training and supporting optimal performance, as well as selecting high performers, is a more effective and efficient approach than simply selecting high performers (Holland et al., 2007). Training involves imparting knowledge and/or teaching skills to a group of individuals. However, training team skills and supporting optimal performance entails more than educating astronauts about the technical aspects of the job. It also requires equipping those astronauts with the resources that are needed to maintain their psychological and physical health in an ICE environment over an extended period of time.

Performance levels are also a consideration in relation to training team skills. When considering optimal performance, any training design should be accompanied by an evaluation to determine the standards of optimal, adequate, or inadequate performance, and what skills help differentiate expert from novice teams. In this way, training can be validated by checking student progression and the performance of teams before and after training. It is therefore recommended that team performance standards and levels be documented in the space flight context before effective training is designed. To date, this type of information is unavailable to researchers, and acquiring such performance data requires a better partnership between research and operations.

Developing the right kind of training for team skills that will support astronaut performance is further complicated by other operational issues. To begin with, it is difficult to get an accurate picture of what knowledge and skills are required for successful performance. Not all tasks, or even types of tasks, can be anticipated. On an Exploration mission, new tasks may arise suddenly, so team training needs to be broad and flexible enough to support unexpected performance requirements. Another operational issue is that space exploration is a relatively new job, and not many

individuals have performed it, particularly for long-duration missions (only four individuals have lived and worked in space for 1 year). While all experienced astronauts are polled for this information on a regular basis, only a limited number of experienced astronauts can describe what kind of training they found useful on the job and what kind of training has not been critical to their performance. This situation makes describing successful performance reliably more difficult and evaluating the relationship between training and performance improvement more challenging, especially when considering the team context.

Astronauts are also required to live and work together. Performance expectations include maintaining a healthy psychological and social environment in addition to achieving technical objectives. Astronaut performance is largely team dependent. While some tasks are performed independently, many more tasks (e.g. robotics, extravehicular activities (EVAs)) require the simultaneous involvement of both crew members and ground support members. Subject matter experts within the various space agencies argue that teamwork skills are critical to accomplishing overall mission objectives safely. The Human Behavior and Performance (HBP) Training Working Group at NASA JSC recently articulated the training requirements that are necessary to promote ISS astronaut performance, and teamwork was one of eight primary categories of training requirements. The group recommended that ISS crew members complete at least one technical training event as a team (Human Behavior and Performance Training Working Group, 2007). Additionally, the NASA Mission Operations Directorate provides teamwork training as one of nine primary space flight resource management skills sets that are provided to flight controllers, directors, and crews during mission operations (Mission Operations Directorate, 2007).

As astronauts perform complex technical tasks that are at the forefront of modern science and human limitations, they currently complete a rigorous technical training curriculum that can span from 2 to 5 years. Adding requirements that allow them to practice or perfect skills is a critical concern for schedulers. If, as research suggests, teaching team members to exchange mental models and perceptions concerning performance can reduce the amount of time that is required to master a skill (Cannon-Bowers and Salas, 1998b; Edwards et al., 2006) (Category II), training team skills results in technical training efficiencies. Accordingly, a meta-analysis of 97 studies, involving 11 different types of interventions, that was conducted by Guzzo et al. (1985) found that training and goal-setting are the most effective organizational interventions that are aimed at increasing motivation and individual performance (Category II).

These findings support the idea that training is one of the best interventions for addressing the psychosocial characteristics of teamwork, and, as such, training offers NASA a great chance to promote crew health and optimal performance pre-flight, in-flight, and post-flight for long-duration missions. Evidence indicates that two facets of training are relevant to team performance: (1) individual training on teamwork and interpersonal skills, and (2) time training as a team.

Teamwork and Interpersonal Skills for the Individual

Space flight evidence regarding teamwork and interpersonal skills training is more limited than ground-based evidence. Prior to starting joint operations on the Russian space station *Mir*, NASA mission specialists provided a discussion and resource guide that defined effective teamwork and highlighted several individual strategies for ensuring team performance for the U.S. astronauts who were preparing for those long-duration operations (Galarza et al., 1999), thus implying that training teamwork skills was at least operationally relevant to long-duration missions.

Many training efforts in industry and in the military focus on developing the interpersonal skills of group members to enhance team performance. Arthur et al. (2003) classify studies in terms of three learning objectives: cognitive, interpersonal, and psychomotor skills. Four different training criteria were also identified:

reaction (self-report), learning (test performance, usually pencil and paper), behavior (on-the-job performance, supervisor ratings, or objective measures), and results (company-category productivity, profits, or return-on-investment). These researchers concluded that cognitive and interpersonal skills training have the largest positive effects on behavioral criteria. This indicates that interpersonal skills training specifically benefits job performance (Category II). Bradley et al. (2003) conclude that interpersonal skills training also contributes to good supervisor ratings of team performance in ongoing teams for both short- and long-duration tasks, and for short-term teams that are engaged in long-duration tasks (Category II). The interpersonal skills that contributed to performance include: role clarification, goal setting, identifying work priorities, group problem solving, team coordination, interpersonal relations and understanding, consensus building, and conflict management. Dependent measures that showed improvements included: cohesion, personal growth, motivation, team performance, work efficiency, and job satisfaction. It may therefore be suggested that interpersonal skills training relates positively to team performance.

Baker et al. (2006) investigated the impact of training teamwork skills on surgical team performance and errors; they found that the training significantly improved patient mortality rates and reduced the amount of surgical errors (Category II). Powell and Hill (2006) noted reductions in adverse patient outcomes, medical errors, nursing attrition, and conflicts after crew resource management (a form of teamwork and psychosocial skills training) was implemented in health care arenas (Category III). In a review of the factors that determine the ability of a team to adapt its performance to successfully handle changing conditions, Burke et al. (2006) found that training teamwork skills and cross-training team members resulted in the most adaptive teams (Category III).

In a laboratory simulation, researchers found that training that is designed to improve individual communication and interaction skills improves team performance under novel work conditions (Marks et al., 2000) (Category I). In a similar study that was done with 60 graduate students in assigned teams, Smith-Jentsch et al. (1996) found that training students how to be appropriately assertive and to speak up about team performance issues significantly improved the ability of a team to adjust its performance. Leedom and Simon (1995) found that providing United States Air Force (USAF) aviators with standardized, behavior-based training on teamwork increased team coordination and improved team task performance.

Other studies suggest that teams that are composed of team members who have more knowledge concerning teamwork perform better than teams that are composed of team members who have less knowledge concerning teamwork (Morgeson and DeRue, 2006; Hirschfeld et al., 2006). In a manufacturing organization, Morgeson and DeRue (2006) observed that individual knowledge concerning teamwork helped to predict team performance. In a field study of 92 teams (1,158 team members) in a USAF officer development program, Hirschfield et al. (2006) found that team member mastery of teamwork knowledge predicted better team task proficiency and higher observer ratings of effective teamwork.

Outside of the field and laboratory setting, however, we find little empirical evidence that relates interpersonal skills to the individual in a space flight or an analog setting. Nevertheless, the overall conclusion of the evidence that has been presented suggests that teamwork and interpersonal skills training promote team performance. Research must still help to determine the best kinds of interpersonal and teamwork skills training as well as the best implementation means for supporting optimal team (i.e., the whole mission team, including flight crew and ground control) performance prior to, during, and after long-duration missions. Furthermore, research must be conducted in analog and/or extreme environments and space flight contexts to examine interpersonal and teamwork skills training so that these findings may be extended to space flight.

Training Team Skills to the Collective Team

Space flight evidence regarding the effectiveness of team training in promoting team performance consists largely of professional opinion and anecdotal stories advocating the importance of team building for astronauts and ground support (Category III and Category IV). Nicholas (1989) argues that some problems that are encountered by crews can only be settled by training the crew as a whole in interpersonal, emotional-support, and group-interaction skills (Category IV). The authors of a 1998 National Academy of Science report on behavioral issues advise that crews and ground support personnel be trained together on interactive techniques prior to flight (National Research Council, 1998) (Category IV). Over the last 3 years, several space shuttle crews have specifically opted to complete ISS Expedition interpersonal training as a team to enhance their "cohesion and performance" (in personal communication, Shultz, 2007) (Category III).

Ground-based research supports the idea that employees who are interacting in stressful environments, with high workloads, or in environments that require coordination at a distance (similar to the manner in which ground support and flight crews operate together) need team training (Harrison et al., 2003; Ilgen et al., 2005) (Category III). In a study of 27 manufacturing teams (263 individuals) who had worked together for an average of 1.9 years, Austin (2003) found that team performance depended on how well individual team members could describe what knowledge resources the team possessed, and how those knowledge resources could be applied to new situations.

This finding supports the notion that giving team members an opportunity to learn about each other's task-related knowledge and skills supports team performance. Research indicates that more experience working together bolsters the performance of a team in a variety of ways, and that team training is one means of ensuring that team members gain some experience working together (Paris et al., 2000). For example, in a study of submarine attack crews, Espevik et al. (2006) found that knowledge concerning team members adds to the number of hits on target, over and above the contribution from operational skills (Category II).

In addition, Espevik et al. (2006) found that the more experience crews had working together, the less physiological arousal the crew experienced during attack simulations. In a study comparing 83 work dyads, Edwards et al. (2006) found that more time spent working and training with their team members made junior and minority team members more likely to contribute to the team, and that teams in which individuals contributed more information performed better than teams in which one individual provided larger portions of information (Category III).

More conflicts are generally associated with more stress, increases in errors, and decreases in productivity (Alper et al., 2000). In a review of 55 studies, Rasmussen and Jeppesen (2006) noted that every study found that the more time team members spent training together, the fewer conflicts and conflict-related performance deficiencies the team members experienced (Category III). This seems highly relevant when considering that current plans for astronaut teams include reducing the time that is spent training together. Reductions in team training will likely increase conflict and related performance decrements as the teams will be less able to create interpersonal ties and share mental models. Indeed, in a review of applied findings from the team performance training that took place in military settings, Cannon-Bowers and Salas (1998a) conclude that it is important for teams to practice complex or off-nominal situations together (Category III). Also, in a review of simulation-based training practices, Salas et al. (2007b) observe that more benefits can be accrued from team performance if teams are encouraged to practice complex and emergency simulations together than if team members are trained in simulations in random groups.

A meta-analysis of 37 work teams found that teams that have densely configured interpersonal ties are more committed to staying together and attain more performance goals (Balkundi and Harrison, 2006). The authors note that team training is one mechanism whereby team familiarity and the density of interpersonal ties can be increased; however, it is important to note that non-work-oriented team training may not be sufficient or worthwhile by itself. Studies with geographically distributed teams that compare task-based team training with more socially oriented time together indicate that team members who are familiar with one another socially, but have little to no experience working together as a team, do not realize the same performance benefits as teams that consists of members who are experienced in working together (Espinosa et al., 2007; Kirkman et al., 2006) (Category II).

In so far as team training requires that team members complete a task or objective as a team, it encourages better team performance (see Table 2-3 for a summary of the evidence that is cited). Interpersonal skills training that is intended to improve team member interactions and other teamwork skills training also encourages better individual and team performance. Although analog and space flight studies are not numerous, the other evidence, as reviewed above, indicates that training may be designed to promote flight crew and ground support team health and optimal performance. However, research is necessary to determine the most appropriate designs for preparing for, enduring, and recovering from long-duration missions. We thus suggest that team training is an essential component of achieving optimal performance, and recommend that steps be taken to examine team training, both at the individual and the group level, within the space flight context.

Cohesion

Festinger (1950) originally defined group cohesiveness as the strength of members' motivations to stay in the group and cited three primary characteristics: interpersonal attraction, task commitment, and group pride. As research accumulated, many attempts have since been made to operationalize and measure cohesion. Studies to determine the strength or willingness of individuals to stick together and act as a unit have most consistently assessed the level of conflict, degree of interpersonal tensions, facility and quality of communications, collective perceptions of team health and performance of the group, and the extent to which team members share perceptions or understandings concerning their operational contexts.

As researchers at the U.S. Army Research Institute (ARI) note in their recent review of cohesion as a construct, the definition of cohesion is ambiguous; therefore, the means of measuring cohesion is complex. The ARI authors conclude that "cohesion can best be conceptualized as a multidimensional construct consisting of numerous factors representing interpersonal and task dynamics" (note that this is the definition of cohesion that will be referred to in this report) (Grice and Katz, 2005). Despite the inexact, less-than-rigorous understanding of cohesion as a construct, the ARI researchers do note that anyone who has worked with or played on a team knows what a cohesive team looks like, and most believe that teams that are more cohesive usually perform better than less-cohesive teams.

Research also provides some understanding of what a cohesive team may look like. Members of cohesive teams sit closer together, focus more attention on one another, show signs of mutual affection, and display coordinated patterns of behavior. Members of cohesive teams who have established a close relationship are more likely to give due credit to their partners. In contrast, those who do not have a close relationship within a team are more likely to take credit for successes and blame others for failure (Thompson, 1967). It is also important to note that team cohesion is distinct from individual morale. Although an individual's low morale may influence team cohesion (and possibly vice versa), it is possible for a team to remain cohesive with low-morale members.

Table 2-3. ***Summary of Findings Presented for Team Skills Training***

Source	Predictor	Outcome	Context	Evidence Type
Guzzo et al., 1985	Training	Increasing motivation and individual performance	Ground-based	Category II
Guzzo et al., 1985	Goal-setting	Increasing motivation and individual performance	Ground-based	Category II
Arthur et al., 2003	Cognitive skills training	Improved job performance	Ground-based	Category II
Arthur et al., 2003	Interpersonal skills training	Improved job performance	Ground-based	Category II
Bradley et al., 2003	Interpersonal skills training (includes goal setting, group problem solving, team coordination, etc.)	Good supervisor ratings of team performance	Ground-based	Category II
Baker et al., 2006	Teamwork skills training	Improved surgical team performance and reduced errors	Ground-based	Category II
Powell and Hill, 2006	Teamwork and psychosocial skills training	Reductions in adverse patient outcomes, errors, etc.	Ground-based	Category III
Burke et al., 2006	Teamwork skills training	More adaptive teams	Ground-based	Category III
Marks et al., 2000	Communication and interaction skills training	Improved team performance	Lab study	Category I
Smith-Jentsch et al., 1996	Team skills training	Improved team performance	Lab study	Category I
Morgeson and DeRue, 2006	Knowledge about teamwork	Improved team performance	Ground-based	Category II
Espevik et al., 2006	Knowledge about team members	Improved team performance	Ground-based	Category II
Edwards et al., 2006	Time spent working and training as a team	Increased team contribution	Ground-based	Category III
Rasmussen and Jeppesen, 2006	Time spent training together as a team	Few conflicts and conflict-related performance deficiencies	Ground-based	Category III
Balkundi and Harrison, 2006	Teams with densely configured interpersonal ties	More committed to achieving performance goals	Ground-based	Category II
Espinosa et al., 2006	Teams with experience working together	Higher performance	Ground-based	Category II

Psychosocial experts within the space flight research community have articulated their concern that interpersonal conflicts and lack of cohesion will impede the abilities of crews to perform tasks accurately, efficiently, or in a coordinated manner during long-duration missions (Hackman, 1996; NASA, 1987; Vinograd, 1974) (Category IV). Indeed, although prescreening precludes individuals with personality or mood disorders from being selected, the likelihood that certain disorders may develop (i.e., poor psychosocial adaptation) due to poor cohesion and/or support is a concern that could ultimately decrease performance in space flight crews.

Space flight evidence regarding cohesion and performance is limited by a paucity of objective team performance data. However, case studies, interviews, and surveys that have been done within the space flight realm provide evidence that issues pertaining to cohesion exist and are perceived as threats to effective operations. For example, breakdowns in team coordination, resource and informational exchanges, and role conflicts (i.e., common

indicators of poor cohesion) were mentioned as contributors to both the *Challenger* and the *Columbia* space shuttle accidents (*Columbia* Accident Investigation Board Report, 2003; Launius, 2004) (Category IV). Likewise, interviews and surveys that were conducted with flight controllers reveal that mission teams are commonly concerned with team member coordination and communications, and that interpersonal conflicts and tensions exist (Caldwell, 2005; Parke et al., 2005) (Category III).

We must again turn to other sources of empirical evidence to inform us of this relationship because space flight research is lacking in this regard. The bulk of evidence (Category I, Category II, and Category III) that is surrounding cohesion and performance comes from non-space domains such as aviation, medicine, the military, and space analogs. Some reports have estimated that "crew error" in aviation contributes to 65% to 70% of all serious accidents (Lautman, 1987; Sumwalt and Watson, 2001) (Category III). Accident investigations and mishap reports note poor teamwork, communication, coordination, and tactical decision-making as significant causal factors in mishap samples (NTSB [National Transportation Safety Board], 1994) (Category III). Team breakdowns are repeatedly implicated in accidents (Merket and Bergondy, 2000; Nagel, 1988) (Category III). In medicine, research indicates that interpersonal conflicts, miscommunications, failures to communicate, and poor teamwork skills contribute significantly to the rate of medical errors (Baker et al., 2006; McKeon et al., 2006; Powell and Hill, 2006) (Category III).

Four meta-analyses (Category I) that were conducted across industries as well as types of performance teams (work, military, sport, educational, project, etc.) provide further ground-based evidence that cohesion is related to performance. The authors of the first of these meta-analyses (Evans and Dion, 1991) found a positive correlation between cohesion and individual performance, but their study did not include group performance criterion measures. Mullen and Copper (1994), in addressing these limitations in a subsequent meta-analysis, found that cohesion positively affects performance. They also found that this relationship was stronger in real (vs. ad hoc) teams, in small (vs. large) teams, and in field studies. Mullen and Copper (1994) noted that successful performance also promotes cohesion. Oliver et al. (2000) analyzed 40 years of military research, and noted positive relationships among cohesion and numerous performance outcomes, including individual and group performance, behavioral health, job satisfaction, readiness to perform, and absence of discipline problems. In the latest of the meta-analyses, Beal et al. (2003) re-analyzed the studies that were included in Mullen and Copper plus additional studies and found that, as the work required more collaboration, the cohesion-performance relationship became stronger and highly cohesive teams became more likely to perform better than less-cohesive teams. This conclusion coincides with Thompson's (1967) cumulated field study finding that cohesion facilitates team processes and team coordination among work teams in various industrial settings (Category III).

In a meta-analysis of 67 ground-based experimental studies, Gully et al. (2002) (Category I) note a significant positive relationship between performance and the generalized beliefs of team members concerning the capabilities of their team across different situations. While most of the research on team cohesion and performance deals with the positive aspects of team attitudes, several studies investigated level of conflict and negative attitudes concerning the team as indicators of cohesion. De Dreu and Weingart (2003) note an important distinction is between interpersonal conflict and task conflict; i.e., that defined, interpersonal conflicts are about relationship issues, whereas task conflicts are about how to handle tasks.

Interpersonal conflict is generally found to be destructive to cohesion and, in turn, team performance; whereas task conflict can improve task performance. Team members may correct each other's misperceptions, offer alternatives, and argue about how to solve a problem (Jehn and Mennix, 2001) (Category III). Interpersonal conflict is thus generally detrimental, as it appears to affect team cohesion. Some level of task-related conflict may be desirable, regardless of its affect on cohesion, because conflict can promote optimal performance. In

contrast, both aspects of cohesion (i.e., interpersonal and task-related) are generally found to influence performance positively. In a study that was conducted with Canadian military groups, path analysis showed that task-related cohesion was positively related to individual job satisfaction, interpersonal cohesion was negatively related to reports of psychological distress, and both types of cohesion were positively related to job performance (Ahronson and Cameron, 2007).

Research that was conducted within Antarctic space analogs also investigated conflict, cohesion, and performance. In one survey of Expeditionary crews conflict that was measured as inter-member hostility was related to the poor ratings of member effectiveness that were meted out by supervisors (Vallacher et al., 1974). In one Antarctic expedition, scientists reported that team members' perceptions of status contributed to conflicts and reduced perceptions of cohesion (Dutta Roy and Deb, 1999) (Category III). Wood et al. (2005) also collected data on human performance in Antarctica over a 10-year period, modeling individual and group effects on adaptation to life in this extreme environment using multilevel analyses (Category III). Positive team climate and cohesion helped to reduce interpersonal tensions, which, in turn, contributed to work satisfaction (Wood et al., 2005).

Cohesion studies that were conducted by the military and in the aviation industries have focused more on task cohesion and the role of shared mental models (SMMs). SMMs, which refer to implicit agreements in team member expectations concerning how things work and what behaviors will result in various conditions, are proposed to characterize cohesive work teams (Baker et al., 2006; Edwards et al., 2006; Hirschfeld et al., 2006). Studies that compare performance during simulated operations and training note that members of high-performing teams coordinate with one another frequently to establish, maintain, and adapt SMMs as the situation evolves (Edwards et al., 2006; Espevik et al., 2006; Wech, 2002) (Category II). Teams that have little to no training on developing or coordinating SMMs demonstrate more errors and are less productive as compared to teams that have received training on building SMMs (Edwards et al., 2006; Espevik et al., 2006; Hirschfeld et al., 2006) (Category II and Category III).

The authors of the studies that manipulate the stressors that flight simulation crews face have found that cohesive teams enhance their performance under stress by shifting from using more time-consuming, explicit coordination strategies to more streamlined, implicit coordination strategies to share mental models and information (Bowers et al., 2002; Driskell et al., 1999; Entin and Serfaty, 1999; Serfaty et al., 1998) (Category I and Category II). Effective teams share more task-critical information than less-effective teams, especially concerning the problem that is at hand, task goals, and team strategies (Bowers et al., 1998; Helmreich and Sexton, 2004; Orasanu and Fischer, 1992) (Category II and Category III). Moreover, members of effective teams tended to anticipate each other's needs and to volunteer information and assistance more frequently (Orasanu and Fischer, 1992; Serfaty et al., 1993) (Category III).

Leadership may also play a role in team cohesion. Although a vast amount of research exists concerning leadership characteristics and leadership and member interaction, as well as how leadership may relate to performance, many of the findings in this area of research are conflicting. Furthermore, many of the studies are conducted at the individual level, and the context in which much of this research has been conducted may not generalize to a space flight setting.

In general, leadership is defined as the ability to influence others toward achieving group goals (Avolio et al., 2003). Although studies have found evidence that supports a relationship between different types of leadership styles and individual performance and morale (Den Hartog et al., 2002; Howell and Avolio, 1993), research that examines leadership influence at the team level is more complex and findings are often mixed. However, the findings of one group of researchers who examined team leadership suggest that leaders who are within teams focus

on leadership in two primary domains: the task at hand (i.e., helping the team achieve a task-related goal), and the development of team members (the interpersonal aspect of team interaction) (Kozlowski et al., 1996). Their findings provide compelling evidence that leaders impact team cognition, motivation/affect, and team behavior within the team setting. This evidence makes the argument for the importance of team leadership research compelling. We therefore recommend further examination of team leadership in the context of a space flight or an analog setting to examine the effects of leadership behavior and team cohesion in relation to the effects on team performance.

In summary, space flight evidence indicates that cohesion is a relevant concern for long-duration missions (see Table 2-4 for a summary of the evidence presented). For example, the delays in communicating with ground team members that are inherent in long-duration flight are likely to impact two key factors of team cohesiveness: the quality of communication and the quality of leader support. However, we must turn to research outside of space flight to provide insight as to the connection between cohesion and performance.

Table 2-4. *Summary of Findings Presented for Cohesion*

Source	Predictor	Outcome	Context	Evidence Type
Thompson, 2002	Cohesive team	Give due credit to members of team	Ground-based	Category II
Hackman, 1996	Lack of cohesion	Poor performance	Ground-based	Category IV
Merket and Bergondy, 2000	Lack of cohesion (team breakdowns)	Increased accident frequency	Ground-based	Category III
Baker et al., 2006	Lack of cohesion (interpersonal conflict, miscommunication, etc.)	Increased medical error	Ground-based	Category III
Mullen and Cooper, 1994	High cohesion (stronger for real teams)	Increased performance	Ground-based	Category I
Oliver et al., 2000	High cohesion	High individual and group performance, behavioral health, and job satisfaction	Ground-based	Category I
Thompson, 2002	High cohesion	Increased team coordination	Ground-based	Category III
Ahronson and Cameron, 2007	High interpersonal cohesion	Decreased psychological distress	Ground-based	Category II
Edwards et al., 2006	SMMs	Increased productivity	Ground-based	Category II and Category III
Bowers et al., 2002; Driskell et al., 1999	Implicit coordination strategies	More effective teams (more cohesive)	Ground-based	Category I and Category II

A large body of ground-based evidence shows that cohesion influences levels of performance, but this evidence is primarily correlational rather than causal. Cohesive teams are more productive than are less cohesive teams, and this situation could be because (1) more productive teams become more cohesive, or (2) more cohesive teams become more productive. Teams preserve their cohesion when they succeed rather than when they fail. Therefore, applied scientists advise that it is important to promote three essential conditions for team performance: ability (i.e., knowledge and skills), motivation, and coordination strategy. Team members need to have sufficient levels of interpersonal and technical skills to perform their jobs at the same time at which they are attaining team objectives. Team members must also be motivated to use their knowledge and skills to achieve shared goals. Team context, which consists of organizational context, team design, and team culture, must create conditions

to avoid problems such as social loafing, free riding, or diffusion of responsibility. These kinds of problems undermine team performance and can have detrimental effects on team cohesion (Thompson, 2002).

From the evidence, it cannot be said that a lack of team cohesion is statistically likely to result in numerous performance errors or an observable failure, but it does seem likely that ignoring the relationship between cohesion and performance will result in suboptimal performance (Grice and Katz, 2005). Although we know that many factors contribute to how cohesion is built and encouraged within a team and that cohesion is positively related to better performance, research cannot effectively determine, in a reasonable amount of time, what minimum level of cohesion is required to avoid catastrophic failure. Instead of investing research and time in such an endeavor, funding would be better used to test and identify effective means of building cohesion and promoting optimal performance in a long-duration mission context. This kind of research would generate enough immediate intellectual and operational benefits to justify the investment of funding.

Psychosocial adaptation

Long-duration space flight is a unique environment with unique conditions. On one hand, research suggests that it may offer salutogenic conditions, a termed that was coined by Antonovsky (1987) to convey the idea that, under certain conditions, stress could actually be beneficial and health promoting (Palinkas, 2003) (Category III). Indeed, space flight offers the thrill of doing what few people have done before and the challenges of discovery; these conditions foster the personal growth of individuals (Suedfeld and Steel, 2002) (Category III). Yet stressful conditions are also inherent to long-duration missions. Working in space involves danger, isolation, and confinement; therefore, space is understood to be an extreme work environment. Survival in space requires the provision of constant shelter or the wearing of protective gear, and it is also subject to equipment malfunctions. Crew members must adapt to a certain level of danger or threat to survive. They must also adapt to certain levels of isolation as contact with others (i.e., outside of the immediate crew) may be very limited and inconsistent at times, and isolation from family and friends may create social rifts and isolation that persist post-flight. Finally, space flight crew members must adapt to being confined to a limited living and working space. Ground-based research involving similar conditions (e.g., submarines, offshore oil rigs, polar stations) has found that such conditions are generally detrimental to psychological health and social well-being over prolonged periods (Braun and Sells, 1962; Britt and Bliese, 2003; Krueger, 2001; NASA, 1987). The exact mechanics are not well understood, but ground-based evidence suggests that social isolation is detrimental to individual health. Epidemiologists have noted higher mortality rates among socially isolated patients (House, 2001) (Category III), and physicians have described more issues with depression and somatic illnesses in conjunction with longer periods of relative social isolation among Antarctic expeditioners (Lugg, 1977; Lugg, 2005) (Category III).

Finally, long-duration missions may require crews and ground operations to operate more or less autonomously over the course of a mission as the degree of crew isolation oscillates in accordance with the distance that the spacecraft travels from the Earth. Crews are likely to have some periods of great control as well as some periods of very little control over what tasks are done, how the tasks are done, and when they are done. Ground operations are likely to necessitate total control at certain points in the mission, and have no opportunity to exercise any control during other parts of the mission. Shifts in operational autonomy are expected to impact psychosocial adaptation to space flight demands (Kanas and Manzey, 2008).

Researchers often conceptualize autonomy in relation to the job controls and demands that are found within a work environment (Theorell and Karasek, 1996). Ground-based evidence suggests that when job demands or personal risks are high and individual perceptions of control are low, health and performance suffer (MacDonald et al., 2001) (Category II). Furthermore, ground-based evidence suggests that under high-demand and low-control conditions, clarity in team member roles reduces the likelihood of individual strain and helps to ensure team co-

ordination and performance (Bliese and Castro, 2000; Schaubroeck and Fink, 1998). Other contextual factors also play an influential role. Specifically, ground-based research has demonstrated that high social support and strong communication among team members may decrease the impact of individual strain, thereby once again buffering any negative effects on team effectiveness and performance (Guzzo and Dickson, 1996; Theorell and Karasek, 1996).

Given all of the conditions and factors just described, the definitive point for research is that psychosocial adaptation is a multilevel construct that includes team and individual adaptation to the psychological and social demands that are inherent in an extreme environment and in teamwork. It is therefore important to understand how these factors (i.e., isolation, physical space, individual and group autonomy, etc.) influence psychosocial adaptation among crew members, as these factors ultimately will impact crew performance (Langfred, 2000).

Suedfeld and Steele (2000) conclude that the objective characteristics of an extreme environment are less important than are the subjective perceptions of the environment in regards to performance. In general, individuals who believe that they are well adjusted perceive fewer physical pains and less mental anguish, and, in turn, learn more and are more productive than individuals who believe that they are not well adjusted (Joshi et al., 1998; LePine et al., 2004; Mocellin, 1995; Staal, 2004; Williams et al., 1996) (Category III). Likewise, individuals who have formed interpersonal networks at work have more access to critical information and resources, and, in turn, are able to accomplish more than less socially adapted individuals who have smaller interpersonal networks (Balkundi and Harrison, 2006; Burke et al., 2006; Johnson et al., 2003; Schaninger, 2002). The process of psychological and social adjustment to environmental conditions and demands is known as psychosocial adaptation. It is important to note, however, that the relationships among psychosocial adaptation, health, learning, productivity, and performance are somewhat reciprocal at both the individual and the team levels (e.g., good health improves psychosocial adaptation and learning, satisfaction with learning and team performance improves psychosocial adaptation, etc.) (Burke et al., 2006; Buunk et al., 1993; House et al., 2003; Israel et al., 1989; Kramer, 1993; Vogt et al., 2008) (Category II and Category III).

The successful completion of technical objectives is not enough to consider an overall long-duration mission successful. The crew must also return home safely with psychological health intact; we are thus concerned with helping individuals and teams adapt quickly and effectively to long-duration space flight. Observations indicate that (1) individual factors help predict who is more likely to adapt effectively to the psychosocial requirements of long-duration missions (Gunderson and Nelson, 1963a; Kanas and Manzey, 2003; Lugg, 1977) (Category III), and (2) contextual factors help to predict how well individuals and teams may be able to adapt and recover under various conditions (Boyd, 2001; Lugg, 1977; Palinkas, 2003; Palinkas, 1991) (Category III). Focusing on these individual and contextual factors will help to identify ways in which to support pre-, in-, and post-flight performance and ensure mission success.

Predicting Individual Ability to Adapt

A significant challenge of collecting data in flight is that the data are collected from a small or limited number of subjects, and many measures of psychosocial adaptation require a comparatively large amount of a subject's time (e.g., extensive questionnaires on a repeated basis, repeated collection and storage of physiological stress data, etc.). The bulk of evidence that is available regarding adaptation to long-duration missions thus comes from space analogs, mainly from Antarctic expeditions. Findings from these Antarctic studies note that adapting is an individual process. Not all individuals successfully adapt to the psychosocial conditions of an isolated, a confined, and an extreme environment such as that in Antarctica; for these individuals, performance and health usually suffer. In an early correlational study comparing expeditionary groups, Gunderson and Nelson (1963b) found that a group rated as less effective also reported being more

bored, less compatible, less motivated, and less socially balanced than did a higher-performing group (Category III). To the extent that these perceptions can be viewed as indicators of adaptation, a better-adapted group appears to be a more effective group.

Regarding individual performance, Palinkas (1987) found no significant differences between group members who wintered-over and members of a control group in terms of long-term performance (Category II). Although wintering over (vs. completing a long-duration expedition without winter) does not appear to have a lasting effect on performance, poor individual adaptation to work requirements in Antarctica was associated with an exaggeration of perceived injustices (Lugg, 1974) (Category III), and a failure to perform well appears to affect continued adaptation. As one low performer became a social isolate as the result of his poor performance (Lugg, 1974), this suggests that the adaptation-performance relationship is reciprocal for at least some individuals (Category III).

Crocq et al. (1974) found that age was not correlated with adaptation among Antarctic expeditioners; however, some anecdotal evidence suggests that the youngest personnel sometimes have more difficulty adapting than the older personnel. Previous medical history and cognitive ability also predict adaptation among Antarctic expeditioners (Lugg, 1974). Crocq et al. (1974) also found that high cognitive ability has a positive relationship with adjustment. Low cognitive ability, however, does not necessarily indicate a correspondingly poor ability to adapt. The various personality characteristics of individual Antarctic station members and attitudes that they hold were found to predict adaptation. Individuals who were low in extroversion and assertiveness adapt better to life in Antarctica (Rosnet et al., 2000). As noted previously, however, ground-based evidence indicates that teams with more moderately extroverted members generally perform better (Allen and West, 2005; Barry and Stewart, 1997). Research must still determine how to balance individual extroversion at levels that are encouraging to both psychosocial adaptation and team performance. In fact, many characteristics influence adaptation, and several are likely to call for balancing within teams that are performing in extreme environments. As Gunderson (1966b) noted: “achievement needs, needs for activity, needs for social relationships and affection, aesthetic needs, needs for dominance or leadership, a sense of usefulness in one’s job, and control of aggressive impulses to be particularly important for adjustment in small Antarctic groups (those groups with less than 5 persons)” (p. 4).

Generalizing the results that were found in Antarctica to those from space flight require caution. Firstly, any generalizations of Antarctic findings to space require the differences between the two environments to be taken into account. Group size, for example, is larger in Antarctica than it is on space flights. Given that group size has been seen to affect aspects of life in Antarctica, the degree to which Antarctic findings involving groups can be generalized to space might be limited. Secondly, any conclusions that are made regarding factors affecting performance in Antarctica are based on relatively few articles.

Ground-studies that were conducted in traditional work environments regarding psychosocial adaptation and performance offer a broader base of evidence and some insight into the general principles of psychosocial adaptation to work; however, the utility of these findings are limited by the critical fact that most employees, unlike long-duration mission participants, do not live exactly where they work. Ground-based studies support the conclusion that some individual factors predict an individual’s ability to adapt. Gender may even play a role; the Vogt et al. (2008) study of stress reactions and hardiness among U.S. Marine recruits reveals that social support significantly bolsters the hardiness of women recruits after stress, but not that of male recruits. Caldwell et al. (2005) found that a small group of pilots and a control group of non-pilots who exhibited more cortical activity were less vulnerable to cognitive performance decrements and emotional distress related to 36-hour sleep decrements. Additionally, LePine et al. (2004) found that selecting adult learners who had a

positive attitude toward a complex training program reduced resulting reports of fatigue and exhaustion (Category II). Independent of any particular stressor or stressful environments, Greenberg et al. (1992) observed that individuals who have more self-esteem generally experience less anxiety under the same or similar conditions as individuals who have less self-esteem (Category II).

The existing evidence provides a starting point, but more focused research is needed to address the gaps in our knowledge. Achieving a better understanding of the individual factors influencing an individual's ability to adapt to long-duration space missions would generate at least two operational benefits: (1) individual factors that predict adaptability could be used to aid selection or assignment decisions, and (2) these individual factors could be used to customize psychosocial support and resources to fit individual and team needs pre-flight, in-flight, and post-flight for long-duration missions.

Contextual Factors Influencing Adaptation

Factors outside of the individual (e.g., duration of stressful conditions, coping resources available) can also help to predict individual adaptation. For example, a slow voyage to Antarctica and living and working in a larger station once in Antarctica predicts adjustment (Lugg, 1974) (Category III). Composition of the group and job skills of group members also predict adapting to the new environment (Lugg, 1974). Contextual factors influence adaptation by contributing to an individual's stress perceptions.

Stress is the disruption of homeostasis through physical or psychological stimuli that are known as stresssors. According to the *Merriam-Webster Dictionary*® (2007), stress is defined as "a physical, chemical, or emotional factor that causes bodily or mental tension and may be a factor in disease causation." Some stress is unavoidable, such as the stress of competition during a game, and some stress is good, as the inverted-U of the performance-anxiety relationship demonstrates (Abramis, 1994). However, some stressors are so acute that even small amounts cause serious performance decrements (Abramis, 1994) (Category II), and chronic (long-term) stress or many acute stressors lead to strain or burnout (Barnett et al., 2007; Freedy and Hobfoll, 1994; Hobfoll et al., 2001; van Gelderen et al., 2007) (Category II and Category III). Adler and Dolan (2006), for example, found that longer peacekeeping mission deployments for 3,339 military personnel were associated with increased reports of depression and post-traumatic stress syndrome (Category III). This indicates that there may be a limit to how long an individual can adapt to a particular environment or related stressors. From a space flight perspective, the Russian space station *Mir* operations indicate that astronauts and cosmonauts are capable of adapting to 6 months in orbit, but reports also indicate that many *Mir* participants who took part in longer-duration flights (in excess of 6 months) developed symptoms of fatigue, irritability, and minor disorders of attention and memory (Boyd, 2001; Kanas et al., 2001) (Category III).

There are individual differences in perceptions of and adaptations to particular stressors, and many different potential stressors are inherent in a long-duration mission. Two typical stressors (isolation and confinement) have already been discussed. More research is needed, however, particularly research involving ISS astronauts, to determine what stressors are most salient to crews and ground support during long-duration missions and how these stressors persistently affect team members post-flight. Research is also needed to determine what coping mechanisms and contextual factors best support psychosocial adaptation within the operational constraints of long-duration missions and when (i.e., pre-flight, in-flight, post-flight) they are likely to be most effective.

It is known, from extensive ground-based evidence, that social support improves adaptation to, resilience to, and recovery from various stressors in traditional and military work environments; and that the more social support provided before, during, and after work from more sources (e.g., family, friends, supervisors),

the better individuals cope in general (Anderson, 2003; Riggio et al., 1993; Seers et al., 1983) (Category II). Social support has traditionally been operationalized as any assistance that individuals receive from others through interpersonal interactions, including information, emotional care, or instrumental resources (Buunk et al., 1993b; Riggio et al. 1993). Individuals who receive less social support are more likely to commit suicide, have accidents, incur injuries, or develop illnesses over their life span than individuals who have more social support available to them (Buunk et al., 1993a; House et al., 2003; Israel et al., 1989; LaRocco et al., 1980; Nowack, 1991) (Category II and Category III). Ground-based research also indicates that social support plays a positive role in team functioning and performance, individual achievement, and employee safety (Bhanthumnavin, 2003; Buunk et al., 1993a; Buunk et al., 1993b; Heaney et al., 1995; Hearns and Deeny, 2007; Nowack, 1991; Schaubroeck and Fink, 1998; Seers et al., 1983; Settoon and Mossholder, 2002) (Category II, Category III, and Category IV). There is thus ample reason to consider social support as an important contextual factor promoting psychosocial adaptation for long-duration missions. Communication lags on longer-duration missions may stress the social support system more than previous experiences in space would lead us to expect. Flight operations would benefit from pre-identifying practical ways in which to provide and sustain social support systems in a long-duration mission context.

Based on the literature, long-duration missions in extreme environments (Antarctica or space) require mission participants to adapt or cope with several inherent emotional stressors (e.g., isolation from family and friends, limited communication opportunities, limited stimulation, shifting work demands and control, etc.) (Kanas and Manzey, 2003; Mocellin and Suedfeld, 1991; Natani and Shurley, 1947; Nelson, 1962; Palinkas, 1991; Vinograd, 1974) (Category III and Category IV). The evidence indicates that (1) optimal performance depends on coping with these stressors, (2) there is considerable individual variance in how, and how well, people cope, and (3) many contextual factors influence how well individuals and teams are able to cope and adapt (see Table 2-5 for a summary of these findings). On the other hand, there is not much evidence on how contextual factors influence an individual's ability to recover from work in similar environments. The critical point for long-duration space flight is to determine the viability and utility of these factors for supporting the psychosocial adaptation to training, flight, and recovery of a crew – by doing so, research will identify ways in which to reduce the negative health impacts that are related to perceived stress and help to optimize performance on long-duration missions.

Risk in Context of Exploration Mission Operational Scenarios

Given that we know selection/composition, training, cohesion, and psychosocial adaptation influence performance, many operationally relevant questions remain for research to address. These include: What mix of crew members is likely to perform best? What kind of team skills training and team training will be most useful for teams that are living and working together on a long-duration mission? What kinds of resources and support will facilitate psychosocial adaptation to a long-duration environment when outside intervention and facilitation is severely limited by communication lags?

Table 2-5. ***Summary of Findings Presented for Psychosocial Adaptation***

Source	Predictor	Outcome	Context	Evidence Type
Braun and Sells, 1962; NASA, 1987	Confinement and isolation	Decreased psychological health and social well-being	Ground-based	Category III
House, 2001	Social isolation	Increased mortality rates	Ground-based	Category III
MacDonald et al., 2001	High job demands and low personal control	Decreased performance	Ground-based	Category II
Joshi et al., 1988; LePine et al., 2004	Adjustment	Performance	Ground-based	Category III
Crocq et al., 1974	High cognitive ability	Lower adjustment	Ground-based	Category III
Rosnet et al., 2000	Low in extro-version and assertiveness	Higher adjustment/ adaptability	Ground-based	Category III
LePine et al., 2004	Positive affect	Increased ability to adapt (less fatigue)	Ground-based	Category II
Greenberg et al., 1992	Self-esteem	Less anxiety	Ground-based	Category II
Lugg, 1974	Voyage duration	Ability to adapt	Ground-based	Category III
Lugg, 1974	Composition of group and job skills of group	Ability to adapt	Ground-based	Category III
Barnet et al., 2007; Hobfoll et al., 2007	Stress	Decreased performance	Ground-based	Category II and Category III
Anderson, 2004; Riggio et al., 1993	Social support	Reduces stress	Ground-based	Category II
Bhanthumnavin, 2003; Buunk et al., 1993; Heaney et al., 1995	Social Support	Team functioning, team performance, individual achievement, and employee safety	Ground-based	Category II, Category III, and Category IV

As previously detailed in this chapter, ground-based evidence demonstrates that long-duration team composition would be hampered by poor selection, ineffective team composition, inadequate training, and poor psychosocial adaptation. A possible qualitative likelihood scale for performance errors during certain mission operational scenarios is as follows:

- Level 1 – will most likely not occur
- Level 2 – could occur
- Level 3 – will most likely occur

Using this scale, the likelihood of performance errors for each type of mission is displayed in Table 2-6 below.

Table 2-6. *Risk of Context of Exploration Mission Operational Scenarios*

Levels of Risk	ISS Six-Person	Lunar Sortie	Lunar Long	Mars
Level 1				
Level 2	X	X		
Level 3			X	X

While crew members often engage in Expeditionary training activities (e.g., National Outdoor Leadership School [NOLS]) to promote team cohesion, there is no scientific evidence regarding what type and method of training offers the best means of promoting team performance for long-duration missions. As the number of crew members that are involved in long-duration missions increases (from three ISS crew members to potentially seven Mars mission crew members), the complexity of crew communications and the likelihood of inter-crew conflict increases exponentially. Anecdotal reports indicate that extensive training requirements and scheduling limitations make it difficult to set aside adequate time for crew members to train as a team. Increasing crew size and new operating systems (associated with the Constellation project) no doubt will create additional difficulties in training crew members as a team.

Poor cohesion, poor composition, inadequate training, and difficulties adapting will have more pronounced consequences during long-term lunar and Mars missions, where there will be fewer resources for mitigating the effect of these factors on performance. Prolonged or pronounced exposure to stressors, such as interpersonal conflict, may produce strain among crew members; and strain is associated with negative physiological and mental health consequences. These health risks may become compounded by the fact that lunar and Mars missions introduce additional restrictions and stressors compared to the mission experiences of astronauts to date.

Currently, the Spaceflight Human System Standards (Standard 5.2.3) states that training shall be provided on the psychosocial phenomena that will be experienced by crews and that additional training regarding crew integration and team dynamics may be included. The current standards are also found in the *Human Integration Design Handbook* (*HIDH*). However, these standards do not define such training or ensure that it will be available to crews prior to taking part in long-duration missions. Given the noted relationship between team composition, team training, cohesion, psychosocial adaptation, and performance, future space flight endeavors would benefit from specifying a "Fitness for Duty Standard" as well as "best practices" of psychosocial training and support for all crews prior to, during, and after flight.

Conclusion

BHP research provides the knowledge, tools, and technologies that support crew health to prevent or mitigate the risk of human performance errors due to poor cohesion and performance, selection/team composition, training, and psychosocial adaptation (Team Risk). These efforts are operationally driven, consistent with human health and performance standards as outlined in the *HIDH*, and aligned with major Constellation milestones. From this, BHP made a prioritized list of gaps and related activities and deliverables. Priorities were determined by considering the operational relevance of each deliverable as well as its role in risk reduction and the advancement of countermeasure development in light of crew needs during Exploration missions.

Veteran astronauts and ground control personnel have expressed the need for training requirements that will improve crew cohesion to reduce the likelihood of performance errors that are caused by inconsistent and suboptimal team dynamics. Some missions may have been jeopardized and, possibly, terminated as a result of interpersonal frictions in the past; therefore, the first priority of BHP insofar as team risk is concerned involves reducing the risk of team conflict and developing appropriate countermeasures. To this end, BHP is collaborating with the JSC Astronaut Office and flight surgeons to systematically collect information directly from the long-duration crew members. BHP is also evaluating conflict management and communication tools for use by crews during space flight, and will provide recommendations that are based on the outcome from these research tasks. BHP is also collaborating with the HBP International Working Group on an HBP competency model that will ensure adequate team training of astronauts by NASA and international space agencies. These efforts will address specific gaps including the following: What are the most likely and serious threats to team cohesion, performance, and crew-ground interaction? What are the most optimal ways in which to compose crews? What are the most optimal ways in which to train crews?

Long-duration missions to remote environments will increase astronaut exposure to extreme isolation and confinement, resulting in higher stress levels and an increased risk of crew morale deterioration. As the methods that are used to deal with crew stress could be critical to the success of the mission, the second priority of BHP insofar as Team Risk is concerned involves providing unobtrusive monitoring technologies for deteriorated crew cohesion, a situation that will ultimately decrease crew performance. The BHP gaps that address this issue are: What additional approaches and countermeasures exist to counter these threats? How can we monitor and measure these threats?

Evidence supports the important role of environmental context in influencing team performance. Research demonstrates that specific factors can influence both team cohesion and team performance; it is therefore important to examine and implement practices that will ensure optimal performance while considering these issues. Therefore, the third priority of BHP insofar as Team Risk is concerned addresses the examination of autonomy and communication. The BHP gaps that cover these issues are: How does increased autonomy impact crew cohesion, crew performance, and crew-ground interaction? What aspects of communication impact crew cohesion, crew performance, and crew-ground interaction?

In summation, the selection of crew members, team training and building, and the psychosocial adaptation of the crew to the mission environment present several opportunities to encourage optimal performance; but more research must be done, in the appropriate contexts, to inform mission designers of how to take advantage of these opportunities.

The BHP Element has identified gaps in knowledge and mitigation strategies that are related to these issues. To close these gaps, the BHP Element needs to pursue more rigorous, longitudinal research designs and a multi-method research program. Space flight history and data are required to identify the performance objectives that are most likely to be influenced by psychosocial team factors, to assess which factors are most salient on the job, to develop relevant measures of cohesion and psychosocial adaptation, and to determine the baselines of individual and team performance. Laboratory-based and space analog studies are needed to pilot countermeasures and monitoring technologies, and to help identify the safest and most efficient means of manipulating factors to optimize performance.

Finally, high-fidelity space analogs or current space flight studies are needed to test the utility of the tools and countermeasures that will be designed to promote optimal performance and support the psychosocial health of astronauts who are on long-duration missions. The funding and support of this research is justified by the poten-

tial benefits of knowing how to promote optimal performance. In essence, the surest way to reduce the risk of failure when we are unable to isolate and eliminate potential error sources is to achieve optimal performance.

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Glossary

Term	Definition
Cohesion	The strength or willingness of individuals to stick together and act as a unit.
Composition	The arrangement or mix of individuals into a group, team, or crew.
Crew	A group of astronauts who are assigned to a mission.
Diffusion of Responsibility	Phenomenon in which, because of the size of a group, individual responsibility is not assigned explicitly. For example, because of the size of the group, individuals allow something to occur that they would not allow if they were alone.
Cut-score	Cut-scores are selected points on the score scale of a test. The points are used to determine whether a particular test score is sufficient for a specific purpose.
Free Riding	Phenomenon in which an individual who is a part of a group allows others in the group to share his or her responsibilities rather than assume those responsibilities as his or her own.
Group	A collection of individuals into one place at one period in time.
Interpersonal Interaction	A communication exchange (verbal and nonverbal) between two or more individuals.
Performance	The execution of an action.
Performance Error	An act that deviates from an established code or a standard of performance.
Performance Standard	Specific requirements concerning how an action should be executed.
Personality	A person's unique set of behavioral or cognitive patterns (usually described using "Big Five" broad factors: openness, conscientiousness, extroversion, agreeableness, and neuroticism).
Psychosocial Adaptation	An individual's social, mental, and emotional adjustment to the stressors that are inherent in a particular environment or state of existence; quality of life as determined by an individual's subjective perception of his/ her situation.
Selection	The choice of one individual for a particular purpose or role.
Shared Mental Model [SMM]	Shared beliefs among team members concerning how things work and what actions will result in various conditions; An organized set of expectations for performance and common understanding of the resources that are available among team members.
Social Loafing	Phenomenon in which individuals make less effort to achieve a goal when they work in a group than when they work alone.
Strain	A state of injury that is induced by prolonged or pronounced exposure to tension or stress.
Stress	Tension resulting from factors that alter a current or expected state of equilibrium.
Stressor	A stimulus that causes stress.
Team	A collection of individuals who are working cooperatively toward a common goal or common set of goals; the collection of individuals who are assigned to support and achieve a particular mission.

Term	Definition
Team Skills Training	Educating or teaching an individual concerning the skills and knowledge that are associated with effective team performance.
Team Training	Educating or teaching skills to a team as a whole, rather than educating individual team members separately.
Training	The act of educating or teaching skills or knowledge; The skills, knowledge, or experience that is obtained through instruction or education.

Chapter 3:
Risk of Performance Errors due to Sleep Loss, Circadian Desynchronization, Fatigue, and Work Overload

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Fatigue occurs during spaceflight and will jeopardize health and performance. This risk may be influenced by artificial and transmitted light exposure, individual vulnerability to sleep loss and circadian dynamics, and work/sleep schedules. Efforts are needed to improve sleep hygiene, and to identify and improve conditions that interfere with sleep quality. Research areas may include: development of a self-assessment tool for cognitive function and fatigue, light therapy for phase shifting, alertness and mood disorders, and other means to improve sleep quality and reduce fatigue. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

Sleep accommodations on short-duration space shuttle flights were Spartan (as shown here), but sleep stations on board the International Space Station strive to provide a stable, comfortable, dark, and quiet environment to encourage the quality and quantity of sleep essential to optimize crew performance and health.

Executive Summary

Data that have been collected during space flight missions consistently indicate that sleep loss, circadian desynchronization, fatigue, and work overload occur, to varying degrees, for some individuals. Few studies of performance have been conducted in flight, however, and the findings that have been generated remain unclear as to how a crew member's performance during space flight is directly impacted by sleep loss. Extensive ground-based scientific literature, including controlled laboratory studies and data that have been gathered from industries, demonstrates that the degree of sleep and circadian disturbances that are often experienced by astronauts result in performance errors and may also impact long-term health.

Space flight evidence regarding sleep loss primarily includes data that were collected through controlled studies (Category II[15]) as well as through self-report (Category III). These evaluations, which have focused on short-duration (fewer than 30-day) missions, have provided data from astronauts' daily sleep logs, polysomnography, and actigraphy. These data have characterized sleep in space, overall, as shorter, less restful, and more interrupted than sleep on Earth. Circadian rhythms may also be misaligned due to scheduling constraints, with the result that fatigue (physical and mental) from work overload has been reported (Scheuring et al., 2007).

Questions, however, remain regarding the nature of sleep and circadian rhythms on long-duration space flight missions. Despite the fact that ISS construction has been under way for 9 years, systematic data collection to address this issue has only been undertaken recently. In light of ground-based evidence on sleep-loss-related performance effects, it is critical to understand the various factors that exist in the space flight and long-duration mission environment, and to identify ways in which sleep and circadian rhythms can be protected for crews who are flying on ISS and shuttle missions. NASA ground support personnel, as well as space flight crews, experience sleep loss, fatigue, circadian misalignment, and work overload. Ground teams that support robotic missions to Mars, as evidenced during the Mars Pathfinder, Spirit, Opportunity, and Phoenix missions, similarly face issues of sleep loss and circadian desynchronization.

As human space flight transitions from LEO (e.g., shuttle, ISS) to Exploration missions to the moon and Mars, and as NASA continues to support robotic missions to Mars and beyond, it becomes more important to characterize human risk factors accurately and adequately and to identify the ways in which to mitigate this performance risk safely and effectively. The first short-duration lunar missions, which will be similar to the shuttle missions, will seem to be fast-paced sprints as compared to the marathon-like races of later, longer lunar outpost missions (and ISS increments). Docking will require shifting of schedules for those in flight and for their support teams on the ground; the hurried schedule will likely include heavy workloads. Longer lunar missions will pose additional challenges to crews, including perpetual non-terrestrial day-night cues, environmental constraints, and extended periods of high-intensity workload. As the evidence reveals, crews on short- and long-duration lunar missions will need to be well-equipped and prepared for the potential performance and long-term health effects of sleep loss and circadian shifting.

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[15]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

Introduction

Sleep disorders plague a staggering number of individuals. The authors of the 2007 Institute of Medicine (IOM) report *Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem* state that as many as "60 to 70 million individuals chronically suffer from a disorder of sleep and wakefulness, hindering daily functioning and adversely affecting health and longevity… a wide range of deleterious long-term health consequences are associated with chronic, or cumulative, sleep loss. These consequences include: hypertension, diabetes, obesity, heart attack, stroke, and psychiatric disorders such as depression or severe anxiety."

In addition to the negative health outcomes that are cited above, another risk that can result from sleep loss is an increase in performance errors. Evidence shows that 24 hours without sleep, or less severe but more chronic sleep loss, can lead to daytime feelings of fatigue and increase performance errors on a variety of tasks that require attention, memory, cognitive and psychomotor speed, and executive functioning (Harrison and Horne, 1998; Durmer and Dinges, 2006; Banks and Dinges, 2007). Research indicates that astronauts, on average, sleep fewer than 6 hours per day (Dijk et al., 2001; Barger and Czeisler, 2008). Several authors of Earth-based sleep-dose-response studies reveal that sleeping 6 hours or fewer per day results in cumulative cognitive performance deficits (Belenky et al., 2003; Van Dongen et al., 2003; Dinges et al., 2005; Mollicone et al., 2008). Moreover, there is a disconnect between subjective and objective measures of sleep loss under these conditions; e.g., individuals who are suffering from sleep deprivation or fatigue may not be able to accurately gauge their degree of impairment, and, therefore, will not take appropriate countermeasures to mitigate the impacts that can arise from these conditions.

Crews who are on orbit and the ground teams who support them face not only the likelihood of recurrent sleep loss but also the risk of circadian desynchronization. Circadian rhythms regulate subjective alertness, cognitive functions, and sleep propensity as well as core body temperature, hormone secretion (including melatonin), and the nocturnal secretion of growth hormone. A misalignment of circadian rhythms results in disturbed sleep and impaired performance and alertness (Ball and Evans, 2001, p.144; Van Dongen and Dinges, 2005). On Earth, shift workers often experience circadian misalignment, especially when they are working over night or rotating shifts; shift work schedules are associated with increased risk of accidents and injuries (Dinges, 1995; Czeisler et al., 2005; Barger et al., 2006). Recent evidence suggests that shift work, which includes exposure to light at night, suppresses the normal nocturnal production of melatonin by the pineal gland; this suppression over time may increase the risk of developing cancer among individuals who are working shifts (Blask et al., 2002; Glickman et al., 2002, Blask et al., 2005; Stevens et al., 2007).

Work overload also poses a risk to the behavioral health of space flight crews. NASA management currently sets limits, which are known as "Fitness for Duty Standards," for the planned number of hours in which astronauts are to complete tasks and events. The planned nominal number of work hours for space crews is 6.5 hours per day; it is recommended that crew members not exceed a 48-hour total work week. NASA researchers have found that maintaining nominal work hours and workload is especially important during critical operations. The NASA definition of a critical overload workload for a space flight crew is 10-hour work days that are undertaken for more than 3 days per week, or more than 60 hours per week (NASA STD-3001, Vol. 1). Not only is the duration of the workday important, but so, too, is the intensity of the workloads for space flight crews. Astronauts who have taken part in high-tempo missions, from the historic Apollo to the current space shuttle missions, have accomplished complex tasks in the most dangerous surroundings while enduring hours of intense concentration. Anecdotal reports from veteran astronauts (Scheuring et al., 2007) indicate that at times of high intensity, workload can result in mental and physical fatigue. Field studies from the medical and aviation industries show that increased and intense workloads, particularly in conjunction with disturbed sleep and fatigue, can lead to

significant health issues and performance errors, which, in turn, can cause increased incidents of injuries, accidents, or death (Barger et al., 2006; Goode, 2003).

In light of the negative health and performance consequences that are associated with sleep, fatigue, circadian, and workload issues, the duration and quality of sleep among astronauts and ground crews is of concern to the designers of current NASA operations and the NASA Constellation Program. The consequences of human system risks for Constellation missions include loss of mission objectives as well as increased health risk during the mission or post-flight. Research addressing sleep quality and the circadian system endeavors to minimize these risks.

The NASA HRP BHP Element (http://humanresearch.jsc.nasa.gov/about.asp) aims to further characterize the risk of performance errors due to sleep loss, fatigue, circadian desynchronization, and work overload in preparation for Exploration missions to the moon and Mars. Operationally relevant monitoring technologies that detect sleep quantity and quality, and individualized countermeasures that prevent or mitigate the risk in long-duration isolated environments, will equip crews for optimal behavioral health and performance. Focused laboratory and ground analog studies as well as space flight studies will provide valuable insights into developing these technologies and countermeasures.

The NASA HRP BHP Element is tasked with managing three risks. These are the risk of: (1) performance errors due to sleep loss, circadian desynchronization, fatigue, and work overload; (2) performance errors due to poor team cohesion and performance, inadequate selection/team composition, inadequate training, and poor psychosocial adaptation; and (3) behavioral and psychiatric conditions. As each of these risks is addressed in a separate evidence report chapter, they should not be construed to exist independently of one another but, rather, should be evaluated in conjunction with the other. Furthermore, the BHP risks overlap with the risks in other HRP Elements and, as such, must also be considered in conjunction with these other risks (see figure 3-1 for an example of these possible overlaps).

The relationships of BHP with the other Elements are further outlined in the HRP IRP, which can be found at http://humanresearch.jsc.nasa.gov/about.asp. The nature of the IRP implies that BHP is continually reviewing and updating integration points with other Elements. Current research efforts are under way through collaborative efforts with the Exploration Medical Capabilities (ExMC) Element, Human Health and Countermeasures (HHC) Element, as well as the SHFH Element. While current research is designed to address identified gaps, it will be necessary to update and revise each of the BHP Evidence Reports as the Element gaps are closed and new gaps emerge. Such information will also inform the human system risk mitigation and assessment strategy of the NASA JSC Space Life Sciences Directorate.

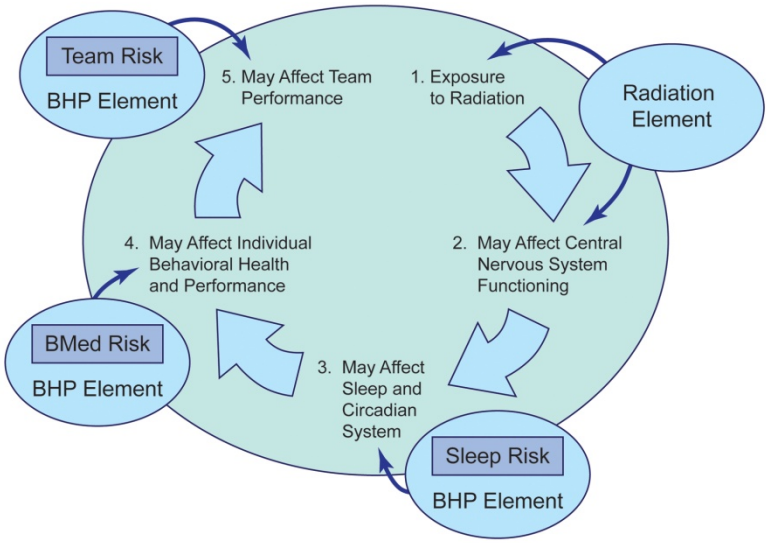

Figure 3-1. ***Sample integration within the BHP Element, and with other HRP Elements.***

Evidence

Ground-based evidence

Studies, which include laboratory investigations (Category I) and field evaluations (Category II and Category III) of population groups that are analogous to astronauts (e.g., medical and aviation personnel), provide compelling evidence that working long shifts for extended periods of time contributes to sleep deprivation and can cause performance decrements, health problems, and other detrimental consequences, including accidents, that affect both the worker and others.

Performance Errors Relative to Sleep Loss and Extended Wakefulness

A meta-analysis (Category I) that was conducted by Pilcher and Huffcutt (1996) examined data that were drawn from 19 research studies to characterize the effects of sleep deprivation on specific types of human performance. Motor skills, cognitive skills, and mood were assessed in terms of: partial sleep deprivation (also known as sleep restriction), which is defined as fewer than 5 hours of sleep in a 24-hour period for 1 or more days; short-term total sleep deprivation (no sleep attained for fewer than 45 hours); and long-term sleep deprivation (no sleep attained for a period in excess of 45 hours). These researchers found that sleep-deprived subjects performed considerably worse on motor tasks, cognitive tasks, and measures of mood than did non-sleep-deprived subjects. The greatest impact on cognitive performance was seen from multiple days of partial sleep deprivation, although short- and long-term sleep deprivation also showed an effect. Meta-analyses of sleep deprivation effects in medical residents found deficits in both laboratory tasks and clinical tasks (Philibert, 2005).

The magnitude of the chronic partial sleep loss that has been experienced by astronauts in flight (Barger and Czeisler, 2008; Monk et al., 1998; Dijk et al., 2001; Kelly et al., 2005; Gundel et al., 1997; Santy et al., 1988; Frost et al., 1976) has been reported to negatively impact cognitive performance in multiple Category I, Category II, and Category III laboratory and field studies (Dinges et al., 1997; Lockley et al., 2004; Landrigan et

al., 2004; Ayas et al., 2006; Barger et al., 2006). Performance can be affected whether sleep loss is in the form of a night of substantially reduced sleep, a night of total sleep deprivation, or a series of less drastic, but more chronic, restricted sleep hours. A 1997 study by Dinges et al. revealed that when sleep is restricted to the level that is commonly experienced by astronauts (i.e., 4 to 6 hours per day), a "sleep debt" accrues and, in less than 1 week, performance deficits during waking hours reach levels of serious impairment.

Chronic reduction of sleep can impact performance in a manner that is similar to that of total sleep deprivation. A study by Van Dongen et al. (2003), which used 48 subjects, evaluated the specific performance effects of chronic sleep restriction in comparison to the effects of 3 nights of total sleep deprivation. Sleep restriction conditions included 14 consecutive nights of 8, 6, or 4 hours of sleep opportunity, with actual sleep quantity validated by polysomnography recordings. Subjects who were subjected to sleep restriction conditions underwent neurobehavioral assessments every 2 hours during their scheduled wakefulness, while subjects who were subjected to the sleep deprivation condition were tested every 2 hours throughout their total 88 hours of sleep deprivation.

The neurobehavioral assessment battery that was used in the Van Dongen et al. (2003) study included the psychomotor vigilance task (PVT). The PVT – which determines alertness and the effects of fatigue on cognitive performance (as determined by lapses in response time and accuracy of responses) by measuring the speed with which subjects respond to a visual or an auditory stimulus (by pressing a response button) – has become a standard laboratory tool for the assessment of sustained performance in a variety of experimental conditions (Dorrian et al., 2005). The PVT detects changes in basic neurobehavioral performance that involve vigilant attention, response speed, and impulsivity; and it has been extensively validated in ground-based laboratory studies to detect cognitive deficits that are caused by a variety of factors (e.g., restricted sleep, sleep/wake shifts, motion sickness, residual sedation from sleep medications) (Dinges and Powell (1985), Van Dongen et al. (2003), Drummond et al. (2005)). The PVT is an optimal tool for repeated use, in contrast to some other cognitive measures, as studies have shown no minimal learning effects and aptitude differences when using the PVT (Van Dongen et al., 2003; Balkin et al., 2004; Dorian et al., 2003).

Results from these laboratory studies indicate that multiple consecutive sleep episodes of 4 or 6 hours significantly erode performance on the PVT and on measures of working memory, and that performance under these two conditions (i.e., 4 or 6 hours) was comparable to the performance that is found under conditions of 1 to 2 days of total sleep deprivation. Surprisingly, by the end of the 14 days of sleep restriction, subjects in the 4- and 6-hour sleep period conditions reported feeling only slightly sleepy. As these reports were taken when performance was at its lowest level, this indicates that the subjects may no longer have been aware of their performance deficits because of inadequate recovery sleep (Van Dongen et al., 2003) (figure 3-2).

Subjects who spent 4 hours in bed reached levels of impairment at 6 days and of severe impairment at 11 days. Subjects who spent 6 hours in bed reached levels of impairment at 7 days. Interestingly, it appears that subjects who spent 8 hours in bed approached levels of impairment. Figure 3-3, which is from Belenky et al. (2003), however, demonstrates that subjects who spent 9 hours in bed did not approach these levels of impairment, indicating that 9 hours in bed may be needed to alleviate the risk of performance errors.

Similar performance effects resulting from chronically restricted sleep can also be seen in the Category I study by Belenky et al. (2003) and in figure 3-3. This study involved 66 subjects who were observed in four conditions (i.e., 3, 5, 7, and 9 hours in bed) for 7 days. PVT testing showed severe impairments in reaction time under the 3-hour condition, with lapses in responses increasing steadily across the 7 days of sleep re-

striction. Subjects who spent 3 hours in bed reached levels of *severe* impairment at 5 days, while subjects who spent 5 hours in bed reached levels of impairment at 4 days.

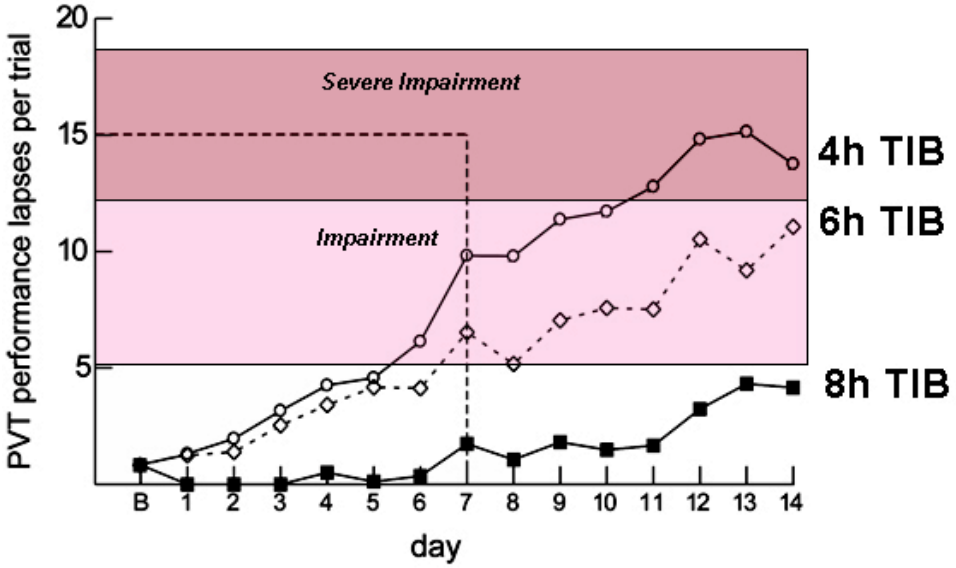

Figure 3-2. ***Performance lapses for time in bed (TIB) over 14 days of sleep restriction (Van Dongen et al., 2003).***

These Category I laboratory studies by Van Dongen et al. (2003) and Belenky et al. (2003) clearly show that subjects suffered performance impairments resulting from total sleep deprivation and/or chronic sleep restriction.

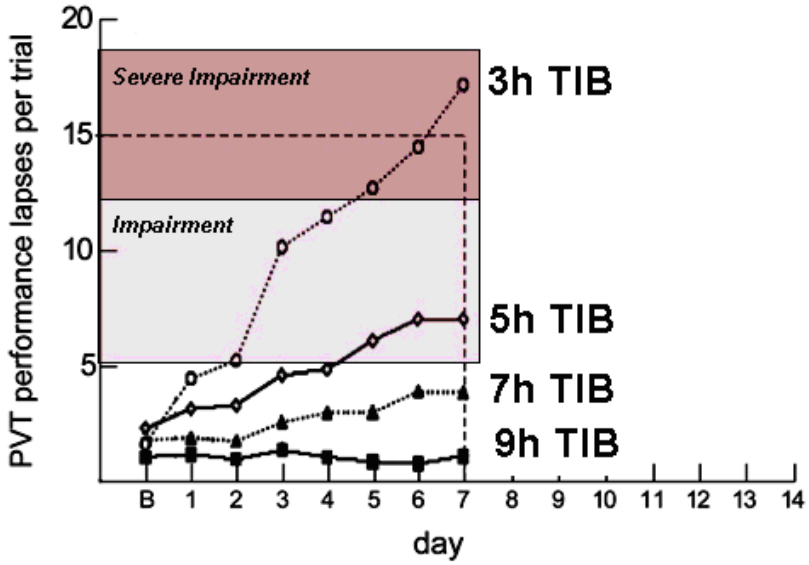

Figure 3-3. ***PVT performance lapses for TIB over 7 days sleep restriction (Belenky et al, 2002).***

Cognitive impairments are present even after an individual has been awake for approximately 17 hours; in fact, recent studies have shown that these decrements are similar to those that result from an elevated blood alcohol level. A compelling Category I laboratory study from Williamson and Feyer (2000) used a cross-over randomized control design to observe cognitive and motor performance after minor sleep deprivation to performance after alcohol consumption. All subjects participated in both alcohol consumption and sleep deprivation, and the order of testing was counterbalanced so that half of the subjects participated in the alcohol consumption part first while the other half participated in the sleep deprivation part first. To avoid carry-over effects from one condition to the next, subjects were provided with a night of rest in a motel between each condition.

Results indicate that, on average, performance with a blood alcohol level of 0.05% remained equivalent to performance after being awake for 16.9 to 18.6 hours. Performance with a blood alcohol level of 0.1% was equivalent to performance after being awake for 17.7 to 19.7 hours, or to restricted sleep of 4 to 5 hours per night for 1 week (Czeisler, 2006). Similar studies that compare performance after a time of sleep deprivation to performance with elevated blood alcohol levels have confirmed these results (Dawson and Reid, 1997; Arnedt et al., 2001). These findings are compelling as the duration of wakefulness (17 hours), which results in decrements that are similar to those that are induced by a 0.05% blood alcohol level, is considered by many to be within the range of a "normal" waking "day"; many individuals can recall an incident in which they had to waken early in the morning and work all day and into the night. Astronauts, who sleep an average of 6 hours per night (Santy et al., 1988; Gundel et al., 1997; Monk et al., 1998; Kelly et al., 2005), may be performing critical tasks 17 hours or more after wakening.

Performance Errors Relative to Sleep Desynchronization and Work Overload

Research suggests that circadian desynchronization and work overload may also impair performance. Specifically, a controlled laboratory study by Wright et al. (2002) evaluated the relationship between circadian rhythms and performance by assessing body temperature, which is regulated by the circadian mechanisms of the body. Body temperature is at its highest near the circadian peak and lowest near the circadian minimum (this is when the body is driven to sleep). It has long been recognized that a positive relationship exists between daily rhythms of body temperature and neurobehavioral performance and alertness in humans (Wright et al., 2002).

The study protocol (Wright et al., 2002) forced circadian desynchronization for 12 consecutive 28-hour days; participants were allowed 9.3 hours of scheduled time in bed and 18.7 hours of scheduled wakefulness. Performance on validated measures was evaluated every 2 hours, beginning 2 hours after the scheduled wake time. The protocol, therefore, assessed performance when the body is normally driven to sleep (which is related to the point at which body temperature at its lowest) relative to performance during normal waking hours, and allowed for assessment of the effects of body temperature independent of (and associated with) sleep hours and time of day. During the circadian peak (when body temperature is high), performance and alertness are high; conversely, near the circadian phase of low body temperature, performance and alertness are low. These results have been replicated in other forced desynchrony and extended wakefulness laboratory protocols (Wyatt et al., 1999).

Results from these laboratory protocols can be extrapolated to field conditions. Studies in the medical industry, where highly educated and trained individuals (e.g., physicians) are subject to circadian shifting and extended work shifts in addition to sleep loss, further demonstrate serious performance errors with populations that are analogous to astronauts. In a two-session, within-subject, Category II experiment that was conducted by Arnedt et al. (2005), the performance of 34 medical interns was observed under four conditions:

after 4 weeks of a light rotation (averaging 44 hours of rotations/week); after 4 weeks of a heavy rotation (averaging 80 hours of rotations/week); after 4 weeks of a heavy rotation with a 0.05% blood alcohol level; and after 4 weeks of a light rotation with a 0.05% blood alcohol level.

Performance measures included the PVT and a simulated driving task. Findings of the Arnedt et al. (2005) experiment indicate that performance impairment after a heavy-call rotation is comparable to the impairment that is associated with a combined 0.04% to 0.05% blood alcohol level and a light-call rotation. Results of this experiment demonstrate that decrements that are created by extended work shifts are similar to the decrements that are created by elevated blood alcohol levels.

Work hours and sleep loss were shown to impact performance in a Category III evaluation by Rogers et al. (2004). A total of 393 registered nurses logged scheduled hours worked, actual hours worked, time of day worked, overtime, days off, and sleep/wake patterns. Questions concerning errors and near-errors were also included. Analysis showed that work duration, overtime, and number of hours worked per week significantly affected the number of errors. The likelihood of making an error increased with longer work hours, and was three times higher when the nurses worked shifts lasting 12.5 hours or more. Working overtime increased the odds of making at least one error, regardless of the originally scheduled length of the shift. Working more than 40 and more than 50 hours per week significantly increased the risk of making an error.

Similar findings were attained in a subsequent Category III evaluation of 2,737 medical interns (Barger et al., 2006). A Web-based survey was conducted across the U.S. in which interns completed 17,003 confidential monthly reports. These 60-item reports contained information concerning work hours, sleep, and activities during the month, number of days off, and the number of extended-duration work shifts (defined as at least 24 hours of continuous work). These interns were also asked to report whether they had made significant fatigue-related or non-fatigue-related medical errors. Other questions assessed how often they had nodded off or fallen asleep during patient care or educational activities.

Analysis revealed a significant relationship between the number of extended-duration work shifts and the reported rates of fatigue-related noteworthy medical errors. Specifically, the number of reported fatigue-related medical errors increased as the number of extended-duration shifts per month increased. At least one fatigue-related significant medical error was reported in 3.8% of months with no extended-duration work shifts; and at least one fatigue-related significant medical error was reported in 9.8% of months that had between one and four extended-duration work shifts and in 16% of months that had five or more extended-duration work shifts (Barger et al., 2006). Furthermore, the frequency of attentional failures was strongly associated with the frequency of extended-duration work shifts. Evidence from this study further corroborates the negative impact that extended-duration work shifts may have on performance, as well as increased accidents and injuries (Barger et al., 2006; Ayas et al., 2006).

Working extended hours or overnight shifts also poses the added difficulty of requiring performance from an individual at a time when the body is driven to sleep by the circadian system. Sleep, alertness, and cognitive functioning are determined by the interaction of two processes: the endogenous circadian pacemaker and the homeostatic drive for sleep (Czeisler et al., 2001). The endogenous circadian pacemaker generates the 24-hour circadian rhythm that regulates subjective alertness and sleep propensity as well as core body temperature, cognitive functions, and melatonin secretion, as described above (Czeisler, 2006). It is also highly sensitive to light, which is its primary synchronizer. Misalignment of the circadian rhythm results in disturbed sleep, impaired performance alertness, waking-hour melatonin secretion, and reduced levels of nocturnal secretion of growth

hormone (Ball and Evans, 2001). The outcome, therefore, can range from performance errors to long-term health decrements.

Individuals who work at night and attempt to sleep during the day suffer because the timing of their sleep/wake schedule remains out of phase with the timing of the environmental light. Night workers are particularly prone to vehicle accidents, and their decreased alertness, performance, and vigilance are likely to blame for a higher rate of industrial accidents and quality control errors on the job, injuries, and a general decline in work productivity rate (Czeisler et al., 2001). Recent information also suggests that as the body normally releases melatonin when it is dark, working under artificial light at night suppresses the release of melatonin, which may increase the risk of developing cancer (Blask et al., 2002; Glickman et al., 2002, Blask et al., 2005; Stevens et al., 2007).

In summation, ground-based evidence demonstrates that sleep loss, circadian desynchronization, and extended work shifts lead to increased performance errors and accidents. The extent to which these risk factors are also present in the space flight environment is therefore an important consideration.

Space flight evidence

Occurrence of Sleep Loss and Fatigue in Space Flight

Space flight research indicates that, overall, sleep quantity and quality in astronauts are markedly reduced in comparison to terrestrial sleep quantity. Seven Category II and Category III studies, which used polysomnographic measurements, actigraphy, or other measures, have consistently shown that astronauts sleep, on average, fewer than 6 hours per day (Table 3-1). This amount of sleep is between 1.5 to 2 hours fewer than the 8 hours that are recommended for astronauts per NASA-STD-3001, Vol. 1.

Table 3-1. ***Space Flight Sleep Studies Summary and Category of Evidence***

Source	Average Hours of Sleep	Missions	Subjects (N)	Measurement Tool	Category of Evidence
Barger and Czeisler, preliminary unpublished data	5.9	STS-104, -109, -111, -112, -113, -114, -115, -116, -118, -120, -121, -122, -123, -124	23 analyzed to date	Actigraphy	II
Dijk et al., 2001	6.5	STS-90, -95	5	Polysomnogram, actigraphy	II
Kelly et al., 2005	6.0	STS-89	4	Sleep logs	III
Monk et al., 1998	6.1	STS-78	4	Sleep physiology	II
Gundel et al., 1997	6.1	*Mir*	4	Sleep physiology	II
Santy et al., 1988	6.0	Space shuttle	58	Post-flight debriefing	III
Frost et al., 1976	5.8	Skylab	3	Physiology	II

A post-flight debriefing survey that was conducted in 1988 (Category III) found that 58 crew members from nine space shuttle missions (ranging in duration from 4 to 9 days) reported sleeping on average 6 hours per day while in space compared to 7.9 hours terrestrially (Santy et al., 1988). Sleep was most reduced during the

first and last days of a mission (total 5.6 and 5.7 hours, respectively). Many crew members reported fewer than 5 hours sleep on some nights, and some crew members slept 2 hours or less (Santy et al., 1988, p. 1096). While NASA flight surgeons recommend 8 hours of sleep per day in space, studies on 101 astronauts have found that, in space, they sleep an average of approximately 6 hours per day.

Note that, in the table, the categories of evidence are limited to Category II and Category III. This limitation is due to the nature of space flight, which requires that researchers evaluate a small number of subjects, rendering it practically impossible to truly replicate a Category I when astronauts are on orbit.

Actigraphy and self-reporting are currently measuring to what degree space flight results in disruption of sleep during both short-duration (shuttle) and long-duration (ISS) missions (Barger and Czeisler, 2008). This study will be the largest and most rigorous of its type. To date, 36 subjects on shuttle missions and six subjects on ISS missions have completed the protocol; a total of 20 subjects from ISS missions are planned to take part in the study, and shuttle data collection will continue until the ISS goal is achieved and/or the shuttle is retired. Data are collected at 90 days before launch for 2 weeks (to establish a baseline), from 11 days before launch until launch, in flight (as soon as possible on orbit until the last flight day), and, after landing, for 7 more days. Preliminary analysis, using 23 subjects over nine shuttle missions, estimated that the average total nightly sleep duration (estimated with actigraphy) was 5.9 hours in flight and 6.9 ± 1.0 hours in the first week after flight. Of the 279 nights in flight that were recorded with actigraphy, 52 (18.6%) included fewer than 6 hours of sleep. These findings confirm previous studies that show an incidence of reduced sleep quantity in space.

Further preliminary analysis shows that sleep quantity may be reduced even more prior to undergoing critical mission operations. Evaluations of nine crew members who were performing between one and three EVAs each, across five missions, estimate that the average total amount of sleep that the crew members had the night before the EVAs was 5.6 ± 1.1 hours. As previously discussed, ground-based studies have consistently reported performance impairments under conditions of acute or chronic reduced sleep.

Objective feedback on sleep quantity is important information to provide to flight surgeons and astronauts who are preparing to engage in critical mission activities; this will be particularly true for the more autonomous Exploration missions. Currently, actigraphy data for some missions are being shared among the researcher, the flight surgeon, and the crew member; the flight surgeons and astronauts, who have commented on the benefit of having this information available, support transitioning the Actiwatch (figure 3-4) protocol to an operational tool (flight surgeons G Beven and S Johnston, personal communication, 2008).

A compelling testimony of sleep disturbances in flight is the degree to which sleep medications are used. A 1999 Category III study reviewed records from 79 space shuttle missions: of the 219 records that were obtained (each record representing one person on one flight), 94% indicated medication use during flight; and of the records that indicated medication use, 45% of them indicated that the medications were taken for sleep disturbances and that these were taken consistently for 9 flight days (Putcha et al., 1999). Two examples of astronaut sleep facilities on the ISS are provided in figure 3-5 and 3-6.

Figure 3-4. ***Image of an Actiwatch activity monitor that is shown next to a ruler to demonstrate the size of the Actiwatch.***

Figure 3-5. ***With most of his body tucked away in a sleeping bag, astronaut Daniel Tani, Expedition 16 flight engineer, poses for a photograph near two extravehicular mobility unit spacesuits in the Quest Airlock of the ISS.***

Figure 3-6. ***Cosmonaut Vladimir Dezhurov of Rosaviakosmos, Expedition 3 flight engineer, works on a laptop computer in the temporary sleep station in the U.S. Laboratory.***

Recent unpublished data from shuttle missions (Barger and Czeisler, 2008) also show a trend of regular use of medication to promote sleep. Of the first 32 crew members studied during 11 missions, 26 (81%) reported taking a sleep-promoting medication in flight. Crew members who used sleep medications reported taking them on approximately half the nights that data were collected aboard the space shuttle; two doses of sleep medication were taken on 7% of the nights when medication was used. The frequent use of sleep medication in flight serves as a strong indication that sleep is disturbed for some crew members.

Sleep structure (i.e., sleep quality) may also be altered in space. A 1997 study (Gundel et al.), which used polysomnography (Category II) to evaluate sleep content, found that latency to the first rapid eye movement (REM) episode was shorter, and slow wave sleep (SWS) was redistributed from the first to the second sleep cycle. Dijk et al. (2001), who also used polysomnography, found a reduction of SWS during the final third of in-flight sleep episodes and post-flight (evaluated at 2, 4, and 5 days post-landing), with an increase in sleep duration and the amount of restorative sleep.

Subjective sleep quality diminished in flight in both the Gundel et al. (1997) and Dijk et al. (2001) studies. Studies by Gundel et al. (1997) and Monk et al. (1998) also revealed decreases in SWS and electroencephalogram (EEG) slow wave activity (SWA), reflecting the decrements in the putative restorative component of sleep that are known as Process S (Borbély and Achermann, 1999). In contrast, ground-based studies of sleep restriction have revealed a rapid increase in EEG SWS and SWA (Brunner et al., 1990). This discrepancy suggests that not only is sleep quantity reduced during space flight, 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).

Individual, Physiological, and Environmental Factors that Contribute to Sleep Loss and Fatigue During Space Flight

Various factors influence the extent to which individuals experience sleep loss and fatigue in space. Differences exist among subjects when experiencing the deleterious effects resulting from inadequate sleep. Some may need less sleep and/or be more resistant to the effects of sleep loss on brain functions. Laboratory and field studies have found this to be the case for 10% to 30% of individuals when sleep loss is mild to moderate (Van Dongen et al., 2004, 2005b; Caldwell et al., 2005). For the majority of astronauts, however, sleep loss and fatigue remain a relevant issue, and self-report of alertness has been shown to be inaccurate under conditions of sleep loss (see above), even in motivated and trained individuals.

The space flight environment affects this risk as well. For instance, recent data indicate that noise levels on the ISS, even during sleep periods, can average more than 70 dB, and that the recordings have "maxed out" at over 90 dB during scheduled sleep episodes (Goodman, 2003). For comparison, a circular saw creates noise levels from 91 to 99 dB. The degree to which noise and environmental disturbances impact sleep during space flight missions remains to be determined.

Recent Category III unpublished data (Barger and Czeisler, 2008) confirm the findings of previous assessments of sleep quantity and quality on orbit. In particular, these findings suggest that the amount and quality of in-flight sleep is reduced in comparison to terrestrial sleep behavior for multiple reasons. Data from 23 astronauts who completed 274 sleep logs on nine shuttle flights indicate that in 163 (59%) of these logs, sleep was recorded as having been disturbed on the previous night. The most frequent causes of sleep disturbance were voids; noise; physical discomfort; other crew member disturbances; and temperature. These physiological and environmental factors may interfere with achieving good sleep quality on either the shuttle or the ISS, thereby depriving crews of the full restoration afforded by sleep. An evidence-gathering effort is under way by BHP researchers to evaluate the impact of these individual, physiological, and environmental factors on sleep and fatigue, and to address several BHP gaps concerning the effects of work-rest schedules, environmental conditions, and flight rules and requirements on sleep, fatigue, and performance.

Occurrence of Circadian Desynchronization in Space Flight

A recent summary of findings from several short-duration evaluations shows that circadian desynchronization can and does affect at least some crew members in space, largely as a result of lighting conditions, scheduling constraints, or other aspects of the space flight environment (Mallis and DeRoshia, 2005).

Limited research is available on circadian rhythms in space. From the studies that have been conducted, there are inconsistencies as to the degree of circadian desynchronization experienced in flight (Mallis and DeRoshia, 2005). As an example, Gundel et al. (1997) assessed the circadian rhythms (using body temperature) of four astronauts over a period of 6 to 8 days during their stay on the Russian space station *Mir*. In comparison to baseline measures, these astronauts displayed a phase delay of more than 2 hours. The phase delay was attributed

to the alterations of external cues (i.e., reduced light/dark modulation) and possibly delayed bedtimes, as well as the fact that the intrinsic period of the circadian pacemaker is longer than 24 hours (Gundel et al., 1997). Monk et al. (1998), however, analyzed the circadian rhythms of four astronauts (using body temperature) prior to, during, and following a 17-day shuttle mission. From this study, the authors determined that circadian rhythms in orbit appear to be very similar in phase and amplitude to those on the ground.

Far fewer analyses have been conducted on circadian rhythms over long-duration missions. A case study involving an astronaut on a mission to *Mir* (Monk et al., 2001), revealed that a 24-hour circadian rhythm was maintained for about the first 3 months, with disruptions in sleep and a reduced circadian amplitude occurring during the last 12 days (Mallis et al., 2004).

Another case study that was conducted over a 438-day *Mir* mission revealed delays in circadian rhythms (Mallis and DeRoshia, 2005). This and other circadian delays are attributed to a variety of factors including: the alterations of external cues, i.e., reduced light/dark modulation (Mallis and DeRoshia, 1995); possibly delayed bedtimes; as well as the fact that the intrinsic period of the circadian pacemaker is longer than 24 hours (Gundel et al., 1997. These inconsistencies in circadian desynchronization may also be due to individual differences, as some individuals (as previously mentioned) are more susceptible to sleep loss or the debilitating effects of shifted work-rest cycles (Dinges, 2004; Mallis and DeRoshia, 2005).

Factors that Contribute to Circadian Desynchronization During Space Flight

Lighting remains the most significant external cue for altering the phase of the circadian rhythm. Lighting is so effective, in fact, that numerous Category I and Category II ground-based laboratory studies have shown that timed exposure to specific types of bright light and blue-enriched (short-wavelength) light serves as an effective countermeasure for circadian phase-shift and performance deficits due to sleep deprivation (Czeisler et al., 1986; Brainard et al., 1988; Czeisler et al., 1989; Brainard et al., 2001; Czeisler et al., 1995; Lockley et al., 2003; Brainard and Hanifin, 2005; Cajochen et al., 2005; Gronfier et al., 2007; Lockley, 2007).

Any natural lighting to which crews are exposed on a spacecraft may impact their circadian adaptation. Note that the ISS and docked shuttle orbit the Earth every 1.5 hours, resulting in 16 sunrises and sunsets every 24 hours, causing the natural lighting cues surrounding the ISS to vary greatly from the terrestrial 24-hour day and night cycle. Indeed, astronauts on shuttle and ISS are no longer exposed to the natural 24-hour 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.

Less-than-optimal artificial lighting conditions have been reported on the ISS (Category IV). Station lighting is provided by both incandescent and fluorescent light sources. Over time, this lighting has degraded due to lamp burnout and the difficulty in supplying replacement lamps on orbit. Over the 9 years of ISS construction, lamps were resupplied piecemeal, with one or two lamps being shipped up by the Soyuz. The resultant decline in on-board lighting eventually was addressed by the first major resupply by STS-114 in July 2005. As soon as the lamps were delivered to the ISS, however, the re-lamping duty was officially given a relatively low priority. Crew members raised this priority significantly, however, because of their desire to improve the illumination on board the station (see Appendix 1 for additional details). This was not only to avoid eyestrain but because, as artificial lighting can impact circadian rhythms and acute alertness, inadequate lighting contributes to circadian desynchronization and fatigue.

Slam shifting, which is an acute shift in the sleep/wake schedule to accommodate a docking or critical task in flight (Leveton et al., 2006), is another risk factor for circadian desynchronization in the current space flight

environment. Slam shifting can result in sleep loss and fatigue for astronauts (Category III). Recent data from the JSC Missions Operations Directorate (MOD) (Korth et al., 2006) reveal that critical operations often require slam shifting. In 2,043 days of ISS operations (2000–2006), slam shifts occurred on 13% of these days, typically before and during critical operations (e.g., dockings/undockings, taxi spacecraft relocations, EVAs). Such schedule changes force critical mission operations to occur against the body's natural circadian rhythm and after sleep deprivation.

Slam shifting also affects the ground teams that are supporting the ISS during critical operations when these NASA teams often are working overnight. As described previously, people whose employment requires that they work overnight shifts must try to remain awake and alert to function well at times when their circadian rhythm and homeostatic drive are promoting sleep. Category IV evidence that is derived from flight surgeons indicates that crew members have said that "the shifting (circadian) was tougher on them than they thought it was going to be" (flight surgeon S Johnston, personal communication, 2007).

Occurrence of Work Overload During Space Flight

Category III evidence reveals work overload occurring during some space flight missions, including those of the Skylab and Apollo Programs. The workload during the second Skylab mission steadily increased over 8 weeks, while crew members of the third Skylab mission reported that they quickly ran into difficulty due to work overload. The fast-paced schedule and workload of the mission had initially caused these crew members to consistently "feel" behind on tasks as well as demoralized. At the start of the 45th day of their 59-day mission, the crew members of Skylab 3 elected to have a sit-down, during which they refused to perform scheduled tasks. Mission Control personnel later acknowledged that the schedule had been such that it had not given the crew members adequate time in which to adjust to their environment (Cooper Jr., 1996). Category III evidence from the Apollo Program also reveals that some of the Apollo crews reported serious mental fatigue while they were performing lunar EVAs (Scheuring et al., 2007). Current shuttle missions to ISS are recognized for their high-tempo nature as crews perform complex, critical tasks. Of the 22 EVAs that were conducted during 2007, nine of these dangerous, and critical, endeavors lasted 7 or more hours.

Space Flight Performance Errors Due to Sleep Loss, Fatigue, Circadian Desynchronization, and Work Overload

While evidence indicates that sleep loss, fatigue, circadian desynchronization, and work overload have occurred during space flight, it remains unclear whether these factors directly affect the performance of a crew in space flight. A limited number of space flight studies have evaluated performance for sleep and fatigue effects, and, of those studies, many of them have very few subjects. In the limited studies in which performance was shown to be affected, questions remain regarding whether sleep loss and fatigue were the root cause. It is also difficult to ascertain causality and relevance to future long-duration missions, when the data from these studies are largely derived from short-duration space flight studies (Table 3-2).

One of the first studies to evaluate cognitive in-flight performance was conducted by Benke et al. in 1993. This Category II evaluation assessed the performance of one cosmonaut in several cognitive tasks at three intervals during a 6-day mission on *Mir*. These tasks evaluated response time and accuracy. In-flight performance on the tasks was compared with pre- and post-flight performance. No significant decrements resulting from a short stay in space were found in this case study.

Table 3-2. ***Space Flight Cognitive Performance Studies***

Study	Year	Mission	No.	Measurement type	Effect	Type of Effect	Mission Days
Manzey and Lorenz	1998	*Mir*	1	Accuracy and response time: four tasks from AGARD-STRES (GRT, MST, UTT); mood and workload assessments	Yes	Pre-launch decrements associated with lowered mood scores; decrements in tracking performance varied in flight, associated w/adaptation (i.e., to space, and back to Earth)	438
Manzey et al.	1998	*Mir*	1	Accuracy and response time: four tasks from AGARD-STRES (GRT, MS, UTT, DT)	Yes	Fine manual control decrements (UTT) due to adaptation; potential decrement in tracking/ memory-search during DT	8
Newman and Lathan	1999	STS-42	4	Memory recall task	No		4
Schiflett et al.	1996	STS-65, STS-78	7	PAWS (battery of performance tests); subjective assessments of cumulative fatigue	Yes	Decrements in memory-search performance, correlated with self-assessment fatigue	14 (STS-65) 15 (STS-78)
Dijk et al.	2001	STS-90, STS-95	5 (STS-90) 1 (STS-95)	PVT (calculation, recall memory, VAS, KSS)	PVT-not sig.	Most lapses in flight; least lapses post-flight	16 (STS-90) 10 (STS-95)
Dijk et al.	2001	STS-90, STS-95	5 (STS-90) 1 (STS-95)	Self-assessment of fatigue	Yes	Fatigue levels worst in flight; best post-flight	16 (STS-90) 10 (STS-95)

Note: AGARD=Advisory Group for Aerospace Research and Development (NATO). STRES=simulated training requirements effectiveness report. GRT=grammatical reasoning task. MST=Memory Search Task. UTT=Unstable Tracking Task. PAWS=Performance Assessment Workstation. VAS=Visual Analog Scale. KSS=Karolinska Sleepiness Scale. DT=dual task.

Manzey et al. (1998) conducted a similar study over an 8-day mission to *Mir*; this again was a short-duration evaluation using one subject. The study involved administering six pre-flight and six post-flight assessments to one subject, with 13 in-flight assessments occurring during the Soyuz approach to *Mir* (high stress) and also during the stay on board *Mir*. Four tasks were administered: grammatical reasoning, MST, UTT, and a DT that consisted of unstable tracking with concurrent memory search. These tasks probe information-processing functions that are known to react sensitively to the adverse effects of environmental stressors or that might become impaired by the direct effects of microgravity on sensory motor processes (Kanas and Manzey, 2000). The speed and accuracy of short-term memory retrieval and logical reasoning were found to be unimpaired under space flight conditions. Decrements, however, were found in fine manual control movements during the UTT. DT interference effects on the tracking task and the memory search were also reflected, increasing from the beginning to the end of the mission.

During the experiment, researchers administered questionnaires to evaluate the crew members' mood, fatigue levels, and assessment of workload. Correlations between reported fatigue and decrements that were observed

during the tasks were revealed. As a result, the investigators proposed that the decrements may have been caused in part by the effects of accumulated fatigue.

Newman and Lathan (1999) conducted a Category II experiment on cosmonauts during space flight and did not find impairments in a memory-search performance task, although tracking disruptions were apparent. A performance monitoring study by Schiflett et al. (1996) included daily assessments of the different mental functions of three astronauts during a 13-day shuttle mission. Impairments and decrements were found in tracking performance, time-sharing efficiency, and memory-search performance in space. The researchers hypothesized that the impairment in memory-search performance in two of the three astronauts was not related to microgravity but, rather, was a side effect of decreased alertness and fatigue.

To further investigate the relationship between sleep and performance on orbit, Dijk et al. (2001) conducted an evaluation of the sleep, circadian rhythms, neurobehavioral performance, and light-dark cycles of five astronauts during two space shuttle flights, STS-90 (Neurolab) and STS-95. The researchers assessed neurobehavioral function and performance by administering several different tests, including the 10-minute PVT; a 4-minute, two-digit addition task; and a memory task. Subjective assessments of performance and effort were also recorded.

Analysis of variance revealed that across performance and mood variables, there was a consistent trend toward worse performance in flight than was noted before or after flight (Dijk et al. 2001). A detailed analysis of the time course of changes involving neurobehavioral measures, which was based on two measures that were derived from the PVT and the probed recall memory test, suggested that most of the study subjects exhibited a decline in performance during the last week before launch, a further decline in flight, and a slow recovery post-flight. While the effect for the number of lapses in attention on the PVT and for the median reaction time was not significant, this lack of effect could be due to the small sample size.

Although findings were not significant, this continuously declining performance appearing in short-duration flight, and the trend of improvement in subjects post-flight correlated with the amount of REM sleep. On return to Earth, subjects experienced a marked increase in REM sleep, and their subjective sleep quality and neurobehavioral performance recovered.

In summation, performance data from space flight thus far reveal some effects on accuracy, response time, and recall tasks; however, the quality of the evidence for performance decrements occurring as a result of fatigue and sleep loss during space flight remains uncertain. To date, no systematic attempt has been made to measure the performance effects of fatigue, sleep loss, circadian desynchronization, and work overload during space flight, and it is unknown whether the effect of these factors on performance significantly impacts the completion of mission objectives. More evaluation is therefore needed to accurately characterize this risk in space, and to understand how sleep loss, fatigue, circadian desynchronization, and work overload in flight translate into performance decrements. Other questions of interest include: Even if performance decrements exist on cognitive assessments, do these indeed translate into potential operational errors? And are decrements, when they exist, related to sleep, fatigue, circadian, and workload issues, or are they instead related to other aspects of the space flight environment? Undoubtedly, thorough evaluation is needed to accurately characterize this risk in space. Testing with the 3-minute PVT, which will be conducted on ISS starting in 2009, will include a larger number of subjects and test sessions to evaluate cognitive performance over the course of long-duration missions.

As noted previously, ground evidence strongly indicates that sleep loss, fatigue, circadian desynchronization, and work overload lead to performance decrements for some individuals. Evidence from space flight clearly

demonstrates the occurrence of sleep loss, fatigue, and circadian desynchronization on orbit. One could therefore conclude that, based on the ground evidence, astronauts do indeed face a realistic risk of performance errors.

It is essential, however, to accurately characterize the performance effects arising from sleep loss, fatigue, circadian desynchronization, and work overload more fully in the space flight environment so that individualized countermeasures can be implemented to prevent or reduce the risk. BHP research activities aim to determine the best measures and tools to assess cognitive performance in space and to characterize the effects of sleep loss, fatigue, extended work shifts, circadian desynchronization, and work overload on cognitive performance in this environment.

Computer-based Simulation Information

As detailed above, astronauts and ground personnel are exposed to many factors that may force their schedules away from the normal 24-hour routine: shift work, extended work hours, timeline changes, slam shifting, prolonged light of a lunar day, a Mars sol on Earth, a Mars sol on Mars, and abnormal environmental cues (e.g., inadequate or inappropriate light exposure). In addition, their quantity of sleep, particularly during critical mission operations, tends to be reduced due to a variety of operational, environmental, and individual factors. Extensive ground-based evidence demonstrates that reduced sleep increases the risk of performance errors, injuries, and accidents. As a result, a validated biomathematical model that instantiates the biological dynamics of sleep need and circadian timing could predict astronaut performance relative to fatigue and circadian desynchronization (Dinges, 2004). Such models could also provide a means by which to optimally schedule targeted countermeasures for maintaining astronaut performance. Various biomathematical models that seek to achieve these goals are under development (Mallis et al., 2004; Dean et al., 2007; Kronauer et al., 2007).

Two biomathematical models are discussed here: the Astronaut Scheduling Assistant, and the Circadian, Neurobehavioral Performance, and Subjective Alertness Model. Both of these models are based on extensive evidence that shows that the temporal dynamics and level of cognitive performance during wakefulness are the result of the interaction of sleep homeostatic drive and circadian timing (e.g., Borbély and Achermann, 1999). Both models incorporate predictions that are based on countermeasures. These predictions allow for the evaluation of the risk and safety of sleep/wake and work schedules during both the planning and the execution of space missions. Prospective studies on the accuracy of these model predictions remain to be done on Earth in conditions that simulate many of the sleep loss and circadian provocations that occur in space flight. Such studies are essential and may indicate the need for additional model parameters and changes in model structure.

The Astronaut Scheduling Assistant software tool, which was developed in 2007 by David Dinges and Hans Van Dongen, is based on a validated biomathematical model that relates cognitive performance to the neurobiology of sleep and wakefulness and to the biological clock. As previously discussed, studies in recent years have documented that the detrimental effects on cognitive performance of chronic sleep loss accumulate linearly across consecutive days of sleep restriction below 7 hours per day (Belenky et al., 2003; Van Dongen et al., 2003; Molicone et al., 2007; Mollicone et al., 2008). This model therefore takes into account cumulative sleep loss and more accurately predicts performance than traditional models (Avinash et al., 2005). For more information, refer to Appendix 2 of this report.

Differential vulnerability to the effects of sleep loss (Van Dongen et al., 2004) and night work (Czeisler et al., 2005) on performance must also be addressed by biomathematical models of astronaut performance because

recent studies have documented large stable (trait-like) differences among individuals in the degree of cognitive deficits that are experienced during sleep loss (Van Dongen et al., 2004; Klerman and Dijk, 2005). Preliminary validation of these techniques indicates that as the number of past data points increases, the model increases the accuracy with which the trait parameters are estimated, resulting in significant improvements in performance prediction accuracy over population average models (figure 3-7) (Van Dongen et al., 2007).

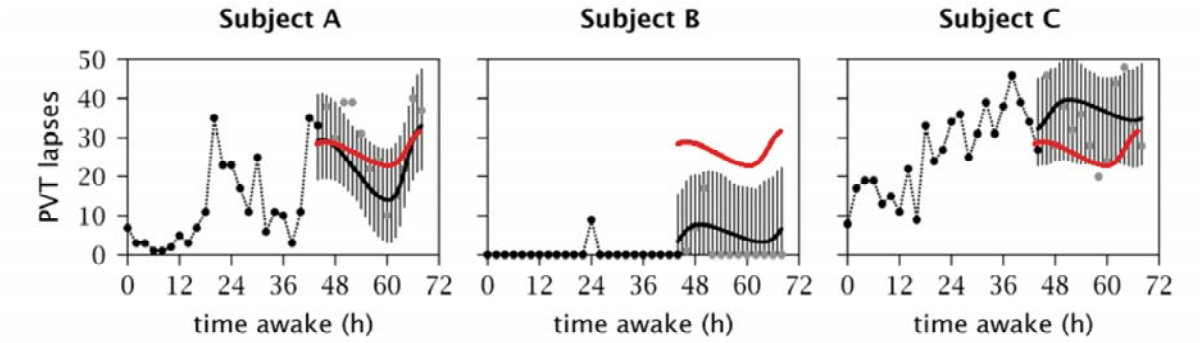

Figure 3-7. ***Future performance of three individuals, measured with the 10-minute PVT, during total sleep deprivation condition is predicted starting from t = 44h of wakefulness, with mean (thick black line) and 95% confidence interval (vertical bars). Individual predictions are based on traits that are identified from prior performance measurements up to t = 44h (block dots). The individualized predictions more accurately forecast the actual future performance of each individual (gray dots) than does the population average prediction (red line).***

The second model that was mentioned previously – the Circadian, Neurobehavioral Performance, and Subjective Alertness Model – predicts the effects of different light/dark and sleep/wake patterns on the circadian biological clock, performance, and alertness. Astronaut performance or alertness for an entire schedule or for a mission-critical time can thus be predicted. The model has been validated with data from shifted sleep-wake (e.g., jetlag or night work), low-light conditions, intermittent bright-light exposure data, and non-24-hour schedules (e.g., Mars), all of which apply to NASA operations. This model has also been used successfully to design a pre-flight light exposure regimen that is associated with the early-morning launch times that are often necessary for shuttle flights.

These methods can be used to design a variety of schedules that are relevant to NASA operations, including shifting sleep/wake (slam shifting) and non-24-hour schedules. Critically, these methods will be able to satisfy the variety of schedules that will be encountered during a Mars mission, where a day is 24 hours and 39 minutes.

Current work includes quantifying individual differences in response to circadian and sleep/wake factors, and incorporating non-light stimuli (e.g., posture and social cues) and information concerning the various wavelengths of light into the model, since the circadian system is responsive to specific wavelengths of light and the wavelength distribution that is found in space differs from that found on Earth (both indoors or outdoors).

This work allows for mathematical simulations that assess the impact of circadian alignment and sleep disruption on performance and alertness.

Risk in Context of Exploration Mission Operational Scenarios

As previously detailed in this report, space flight evidence shows that astronauts lose sleep during flight, and ground-based evidence shows that sleep loss, fatigue, extended work shifts, circadian desynchronization, and work overload lead to performance errors, injuries, and accidents.

A possible qualitative likelihood scale for performance errors during certain mission operational scenarios is

- Level 1 – will most likely not occur
- Level 2 – could occur
- Level 3 – will most likely occur

Using this scale, **the risk of performance errors due to sleep loss, fatigue, circadian desynchronization, and work overload is considered a Level 2 risk for ISS, lunar sortie, lunar long, and Mars missions.** As this section addresses risk in the context of Exploration mission operational scenarios, the Level 2 risk for ISS will not be addressed.

Lunar sortie

Early, short-duration lunar missions will be fast-paced "sprints" that are similar in nature to current shuttle missions. Representatives from MOD anticipate that crew rotations and schedule shifting will still be required during lunar sortie missions, particularly at the beginning and end of a mission when rendezvous between vehicles (the crew exploration vehicle and the lunar lander) will need to occur (S Curtis, personal communication). While shifting should not be prevalent for the duration of the lunar sortie stay, crews will be required to shift while they are conducting critical mission tasks (S Gibson, personal communication, 2008).

In addition, the day-night cues on the surface of the moon will be different than the day-night cues on Earth. The elevated portions on the rim of Shackleton crater, which is a proposed landing site that is near the South Pole of the moon, may be exposed to light as much as 90% of the time (flight surgeon R Scheuring, personal communication, 2007). Anecdotal reports of individuals conducting 2- to 3-week exploration missions in the Arctic, where light exposure is, as it is on the moon, close to continuous, indicates that exposure to constant light may result in an individual being unable to detect a need for sleep and/or rest (flight surgeon R Scheuring, personal communication, 2007). If daily EVAs are conducted on the lunar surface, this level of sunlight exposure may stimulate the same physiological response as are experienced during Arctic expeditions. The high-tempo operations of multiple EVAs on the lunar surface could lead to work overload, extended wake durations, cumulative sleep loss, and excessive fatigue.

If the landing site is not at the lunar poles, however, but is at more equatorial locations, the day-night cycle on the moon involves 2 weeks of light exposure and 2 weeks of darkness. Either way, the natural lighting conditions will not be the same as those experienced on Earth due to the 24-hour clock. This means that astronauts will not be able to depend on natural lighting cues to help with their circadian rhythms.

Additional factors that are associated with sleep and circadian issues in the current space flight environment – e.g., high-tempo workloads and adaptation to the space flight environment – will remain risk factors on lunar sortie missions. Subsequently, performance errors remain a plausible risk during the short-duration missions to the moon and could occur during the lunar sortie mission scenario.

Lunar long

Long-duration lunar missions will be marathon-like events that are similar in nature to the current ISS increments. During these missions, both ground and flight crews will experience high-tempo operations and shift work. As was noted above, unfamiliar day-night cues could affect the circadian system and the subjective need to sleep. As a result, for long-duration lunar missions, it is estimated that human performance errors due to sleep loss, fatigue, extended work shifts, circadian desynchronization, and work overload could occur.

Mars

For a Mars mission, this risk remains relevant and important, although certain aspects of the risk may vary for the different mission phases. The initial transit to Mars is anticipated to be similar to the ISS long-duration experience with regard to sleep loss, extended work durations, and workload. It is anticipated that this transit will exclude the slam shifting and high-tempo schedules that are similar to the dockings and critical mission activities that were experienced during the building of the ISS.

On the surface of Mars, work activities may consume a large part of crew time; the slam shifting that can lead to circadian desynchronization should be absent from a Mars scenario as the crews will, of necessity, manage their own timelines. It is suspected, however, 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, and the martian sky 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 (Murphy, 1997). The spectrum of light wavelengths is also different on Mars than on Earth. This difference in light exposure may complicate the entrainment of circadian rhythms, since the circadian system is most sensitive to blue wavelengths (Brainard et al., 2001), which are less prevalent on Mars than on Earth (Murphy, 1997).

Additionally, Mars has a day-night cycle (lasting 24 hours 39 minutes) that differs from that on Earth, which, as evidenced by recent ground studies, may pose challenges to performance. Sleep disruption and subjective decrements in alertness and performance were reported to be very burdensome to the scientists and engineers at the NASA Jet Propulsion Laboratory who lived on a Mars sol schedule while working on the Mars exploration rovers (MERs) (Bass et al., 2004; Czeisler et al., 2001). A study by DeRoshia et al. (2007) on self-report findings from MER operations personnel showed increased fatigue levels among 82% of the participants, as well as increased levels of sleepiness and irritability. Reduced levels of concentration and energy were also reported by most of the participants. The degree to which the physiological challenge of living on the Mars sol can threaten the success of a mission is described further in the appendix of the DeRoshia et al. report.

Subjects who were living on a laboratory-simulated Mars sol schedule experienced sleep disruption and decrements in alertness and performance (Wright et al., 2006; 2001). Most humans cannot adapt to this non-24-hour day without adequate countermeasures (Gronfier et al., 2007). Performance and circadian entrainment data have just been collected from the Mars Phoenix scout lander (MPSL) mission (May 25 – Sep 1, 2008) ground crew who were living on a Mars sol (L Barger, unpublished results, 2008). From these previous studies and a preliminary review of the MPSL data, it is expected that future crews who are traveling to Mars and the ground crews who will support the Mars missions will experience similar decrements in sleep, circadian alignment, performance, and alertness. As a result, for Mars missions, it is estimated that human performance errors that are due to sleep loss, fatigue, extended work shifts, circadian desynchronization, and work overload could occur.

Implications for future space flight

The behavioral consequences of performance errors due to sleep loss, circadian desynchronization, extended work shifts, fatigue, and work overload on ISS are currently being evaluated. Cognitive decrements that are caused by fatigue, inadequate light exposure, circadian dynamics, and work-sleep schedules, will more profoundly affect crews who are on a long-term lunar or Mars mission, where fewer resources will be available to mitigate these factors. The risk factors may become compounded by the fact that lunar and Mars missions bring additional restrictions. For example, returning to Earth from a lunar mission is not a readily available option, and returning to Earth during a Mars mission is not an option at all.

Currently, NASA STD-3001, Vol. 1 provides standards regarding a normal, uninterrupted sleep period; standards for circadian shifting caused by schedule demands; and limits for the amount of work that can be performed within 1 day and 1 week. The current standards, however, do not provide specific limits for performance thresholds. BHP anticipates developing normative databases for space flight using tools and measures that have been initially tested and verified in laboratories and high-fidelity analogs such as NEEMO [NASA Extreme Environment Mission Operations] and, subsequently, space flight. In mission analogs, astronauts can establish individual and group baselines as well as normative data for an environment that can be compared with space flight.

Flight designers and flight surgeons are concerned that crew members, and especially ground control personnel, may not be obtaining the minimum recommended rest periods: actual work-sleep time is not the same as the time that is planned. Evidence shows that, overall, sleep is shorter and interrupted in flight. During critical mission phases, schedule shifting and workload demands are strenuous for both ground and flight teams. It is important to ensure that the current NASA STD-3001, Vol. 1 standards are enforced to protect work-rest schedules for both ground and flight crews, particularly during high-tempo operations. If crews are shifted or have to perform during this allotted sleep time, recovery time needs to be allowed and individualized countermeasures need to be readily available.

Conclusion

Ground evidence clearly demonstrates the risk of performance errors due to sleep loss, fatigue, circadian desynchronization, and work overload. Reviews in the aviation and medical industry have consistently attributed accidents, injuries, and even death to performance errors arising from sleep and circadian issues. Furthermore, long-term health consequences serve as another potential outcome. The WHO International Agency for Research on Cancer Monograph Working Group recently concluded that, on the basis of published evidence, “shift work that involves circadian rhythm disruption is probably carcinogenic to humans” (Straif et al., 2007).

Space flight evidence shows that astronauts are regularly subject to shifting their sleep/wake schedules, long work hours, complex tasks, and sleep loss. The ground teams that support flight crews and robotic missions endure similar issues. As NASA transitions from LEO to lunar and Mars missions, flight and ground crews will certainly continue to face the challenges that are associated with acquiring adequate sleep, circadian desynchronization, fatigue, extended work shifts, and workload demands.

As space flight performance data are limited, BHP research aims to further characterize performance in the space flight environment using validated tools that detect cognitive deficits that are related to fatigue. Evaluations of gross motor performance in space flight are also anticipated. BHP research efforts will further describe the nature of sleep in space over long-duration missions, and tasks are under way to determine which factors en-

hance or infringe on sleep and disrupt circadian rhythms in space. The space flight environment is reported to be noisy, poorly lit, and, for some, uncomfortable. Shifting schedules and heavy workloads, particularly for the shuttle astronauts, can pose additional challenges. Adequately assessing the environment and making recommendations to improve on it, as well as understanding individual vulnerabilities to sleep loss, is an essential part of preparing for future missions to the moon and Mars.

Astronauts have proven to be resourceful in mitigating sleep loss, circadian desynchronization, fatigue, extended work shifts, and work overload. Lighting, medication, good sleep hygiene, and improved scheduling serve as effective countermeasures for space flight crews. Much remains unknown concerning the best ways in which to implement these countermeasures, however, particularly over time. Some medications, for instance, are suspected to work differently in space than they do on Earth. Non-sleep medications may be required in flight, and the potential interactions between these and the sleep medications that are prescribed in space flight have yet to be determined. Similarly, additional research will aid in the use of artificial lighting as a countermeasure for increasing acute alertness as well as facilitating the alignment of circadian rhythms. The long-term safety and efficacy of light as a non-pharmaceutical aid for alertness, circadian shifting, and sleep will inform requirements for the lunar and Mars crew habitats as well as recommendations to the crews, flight controllers, and flight medical operations.

Continued research efforts are necessary to address the psychological and physiological health of individuals during and following space flight missions. The sleep and circadian systems affect immunology, hormone production, GI function, and cardiovascular health; sleep disruption can also serve as a contributing factor for the risk of behavioral conditions (Chapter 1) as well as for the risk that is related to poor team cohesion and psychosocial adaptation (Chapter 2). Similarly, countermeasures that are developed to aid the sleep and circadian system can also serve to enhance other aspects of health; as an example, research indicates that bright light can serve as an effective treatment for Seasonal Affective Disorder (Glickman et al., 1998). Addressing the sleep and circadian system thus further addresses other risks within BHP as well as enhances other discipline research areas that are related to the human system and health outcomes from living and working in the space flight environment.

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Appendix 1: International Space Station Lighting

The following information was provided by James Maida, Habitability and Human Factors Branch, NASA Johnson Space Center, and Charles Bowen, Ph.D., Human Factors Design Engineering Specialist from the Lockheed Martin Human Factors Design Team. This information illustrates the dim lighting that crew members experience on board the ISS.

The best-case average illumination on board Node 1 of the ISS with eight out of eight fluorescent lamps burning is 13.82 foot-candles (fc). In contrast, on Mar 31, 2005, Node 1 was down to only one lamp burning, with an illuminance of 0.55 fc. Since color vision fails at approximately 0.30 fc, that lighting level is unacceptable for most tasks. The dim illumination in Node 1 presented a safety issue that was addressed, initially, by moving lamps from another area. The problem was ultimately solved by a resupply of the ISS by STS-114, which flew in Jul 2005.

In other examples, when the U.S. Laboratory on ISS has all 12 lamps burning, the illumination is 57.79 fc. When only four of the 12 lamps are burning, illumination is reduced to 16.48 fc. Finally, in an airlock that has all four of its fluorescent lamps working, the illuminance is 17.55 fc. When the airlock is down to one lamp, the illuminance can be as low as 2.62 fc.

The above illuminances were determined by the radiance illuminance model of the Lawrence Berkeley National Laboratory, Berkeley, Calif., with modifications for space flight applications.

Required illuminances for various tasks include: maintenance, 25 fc; transcribing, 50 fc; repair, 30 fc; reading, 50 fc; and night lighting, 2 fc.

Foot-candles can be converted to the international unit of lux by multiplying by 10. Thus, 10 fc = 100 lux.

Appendix 2: Mathematical Models of Human Circadian Rhythms and Performance

NASA currently uses two different mathematical models of human circadian rhythms and performance: the Astronaut Scheduling Assistant, and the Circadian, Neurobehavioral Performance, and Subjective Alertness Model.

At the heart of the Astronaut Scheduling Assistant is a comprehensive set of mathematical equations, numerical strategies, and computer program routines that enables the prediction of changes in astronauts' neurobehavioral performance capability over time. The model core makes predictions of neurobehavioral performance capability that are based on sleep and sleep loss (acute and chronic), naps, circadian rhythms, and light exposure, which means that the model also incorporates predictions that are based on countermeasures. These predictions allow for the evaluation of risk and safety of sleep/wake/work schedules during both the planning and the execution of space missions. Prospective studies on the accuracy of these model predictions that simulate the conditions of many of the sleep loss and circadian provocations that occur in space flight remain to be done on Earth. Such studies are essential, and may indicate the need for additional model parameters and changes in model structure.

Future work involves modifying the Astronaut Scheduling Assistant by integrating adaptive Bayesian performance prediction methods that use the results of an individual's past performance to identify individual

specific trait parameters (e.g., rate of homeostatic decay, magnitude of circadian fluctuation in performance, etc.) prior to predicting future performance with an individual-specific model.

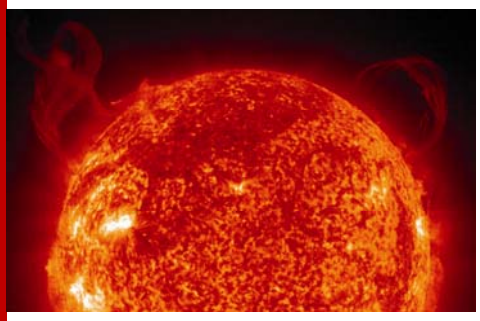
The Circadian, Neurobehavioral Performance, and Subjective Alertness Model approach has been directed towards increasing the accuracy of predictions and adding operationally relevant features. For example, melatonin is now incorporated as a circadian marker rhythm to accurately predict the phase and amplitude of the circadian pacemaker. Incorporation of wavelength-specific inputs is in progress. This model has recently been amended to allow the determination of an optimal light countermeasure regime for a given shift in sleep/wake or work schedule to improve performance at a desired time; this includes a schedule/countermeasure design prototype program that allows a user to interactively design a schedule and automatically design a countermeasure regime.

A current BHP in-flight effort is collecting sleep-wake data through use of actigraphy. These data, which are accumulated from actual astronauts in flight, will be integrated into the Circadian, Neurobehavioral Performance, and Subjective Alertness Model.

Space Radiation

Risk of Radiation Carcinogenesis

Risk of Acute Radiation Syndromes Due to Solar Particle Events



Risk of Acute or Late Central Nervous System Effects from Radiation Exposure

Risk of Degenerative Tissue or Other Health Effects from Radiation Exposure

Chapter 4:
Risk of Radiation Carcinogenesis

Francis A. Cucinotta
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GSI Germany

Occupational radiation exposure from the space environment may increase cancer morbidity or mortality risk in astronauts. This risk may be influenced by other space flight factors including microgravity and environmental contaminants. A Mars mission will not be feasible unless improved shielding is developed or transit time is decreased. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

Pictured is the Crab Nebula, a 6-light-year-wide expanding remnant of the supernova explosion of a star; the colors indicate the different expelled elements. Astronauts in space are exposed to protons and high-energy and charge ions that are released by events such as supernovae, along with secondary radiation, including neutrons and recoil nuclei that are produced by nuclear reactions in spacecraft and tissue. Ground studies and system biology models of cancer risk reduce uncertainties in risk projection models and pave the way for biological countermeasure development to protect astronauts on future Exploration missions.

Executive Summary

Astronauts who are on missions to the ISS, the moon, or Mars are exposed to ionizing radiation with effective doses in the range from 50 to 2,000 mSv (milli-Sievert) as projected for possible mission scenarios (Cucinotta and Durante, 2006; Cucinotta et al., 2008). The evidence of cancer risk from ionizing radiation is extensive for radiation doses that are above about 50 mSv. Human epidemiology studies that provide evidence for cancer risks for low-linear energy transfer (LET) radiation such as X rays or gamma rays at doses from 50 to 2,000 mSv include: the survivors of the atomic-bomb explosions in Hiroshima and Nagasaki, nuclear reactor workers (Cardis et al., 1995; 2007) in the United States, Canada, Europe, and Russia, and patients who were treated therapeutically with radiation. Ongoing studies are providing new evidence of radiation cancer risks in populations that were accidentally exposed to radiation (i.e., from the Chernobyl accident and from Russian nuclear weapons production sites), and continue to analyze results from the Japanese atomic-bomb survivors from Hiroshima and Nagasaki. These studies provide strong evidence for cancer morbidity and mortality risks at more than 12 tissue sites, with the largest cancer risks for adults found for leukemia and tumors of the lung, breast, stomach, colon, bladder, and liver. There is also strong evidence for inter-gender variations due to differences in the natural incidence of cancer as well as additional cancer risks for the breast and the ovaries and a higher risk from radiation for lung cancer in females (National Council on Radiation Protection and Measurements (NCRP), 2000). Human studies also provide evidence for a declining risk with increasing age at exposure, although the magnitude of this reduction above age 30 years is uncertain (NCRP, 2000; Biological Effects of Ionizing Radiation (BEIR), 2006). Genetic and environmental factors that contribute to radiation carcinogenesis are also being explored to support the identification of individuals with higher or reduced risk.

In space, astronauts are exposed to protons and high-Z high-energy (HZE) ions together with secondary radiation, including neutrons and recoil nuclei, which are produced by nuclear reactions in spacecraft or tissue. Whole body doses of 1 to 2 mSv/day accumulate in interplanetary space, and approximately half of this value accumulates on planetary surfaces (Cucinotta et al., 2006; NCRP, 2006). Radiation shielding is an effective countermeasure for solar particle events (SPEs), which are chiefly made up of protons with energies that are largely below a few hundred MeV. The intermediate dose-rates (<500 mSv/hour) and scarcity of data on the biological effectiveness of protons as compared to low-LET radiation make optimization of SPE shielding uncertain at this time, however. The energy spectrum of galactic cosmic rays (GCRs) peaks near 1,000 MeV/nucleon; consequently, these particles are so penetrating that shielding can only partially reduce the doses that are absorbed by the crew (Cucinotta et al., 2006). Thick shielding poses obvious mass problems to spacecraft launch systems, and would only reduce the GCR effective dose by no more than 25% using aluminum, or about 35% using more efficient polyethylene. Therefore, with the exception of solar proton events, which are effectively absorbed by shielding, current shielding approaches cannot be considered a solution for the space radiation problem (Cucinotta et al., 2006; Wilson et al., 1995). In traveling to Mars, every cell nucleus within an astronaut would be traversed by a proton or secondary electron every few days, and by an HZE ion every few months (Cucinotta et al., 1998b). The large ionization power of HZE ions makes them the major contributor to the risk, in spite of their lower cell nucleus hit frequency compared to protons.

Epidemiological data, which are largely derived from the atomic-bomb survivors in Japan (Preston et al., 2003), provide a basis for risk estimation for low-LET radiation. However, because no human data exist for protons and HZE ions, space risk estimates must rely entirely on experimental model systems and biophysical considerations. Projections to predict cancer risks in astronauts are currently made using the double detriment life-table for an average population such as is found in the U.S., which is made up of age- and gender-dependent rates of death from cancer and all causes of death combined with a model of radiation cancer mortality rate (NCRP, 2000). The model that is used for the radiation cancer mortality rate is based on epidemiological studies of atomic-bomb survivors, which are assumed to be scalable to other populations, dose-rates, and radiation types.

The two scaling parameters with large uncertainties are the radiation quality factor, which estimates the increased effectiveness of HZE nuclei as compared to gamma rays for the same dose, and the dose- and dose-rate effectiveness factor (DDREF). The DDREF estimates the reduction of a risk at low doses (<200 mGy) or dose-rates (<0.05 Gy/hour) compared to an acute exposure. Maximum acceptable levels of risk for astronauts are typically set at a 3% fatal risk (Cucinotta and Durante, 2006; NCRP, 1997b; 2000), but the large uncertainties in projections and the likelihood of other fatal or morbidity risks for degenerative diseases precludes a go/no-go decision at this time for Mars exploration. The scaling of mortality rates for space radiation risks to astronauts to the atomic-bomb survivors introduces many uncertainties into risk estimates (Cucinotta et al., 2001; Cucinotta and Durante, 2006), and there are also important questions with regard to the correctness of any scaling approach because of qualitative differences in the biological effects of HZE ions and gamma rays.

Acceptable levels of risk must be guided by societal or ethical norms. Debate continues on what level is acceptable for space radiation cancer risks for the exploration of the moon or Mars. Although a historical perspective is summarized herein, we note that the strong possibility of non-cancer mortality and morbidity risks must also be considered for a Mars mission. Improvements in safety in other areas of space flight should place pressure on radiation protection to improve and lower the risks to astronauts from space radiation.

Ground-based experimentation (Durante and Cucinotta, 2008) is key to solving the problem of space radiation cancer risk estimation because flight experiments are difficult, expensive, and poorly reproducible; the dose-rate is too low to get useful data in reasonable time; and, in the past, experiments have yielded no major findings (Kiefer and Pross, 1999; Schimmerling et al., 2003; Durante and Kronenberg, 2005). As part of its Space Radiation Program, NASA has invested in the NASA Space Radiation Laboratory (NSRL) at Brookhaven National Laboratory (Upton, N.Y.) to simulate the high-energy protons and heavy ions that are found in space. NSRL, which opened for research in October 2003, has produced experimental data in the past few years that are of great relevance for reducing uncertainty on risk assessment.

Although studies with animals are an important component of space radiation research, they are time-consuming and expensive in light of the large number of radiation types, doses, and dose-rates that are of concern to NASA. Systems biology models of cancer risk that can be used to extrapolate radiation quality over the broad range of nuclear types and energies and fluence rates in space suggest that effective mitigation measures are a promising new approach to these problems. Mechanistic research performed at NSRL with two-dimensional (2D) human cell culture and three-dimensional (3D) human coculture models (Barcellos-Hoff et al., 2005) as well as animal studies in murine models is being pursued to establish level of risk, reduce uncertainties in risk projection models, guide the extrapolation from experiment to astronauts, and pave the way for biological countermeasure development (Cucinotta and Durante, 2006).

Introduction

As noted by Durante and Cucinotta (2008), cancer risk that is caused by exposure to space radiation is now generally considered the main hindrance to interplanetary travel for the following reasons: large uncertainties are associated with the projected cancer risk estimates; no simple and effective countermeasures are available, and significant uncertainties prevent scientists from determining the effectiveness of countermeasures. Optimizing operational parameters such as the length of space missions, crew selection for age and gender, or applying mitigation measures such as radiation shielding or use of biological countermeasures can be used to reduce risk, but these procedures are clouded by uncertainties.

Space radiation is comprised of high-energy protons and high-charge (Z) and -energy (E) nuclei (HZE) whose ionization patterns in molecules, cells, and tissues, and the resulting initial biological insults, are distinct from typical terrestrial radiation, which consists largely of X rays and gamma rays that are characterized as low-LET radiation. GCRs, which originate outside of our galaxy (probably from supernovas), are comprised mostly of highly energetic protons with a small component of HZE. Prominent HZE nuclei include: helium (He), carbon (C), oxygen (O), neon (Ne), magnesium (Mg), silicon (Si), and iron (Fe). GCR energy spectra peaks, which have median energies of about 1,000 MeV/amu, and nuclei with energies as high as 10,000 MeV/amu, make important contributions to the dose-equivalent.

Ionizing radiation is a well-known carcinogen on Earth (BEIR, 2006). The risks of cancer from X rays and gamma rays have been established at doses above 50 mSv (5 rem), although there are important uncertainties and ongoing scientific debate concerning cancer risk at lower doses and at low dose-rates (<50 mSv/hour). The relationship between the early biological effects of HZE nuclei and the probability of cancer in humans is poorly understood, and it is this missing knowledge that leads to significant uncertainties in projecting cancer risks during space exploration (Cucinotta and Durante, 2006; Durante and Cucinotta, 2008).

Uncertainties in cancer projections

For space radiation risk assessments, the major uncertainties in cancer prediction are

- Radiation quality effects on biological damage related to the qualitative and quantitative differences between space radiation compared to X rays
- Dependence of risk on dose-rates in space related to the biology of deoxyribonucleic acid (DNA) repair, cell regulation, and tissue or organism responses
- Predicting SPEs, including temporal, energy spectra, and size predictions
- Extrapolation from experimental data to humans and between human populations
- Individual radiation-sensitivity factors, including genetic, epigenetic, dietary, or “healthy worker” effects

The minor uncertainties in cancer risk prediction are

- Data on GCR environments
- Physics of shielding assessments related to transmission properties of radiation through materials and tissue
- Microgravity effects on biological responses to radiation
- Errors in human data (statistical, dosimetry, or recording inaccuracies)

Quantitative methods have been developed to propagate uncertainties for the several factors that contribute to cancer risk estimates (NCRP, 1997a; Cucinotta et al., 2001; 2006). A description of uncertainty analysis using Monte Carlo techniques is provided below. Current estimates of levels of uncertainty, which are represented as fold changes of the upper 95% confidence interval (C.I.) over the median risk projection, are illustrated in figure 4-1, and a comparison of the risks for adults for both terrestrial and space exposures is shown in figure 4-2. The contribution of microgravity effects on space radiation risk has not yet been estimated but it is expected to be small (Kiefer and Pross, 1999). Changes in oxygen levels or in immune dysfunction (Smyth et al., 2006) are of concern during space flight. Their effects on radiation cancer risks are largely unknown.

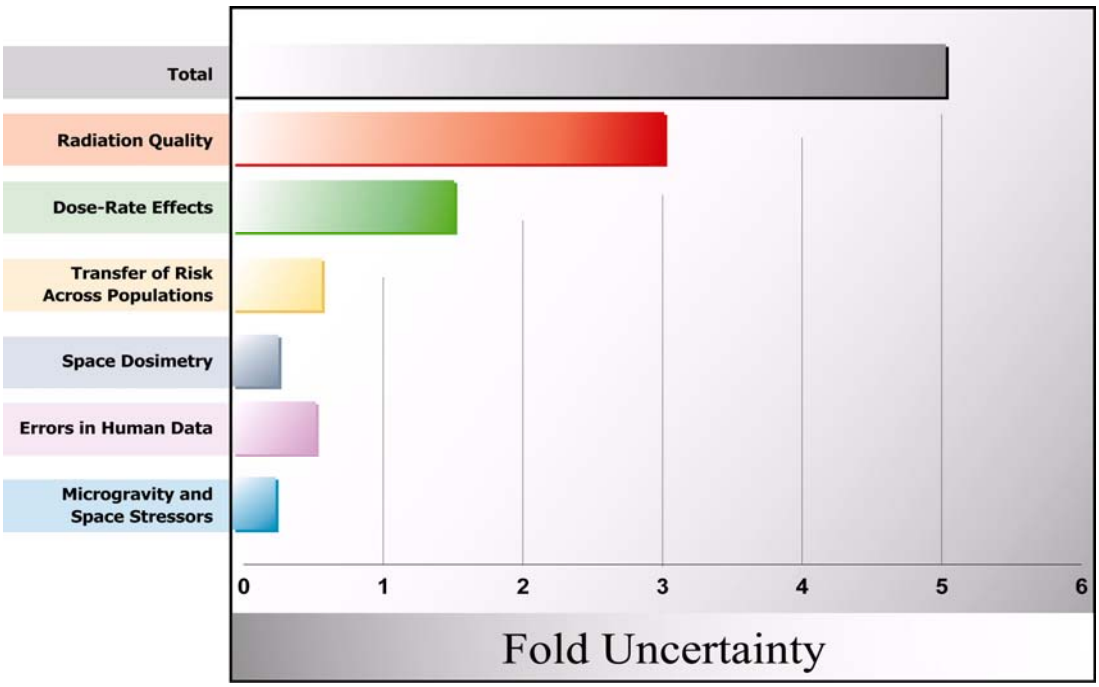


Figure 4-1. ***Estimates of fold uncertainties from several factors that contribute to cancer risk estimates from space radiation exposures. The uncertainties are larger for astronauts who are in space as compared to typical exposures on Earth, as illustrated.***

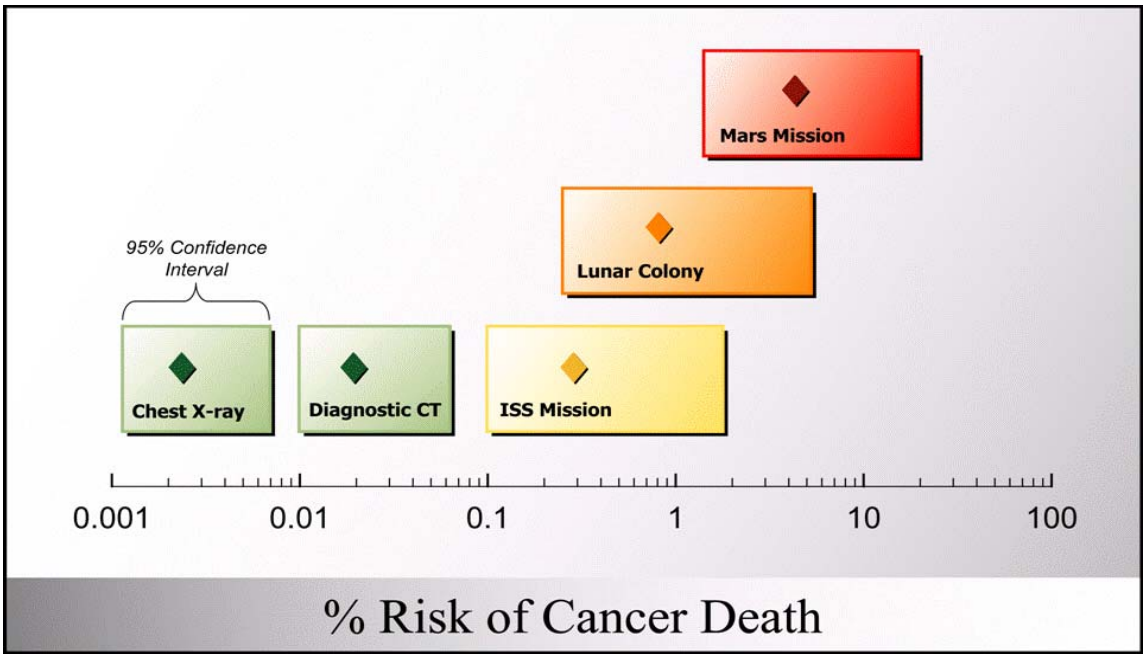


Figure 4-2. ***Uncertainties in risk projection for terrestrial and space exposures. The uncertainties are larger for astronauts who are in space as compared to typical exposures on Earth, as illustrated here. This figure shows the current estimates of cancer risks (diamonds) and 95% confidence bands 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.***

Radiation affects cells and tissues either through direct damage to the cellular components or through the production of highly reactive free radicals from water (Goodhead, 1994). Both of these mechanisms can generate sufficient damage to cause cellular death, DNA mutation, or abnormal cellular function. The extent of damage is generally believed to be dependent on the dose and type of particle with a linear dose-response curve (Goodhead, 1994). This is true for high and moderate radiation exposure, but it is extremely difficult to measure for lower doses where it is not easy to discern the effects of radiation exposure from those that are triggered by the normal oxidative stress with which cells and tissues deal constantly. The HZE nuclei are unique components of space radiation that produce densely ionizing tracks as they pass through matter; when they traverse a biological system, they leave streaks or tracks of damage at the biomolecular level that fundamentally differ from the damage that is left by low-LET radiation sources such as gamma rays and X rays. In the nucleus of a cell, where the genetic material is stored, the traversal of a heavy ion can produce tracks of clustered DNA damage (Cucinotta and Durante, 2006), as illustrated in figure 4-3.

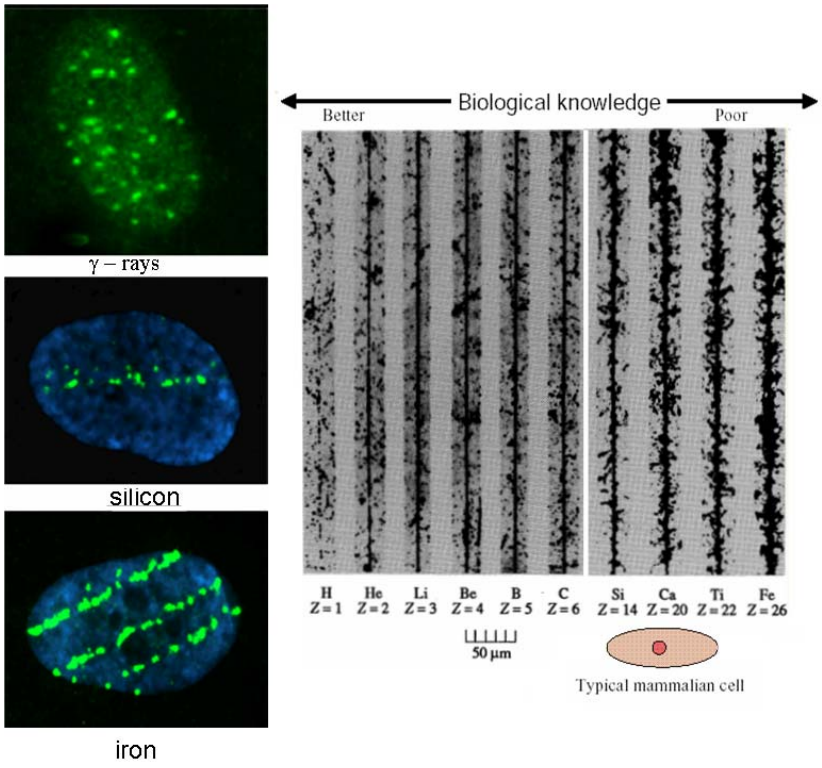


Figure 4-3. ***Comparison of particle tracks in nuclear emulsions and human cells (Cucinotta and Durante, 2006). The right panel shows tracks of different ions, from protons to Fe, in nuclear emulsions, clearly showing the increasing ionization density (LET=ΔE/Δ x) along the track by increasing the charge Z. The left panel shows three nuclei of human fibroblasts exposed to gamma rays or to Si- or Fe-ions, and immunostained for detection of γ-H2AXP. Each green focus corresponds to a DNA double strand break (DSB). While in the cell that is exposed to sparsely ionizing gamma rays foci of the histone variant, H2AX, are uniformly distributed in the nucleus, the cells that are exposed to HZE particles present DNA damage along tracks (one Si- and three Fe-particles, respectively), and the spacing between DNA DSB is reduced at a very high LET.***

HZE nuclei impart damage via the primary energetic particle as well as from fragmentation events that produce a spectrum of other energetic nuclei, including protons, neutrons, and heavy fragments (Wilson et al., 1995; Cucinotta et al., 1998a; 2006); a large penumbra of energy deposition extends outward from the primary particle

track (Cucinotta et al., 2000a). Secondary radiation that is produced in shielding materials can be controlled through the use of materials that have light atomic constituents (e.g., hydrogen and carbon). However, a large percentage of secondary radiation is produced within tissue and is, therefore, not practically avoidable. Due to the large amount of energy that is deposited as these particles traverse biological structures, the HZE nuclei are capable of producing the greatest amount of cellular damage, which means that they are of great concern for astronaut safety. The lack of epidemiological data and sparse radiobiological data on the effects for these radiation types leads to a high level of uncertainty when formulating risk estimates of long-term health effects following exposure to GCRs and SPEs.

Types of cancer caused by radiation exposure

A broad spectrum of tissue types contributes to the overall cancer risk that is observed with low-LET radiation (Table 4-2), including lung, colorectal, breast, stomach, liver, and bladder cancers as well as several types of leukemia, including acute myeloid leukemia and acute lymphatic lymphoma (NCRP, 2000; Preston et al., 2003; BEIR, 2006). It is not known whether the same spectrum of tumors will occur for high-LET radiation as with low-LET radiation, and some differences should be expected. Relative biological effectiveness (RBE) factors describe the ratio of a dose of high-LET radiation to that of the X rays or gamma rays that produce the identical biological effect. RBEs that are observed in mice with neutrons vary with the tissue type and strain of the animal (NCRP, 1990; Fry and Storer, 1987), which provides evidence that the spectrum of tumors in humans who are exposed to space radiation will be distinct from that in humans who are exposed to low-LET radiation. These likely differences are not described by the models that are used currently at NASA to project space radiation risks.

Age, latency, gender, and individual sensitivity issues

As cancer is a genetic disease with important epigenetic factors, individual susceptibility issues are an important consideration for space radiation protection. Females have a higher cancer risk from radiation than males, largely due to the additional risks to the breast and ovary; but studies show that there is also a much higher risk of lung cancer after radiation exposure in females than in males (NCRP, 2000). Risk at a sufficiently high age would be expected to decrease with age at exposure because the distribution of latency for tumor development would extend beyond the expected life span at older exposure ages. There may also be a reduction in the number of cells that are at risk at older age due to senescence or other biological factors (Campisi, 2003; 2007). However, the possibility that radiation acts more as a tumor promoter than as an initiator, and the fact that the animal data for high-LET radiation show tumors developing at earlier times than with low-LET radiation, suggests that the age dependence of space cancer risk is inadequately understood at this time.

Genetic factors and environmental factors also impact the risk of cancer from radiation. Studying the mechanisms of genetic sensitivity provides important insights into the understanding of radiation risks to astronauts (Durante and Cucinotta, 2008). Studies of historical data sets, such as the atomic-bomb survivors, show that subsets of the exposed cohorts could have a higher-than-average radiation risk (Ponder, 2001). A well-known example is *ataxia telangiectasia* (AT) patients, who dramatically demonstrate the importance of genetic susceptibility to radiation damage in cancer treatment. Other examples that are related to DNA repair genes include BRCA1&2 (Ponder, 2001, p. 53), NBS (Pluth et al., 2008), and Artemis (Wang et al., 2005), as well as the many other so-called high-penetrance genes that are involved in cancer susceptibility (Ponder, 2001).

Ataxia telangiectasia mutated (ATM) homozygotes only represent a small fraction of the radiosensitive patients, although these patients appear to be the most sensitive. ATM heterozygotes, who are also cancer-prone, are suspected to represent a large fraction of the extreme radiosensitive patients (Thompson et al., 2005).

It has been shown that cells that are heterozygous for ATM mutations are slightly more sensitive to radiation-induced neoplastic transformation than are the wild-type cells (Sminelov et al., 2001). An increased sensitivity of ATM heterozygotes has been also proved in vivo, measuring the induction of cataracts in ATM homozygotes, heterozygotes, and wild-type mice exposed to 0.5- to 4-Gy X rays (Worgul et al., 2002).

An important issue to address is how low-penetrance genes impact sensitivity to radiation-induced cancer. A recent study on subjects who were exposed to high radiation doses to treat ringworm of the scalp (*tinea capitis*) in Israel revealed a strong familial risk of radiation-induced meningioma (Flint-Ritcher and Sadetzki, 2007), suggesting that radiation carcinogenesis might be an issue for a genetically predisposed subgroup of the general population rather than a random event (Hall, 2007).

It is not known whether individuals who display hypersensitivity to low-LET radiation will also be equivalently hypersensitive to HZE nuclei, or whether findings at high dose and dose-rates will hold at low dose-rates and doses. Mice that are heterozygous for the ATM gene are more sensitive to cataractogenesis than are wild-types, not only after exposure to X rays but also after localized irradiation with high-energy Fe-ions (Hall et al., 2006). However, other studies show that high-LET irradiation has a reduced dependence on genetic background compared to low-LET irradiation (George et al., 2009).

A predictive assay that is able to identify radiation hypersensitive or cancer-prone subjects could be useful in crew selection for long-term space flights. Alternatively, identifying resistant individuals could substantially lower mission costs. Although this assay is neither scientifically achievable nor within society norms in most countries at the present time, ultimately, for a high-risk and high-cost endeavor such as a mission to Mars, screening astronauts for increased resistance to space radiation may be sought to reduce the costs of the missions.

Current NASA permissible exposure limits

Permissible exposure limits (PELs) for short-term and career astronaut exposures to space radiation have been approved by the NASA Chief Health and Medical Officer, and requirements and standards for mission design and crew selection have been set. This section describes the cancer risk section of the PELs.

Career Cancer Risk Limits

The astronaut career exposure to radiation is limited to not exceed 3% of the risk of exposure-induced death (REID) from fatal cancer. NASA policy is to assure that this risk limit is not exceeded at a 95% confidence level (CL) by using a statistical assessment of the uncertainties in the risk projection calculations to limit the cumulative effective dose (in units of Sievert) that is received by an astronaut throughout his or her career. These limits are applicable to missions of any duration in LEO and to lunar missions of less than 180 days duration. For longer missions that are outside LEO, further considerations of non-cancer mortality risks and approaches to reduce uncertainty in cancer risk projection models must occur before these missions can be safely assured.

Cancer Risk to Dose Relationship

The relationship between radiation exposure and risk is both age- and gender-specific due to latency effects and differences in tissue types, sensitivities, and life spans between genders. These relationships are estimated using the methods that are recommended by the NCRP (NCRP, 2000) and more recent radiation epidemiology information (Preston et al., 2003; Cucinotta et al., 2006). Table 4-1 lists examples of career effective dose (E) limits for an REID=3% for missions that are of 1-year duration or less. Limits for other career or mission lengths will vary and should be calculated using the appropriate life-table formalism. Tissue contributions to effective doses are defined below, as are dose limits for other career or mission lengths. Estimates of average life-loss

that are based on low-LET radiation are also listed in Table 4-1; however, higher values should be expected for high-LET exposures such as GCRs.

Table 4-1. ***Example Career Effective Dose Limits in Units of milli-Sievert (mSv) for 1-year Missions and Average Life-loss for an Exposure-induced Death for Radiation Carcinogensis (1 mSv = 0.1 rem)***

	E(mSv) for 3% REID (Ave. Life Loss per Death, yr)	
Age, yr	**Males**	**Females**
25	520 (15.7)	370 (15.9)
30	620 (15.4)	470 (15.7)
35	720 (15.0)	550 (15.3)
40	800 (14.2)	620 (14.7)
45	950 (13.5)	750 (14.0)
50	1,150 (12.5)	920 (13.2)
55	1,470 (11.5)	1,120 (12.2)

The Principle of As Low As Reasonably Achievable

The as low as reasonably achievable (ALARA) principle is a legal requirement intended to ensure astronaut safety. An important function of ALARA is to ensure that astronauts do not approach radiation limits and that such limits are not considered as "tolerance values." ALARA is especially important for space missions in view of the large uncertainties in cancer and other risk projection models. Mission programs and terrestrial occupational procedures resulting in radiation exposures to astronauts are required to find cost-effective approaches to implement ALARA.

Method of evaluating career limits

Radiation Doses and Risk Limits

Cancer risk is not measured directly but is calculated using radiation dosimetry and physics methods. The absorbed dose D (in units of Gray) is calculated using measurements of radiation levels that are provided by dosimeters (e.g., film badges, thermoluminescent dosimeters (TLDs), spectrometers such as the tissue-equivalent proportional counter (TEPC), area radiation monitors, biodosimetry, or biological markers) and corrections for instrument limitations. The limiting risk is calculated using the effective dose, *E* (in units of mSv), and risk conversion life-table methodologies.

For the purpose of determining radiation exposure limits at NASA, the probability of fatal cancer is calculated as shown on the following page.

1. The body is divided into a set of sensitive tissues, and each tissue, T, is assigned a weight, w_T, according to its estimated contribution to cancer risk, as shown in Table 4-2.

Table 4-2. *Tissue Weighting Factors*

Tissue or Organ	Tissue Weighting Factor, w_T
Gonads	0.20
Bone Marrow (red)	0.12
Colon	0.12
Lung	0.12
Stomach	0.12
Bladder	0.05
Breast	0.05
Liver	0.05
Esophagus	0.05
Thyroid	0.05
Skin	0.01
Bone Surface	0.01
Remainder*	0.05

*For purpose of calculation, the remainder is composed of the following additional tissues and organs: adrenals, brain, upper intestine, small intestine, kidney, muscle, pancreas, spleen, thymus, and uterus.

2. The absorbed dose, D_T, that is delivered to each tissue is determined from measured dosimetry. Different types of radiation have different biological effectiveness, depending on the ionization density that is left behind locally (e.g., in a cell or a cell nucleus) by the passage of radiation through matter. For the purpose of estimating radiation risk to an organ, the quantity characterizing this ionization density is the LET (in units of keV/μm).

3. For a given interval of LET, between L and ΔL, the dose-equivalent risk (in units of Sievert, where 1 Sv = 100 rem) to a tissue, T, $H_T(L)$ is calculated as

$$H_T(L) = Q(L)D_T(L), \tag{1}$$

where the quality factor, $Q(L)$, is obtained according to the International Commission on Radiation Protection (ICRP) prescription that is shown in Table 4-3. This way of calculating $H_T(L)$ differs from the method that is used by the ICRP, in which a tabulated set of weighting factors is given instead of the quality factor. The method that is used here is considered to yield a better approximation by using the quality factor as the weight that is most representative of cancer risk; the ICRP method, by contrast, may overestimate the risk, especially for high-energy protons. Neutron contributions are evaluated by their contribution to $D_T(L)$.

Table 4-3. *Quality Factor – Linear Energy Transfer Relationship*

Unrestricted LET, keV/μm in Water	Q(LET)
<10	1
10 to 100	0.32 LET – 2.2
>100	300/ Sqrt(LET)

4. The average risk to a tissue T, due to all types of radiation contributing to the dose, is given by

$$H_T = \int D_T(L)Q(L)dL, \tag{2}$$

or, since $D_T(L) = LF_T(L)$, where $F_T(L)$ is the fluence of particles with LET=L, traversing the organ,

$$H_T = \int dLQ(L)F_T(L)L. \tag{3}$$

5. The effective dose is used as a summation over radiation type and tissue using the tissue weighting factors, w_T,

$$E = \sum_T w_T H_T. \quad (4)$$

6. For a mission of duration t, the effective dose will be a function of time, $E(t)$, and the effective dose for mission i will be

$$E_i = \int E(t)dt. \quad (5)$$

7. The effective dose is used to scale the mortality rate for radiation-induced death from the Japanese survivor data, applying the average of the multiplicative and additive transfer models for solid cancers and the additive transfer model for leukemia by applying life-table methodologies that are based on U.S. population data for background cancer and all causes of death mortality rates. A DDREF of 2 is assumed.

Evaluation of Cumulative Radiation Risks

The cumulative cancer fatality risk (%REID) to an astronaut for occupational radiation exposures, N, is found by applying life-table methodologies that can be approximated at small values of %REID by summing over the tissue-weighted effective dose, E_i, as

$$Risk = \sum_{i=1}^{N} E_i R_0(age_i, gender), \quad (6)$$

where R_0 are the age- and gender-specific radiation mortality rates per unit dose. The effective dose limits that are given in the Table 4-1 illustrate the effective dose that corresponds to a 3% REID for missions with a duration of as long as 1 year. Values for multiple missions or other occupational exposure are estimated using Eq(6) or directly from life-table calculations. For organ dose calculations, NASA uses the model of Billings et al. (1973) to represent the self-shielding of the human body in a water-equivalent mass approximation. Consideration of the orientation of the human body relative to vehicle shielding should be made if it is known, especially for SPEs (Wilson et al., 1995).

Confidence levels for career cancer risks are evaluated using methods that are specified by the NCRP in Report No. 126 (NCRP, 1997a), which was modified to account for the uncertainty in quality factors and space dosimetry (Cucinotta et al., 2001; 2006). The uncertainties that were considered in evaluating the 95% CLs are the uncertainties in

1. Human epidemiology data, including uncertainties in

   a. statistics limitations of epidemiology data,
   b. dosimetry of exposed cohorts,
   c. bias, including misclassification of cancer deaths, and
   d. the transfer of risk across populations.

2. The DDREF factor that is used to scale acute radiation exposure data to low-dose and dose-rate radiation exposures.

3. The radiation quality factor (Q) as a function of LET.

4. Space dosimetry.

The so-called "unknown uncertainties" from the NCRP Report No. 126 (1997a) are ignored by NASA. The statistical distribution for the estimated probability of fatal cancer is evaluated to project the most likely values and the lower and upper 95% C.I.'s that are reported within brackets. For example, for the average adult who is exposed to 100 mSv (10 rem) of gamma rays, the estimated cancer risk is 0.4 % and the 95%. C.I.'s are estimated as [0.11%, 0.82%] where 0.11% is the lower 95% level and 0.82% is the upper 95% CL. To assure that the career risk limit is not exceeded with a safety margin corresponding to a 95% CL, the upper CL (i.e., the worse case) is considered in developing mission constraints and for crew selection. Approximate fold-uncertainties for several NASA missions are shown in Table 4-4.

Table 4-4. ***Approximate Fold-uncertainty Defined as a Ratio of Upper 95% Confidence Level to Point Risk Projection***

Type of Exposure	Fold-uncertainty at Upper 95% C.I.
Medical Diagnostic	2.0
ISS Environment	3.1
SPE	2.5
Deep Space or Lunar Surface GCR	4.0

Evidence

The evidence and updates to projection models for cancer risk from low-LET radiation are reviewed periodically by several prestigious bodies, which include the following organizations:

- The NAS Committee on the Biological Effects of Ionizing Radiation
- The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR)
- The ICRP
- The NCRP

These committees release new reports about every 10 years on cancer risks that are applicable to low-LET radiation exposures. Overall, the estimates of cancer risks among the different reports of these panels will agree to within a factor of two or less. There is continued controversy for doses that are below 50 mSv, however, and for low dose-rate radiation because of debate over the linear no-threshold hypothesis that is often used in statistical analyses of these data. The BEIR VII report (BEIR, 2006), which is the most recent of the major reports, is used in the following summary. Evidence for low-LET cancer effects must be augmented by information on protons, neutrons, and HZE nuclei that is only available in experimental models. Such data have been reviewed by NASA several times in the past and by the NCRP (1989; 2000; 2006).

Epidemiology data for low-linear energy transfer radiation

Life Span Studies of Atomic Bomb Survivors

The life span study (LSS) of the survivors of the atomic bombs in Hiroshima and Nagasaki, Japan, includes approximately 130,000 persons who were registered in 1950. Among these were 93,000 persons in Hiroshima and Nagasaki in 1945, and 37,000 persons who were living in these same cities in 1950. There is a gap in knowledge of the earliest cancer that developed in the first few years after the war, which impacts the assessment of leukemia to an important extent and for solid cancers to a minor extent. Some of the persons in the total data set were censured, leading to about 86,000 persons who have been followed in the study. Table 4-5 shows summary statistics of the number of persons and deaths for different dose groups. These comparisons show that the doses that were received by the LSS population overlap strongly with the doses that are of concern to NASA Exploration mission (i.e., 50 to 2,000 mSv).

Figure 4-4 shows the dose response for the excess relative risk (ERR) for all solid cancers from Preston et al. (2003). Tables 4-6 and 4-7 show several summary parameters for tissue-specific cancer mortality risks for females and males, respectively, including estimates of ERR, excess absolute risk (EAR), and percentage attributable risks. Cancer incidence risks from low-LET radiation are about 60% higher than cancer mortality risks (Preston et al., 2007).

Table 4-5. Number of Persons, Cancer Deaths, and Non-cancer Deaths for Different Dose Groups in the Life Span Study (BEIR, 2006)

	DS86 Weighted Colon Dose, mSv							
	Total	**0-50**	**50–100**	**100–200**	**200–500**	**500–1,000**	**1,000–2,000**	**>2,000**
No. Subjects	86,572	37,458	31,650	5,732	6,332	3,299	1,613	488
Cancer Deaths	9,335	3,833	3,277	668	763	438	274	82
Non-cancer Deaths	31,881	13,832	11,633	2,163	2,423	1,161	506	163

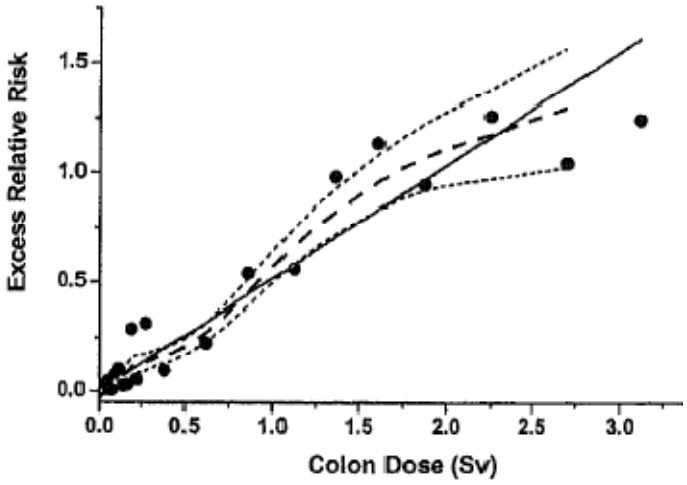


Figure 4-4. ***From Preston et al. (2003): Solid cancer dose-response function average over sex for attained age 70 after exposure at age 30. The solid straight-line is the linear slope estimate; the points are dose-category-specific ERR estimates; the dashed curve is a smoothed estimate that is derived from the points; and the dotted curves indicate upper and lower one-stand-error bounds on the smoothed estimate.***

Table 4-6. ***From Preston et al. (2003): Tissue-specific Cancer Mortality Risk Summary Statistics (i.e., ERR, EAR, and Attributable Risks) for Females and Males, Respectively***

LSS Female Site-specific Summary Mortality Rate Estimates: Solid Cancers 1950–1997

Site/system	Deaths (>0.005 Sv)	ERR/Sv[a] (90% CI)	EAR/10^4PY[b]-Sv[c] (90% CI)	Attributable risk (%)[d] (90% CI)
All solid cancer	4,884 (2,948)	0.63 (0.49; 0.79)	13.5 (7.4; 16.3)	9.2 (7.4; 11.0)
Oral cavity	42 (25)	–0.20 (<–0.3; 0.75)	–0.04 (<–0.3; 0.14)	–4.1 (<–6; 14)
Digestive system				
Esophagus	67(44)	1.7 (0.46; 3.8)	0.51 (0.15; 0.92)	22 (6.6; 42)
Stomach	1,312 (786)	0.65 (0.40; 0.95)	3.3 (2.1; 4.7)	8.8 (5.5; 12)
Colon	272 (150)	0.49 (0.11; 1.1)	0.68 (0.76; 1.3)	9.0 (3.4; 17)
Rectum	198 (127)	0.75 (0.16; 1.6)	0.69 (0.16; 1.3)	11.3 (2.6; 22)
Liver	514 (291)	0.35 (0.07; 0.72)	0.85 (0.18; 1.6)	6.2 (1.3; 12)
Gallbladder	236 (149)	0.16 (–0.17; 0.67)	0.18 (–0.21; 0.71)	2.6 (–2.9; 10)
Pancreas	244 (135)	–0.01 (–0.28; 0.45)	–0.01 (–0.35; 0.52)	–0.2 (–5.0; 7.6)
Respiratory system				
Lung	548 (348)	1.1 (0.678; 1.6)	2.5 (1.6; 3.5	16 (10; 22)
Female breast	272 (173)	0.79 (0.29; 1.5)	1.6 (1.2; 2.2)	24 (18; 32)
Uterus	518 (323)	0.17 (–0.10; 0.52)	0.44 (–0.27; 1.3)	2.7 (–1.6; 7.9)
Ovary	136 (85)	0.94 (0.07; 2.0)	0.63 (0.23; 1.2)	15 (5.3; 28)
Urinary system				
Bladder	67 (43)	1.2 (0.10; 3.1)	0.33 (0.02; 0.74)	16 (0.9; 36)
Kidney	31 (21)	0.97 (<–0.3; 3.8)	0.14 (<–0.1; 0.42)	14 (<–3; 42)
Brain/CNS[d]	17 (10)	0.51 (<–0.3; 3.9)	0.04 (<–0.02; 0.2)	11 (<0.05; 57)

[a]ERR/SV for age at exposure 30 in an age-constant linear ERR model; [b]Excess absolute risk per 10,000 persons per year; [c]Average EAR computed from ERR model; [d]Attributable risk among survivors whose estimated dose is at least 0.005 Sv; CNS – central nervous system.

Table 4-7. ***From Preston et al. (2003): Tissue-specific Cancer Mortality Risk Summary Statistics (i.e., ERR, EAR, and Attributable Risks) for Male***

LSS Male Site-specific Summary Mortality Rate Estimates: Solid Cancers 1950–1997

Site/system	Deaths (>0.005 Sv)	ERR/Sv[a] (90% CI)	EAR/10^4PY[b]-Sv[c] (90% CI)	Attributable risk (%)[d] (90% CI)
All solid cancer	4,451 (2,554)	0.37 (0.26; 0.49)	12.6 (9.4; 16.2)	6.6 (4.9; 8.4)
Oral cavity	68 (37)	–0.20 (<–0.3; 0.45)	–0.12 (<–0.3; 0.25)	–5.2 (<–6; 11)
Digestive system				
Esophagus	224 (130	0.61 (0.15; 1.2)	1.1 (0.28; 2.0)	11.1 (2.8; 21)
Stomach	1,555 (899)	0.20 (0.04; 0.39)	2.1 (0.43; 4.0)	3.2 (0.07; 6.2)
Colon	206 (122)	0.54 (0.13; 1.2)	1.1 (0.64; 1.9)	12 (6.9; 21)
Rectum	172 (96)	–0.25 (<–0.3; 0.15)	–0.41 (<–0.4; 0.22)	–5.4 (<–6, 3.1)
Liver	722 (408)	0.59 (0.11; 0.68)	2.4 (1.2; 4.0)	8.4 (4.2; 14)
Gallbladder	92 (52)	0.89 (0.22; 1.9)	0.63 (0.17; 1.2)	17 (4.5; 33)
Pancreas	163 (103)	–0.11 (<–0.3; 0.44)	–0.15 (<–0.4; 0.58)	–1.9 (<–6; 7.5)
Respiratory system				
Lung	716 (406)	0.48 (0.23; 0.78)	2.7 (1.4; 4.1)	9.7 (4.9; 15)
Prostate	104(53)	0.21 (<–0.3; 0.96)	0.18 (<–0.2; 0.75)	4.9 (<–5; 20)
Urinary system				
Bladder	82 (56)	1.1 (0.2; 2.5)	0.7 (0.1; 1.4)	17 (3.3; 34)
Kidney	36 (18)	–0.02 (<–0.3; 1.1)	–0.01 (–0.1; 0.28)	–0.4 (<–5; 22)
Brain/CNS	14 (9)	5.3 (1.4; 16)	0.35 (0.13; 0.59)	62 (23; 100)

[a]ERR/SV for age at exposure 30 in an age-constant linear ERR model; [b]Excess absolute risk per 10,000 persons per year; [c]Average EAR computed from ERR model; [d]Attributable risk among survivors whose estimated dose is at least 0.005 Sv.

Other Human Studies

The BEIR VII report (BEIR, 2006) contains an extensive review of data sets from human populations, including nuclear reactor workers and patients who were treated with radiation. The recent report from Cardis et al. (2007) describes a meta-analysis for reactor workers from several countries. A meta-analysis at specific cancer sites, including breast, lung, and leukemia, has also been performed (BEIR, 2006). These studies require adjustments for photon energy, dose-rate, and country of origin as well as adjustments made in single population studies. Table 4-8 shows the results that are derived from Preston et al. (2002) for a meta-analysis of breast cancer risks in eight populations, including the atomic-bomb survivors. Median ERR varies by slightly more than a factor of two, but confidence levels significantly overlap. Adjustments for photon energy or dose-rate and fractionation have not been made. These types of analysis lend confidence to risk assessments as well as show the limitations of such data sets.

Of special interest to NASA is the age at exposure dependence of low-LET cancer risk projections. The BEIR VII report (BEIR, 2006) prefers models that show less than a 25% reduction in risk over the range from 35 to 55 years, while NCRP Report No. 132 (NCRP, 2000) shows about a two-fold reduction over this range.

Table 4-8. ***Results from Meta-analysis of Breast Cancer Risk from Eight Population Groups, Including the Life Span Study of Atomic-bomb Survivors and Several Medical Patient Groups Exposed to X Rays, as described in Preston et al., 2002***

Summary of Parameter Estimates for the Final Pooled ERR Model

Cohort	Reference age for the ERR/Gy estimate	ERR/Gy[a]	Percentage change per decade increase in age at exposure	Exponent of attained age	Background SIR[b]
LSS	attained age 50	2.10 (1.6; 2.8)	Not included[b]	–2.0 (–2.8; –1.1)	1.01 (0.9; 1.1)
TBO	attained age 50	0.74 (0.4; 1.2)	Not included	–2.0 (–2.8; –1.1)	0.96 (0.7; 1.2)
TBX	attained age 50	0.74 (0.4; 1.2)	Not included	–2.0 (–2.8; –1.1)	0.73 (0.6; 0.9)
THY	attained age 50	0.74 (0.4; 1.2)	Not included	–2.0 (–2.8; –1.1)	1.05 (0.7; 1.5)
BBD	age at exposure 25	1.9 (1.3; 2.8)	–60% (–71%; –44%)	Not included[c]	0.98 (0.8; 1.2)
APM	all ages	0.56 (0.3; 0.9)	Not included	Not included	1.45 (1.1; 1.8)
HMG	all ages	0.34 (0.1; 0.7)	Not included	Not included	1.07 (0.8; 1.3)
HMS	all ages	0.34 (0.1; 0.7)	Not included	Not included	1.05 (0.9; 1.2)

[a]95% C.I.'s within parentheses; [b]SIR = standardized incidence ratio; [c]"Not included" means that the risk is assumed not to vary with age at exposure (attained age).

Review of space flight issues

In considering radiation risks for astronauts, it is useful to consider the historical recommendations that NASA has received from external advisory committees. These have formed the basis for the dose limits and risk projection models (Cucinotta et al., 2002). Early radiation effects usually are related to a significant fraction of cell loss that exceeds the threshold for impairment of function in a tissue. These "deterministic" effects are so called because the statistical fluctuations in the number of affected cells are very small compared to the number

of cells that are required to reach the threshold (ICRP, 1991). Maintaining dose limits can ensure that no early effects occur; these are expected to be accurately understood. As late effects can result from changes in a very small number of cells, statistical fluctuations can be large and some level of risk is incurred even at low doses. Referring to them as "stochastic" effects recognizes the predominance of statistical effects in their manifestation.

In recommendations by the NAS in 1967 (NRC, 1967), it was noted that radiation protection in human space flight is philosophically distinct from the protection practices of terrestrial workers because of the high-risk nature of space missions. This report by the NAS from 1967 did not recommend "permissible doses" for space operations, noting the possibility that such limits may jeopardize the mission, but instead estimated what the likely effects would be for a given dose of radiation.

In 1970, the NAS Space Science Board (NRC, 1970) recommended guidelines for career doses to be used by NASA for long-term mission design and human operations. At that time, NASA employed only male astronauts and the typical age of astronauts was 30 to 40 years. A "primary reference risk" was proposed that was equal to the natural probability of cancer over a period of 20 years following the radiation exposure (using the period from 35 to 55 years of age); this was essentially a doubling dose. The estimated doubling dose of 382 rem (3.82 Sv), which ignored a dose-rate reduction factor, was rounded to 400 rem (4 Sv). The NAS panel noted that its recommendations were not risk limits but, rather, a reference risk, and that a higher risk could be considered for planetary missions or a lower level of risk for a possible space station mission (NRC, 1970). Ancillary reference risks were described to consider monthly, annual, and career exposure patterns. However, the NAS recommendations were implemented by NASA as dose limits that were used operationally for all missions until 1989.

At the time of the 1970 NAS report, the major risk from radiation was believed to be leukemia. Since that time, the maturation of the data from the Japanese atomic-bomb survivors has led to estimates of higher levels of cancer risk for a given dose of radiation, including the observation that the risk of solid tumors following radiation exposure occurs with a higher probability than that of leukemias, although with a longer latency period before expression. Figure 4-5 illustrates the changing estimates of cancer risks for an average adult worker since 1970. Together with the maturation of the atomic-bomb data, reevaluation of the dosimetry of the atomic-bomb survivors, scientific assessments of the dose response models, and dose-rate dependencies have contributed to the large increase in risk estimate over this time period (1970–1997). The possibility of future changes in risk estimates can, of course, not be safely predicted today; it is possible that such changes could potentially impact NASA mission operations. Thus, protection against uncertainties is an ancillary condition to the ALARA principle, suggesting that conservatism be exercised as workers approach dose limits.

By the early 1980s, several major changes had occurred that led to the need for a new approach in defining dose limits for astronauts. At that time, NASA requested that the NCRP reevaluate the dose limits that were to be used for LEO operations. Considerations included the increases in estimates of radiation-induced cancer risks, the criteria for risk limits, and the role of the evolving makeup of the astronaut population from male test pilots to a larger, diverse population of astronauts (~100), including mission specialists, female astronauts, and career astronauts of higher ages who often participate in several missions. In 1989, NCRP Report No. 98 (NCRP, 1998) recommended age- and gender-dependent career dose limits using a 3% increase in cancer mortality as a common risk limit. This limiting level of 3% excess cancer fatality risk was based on several criteria, including a comparison to dose limits for ground radiation workers and to rates of occupational death in less-safe industries. It was noted that astronauts face many other risks, and that an overly large radiation risk was not justified. It also should be noted that the average years of life loss from radiation-induced cancer death, which is about 15 years for workers over age 40 years and 20 years for workers between age 20 and 40 years, is less than that of other occupational injuries. A comparison of radiation-induced cancer deaths to cancer fatalities in the U.S.

population is also complex because of the smaller years of life loss in the general population, where most cancer deaths occur above age 70 years.

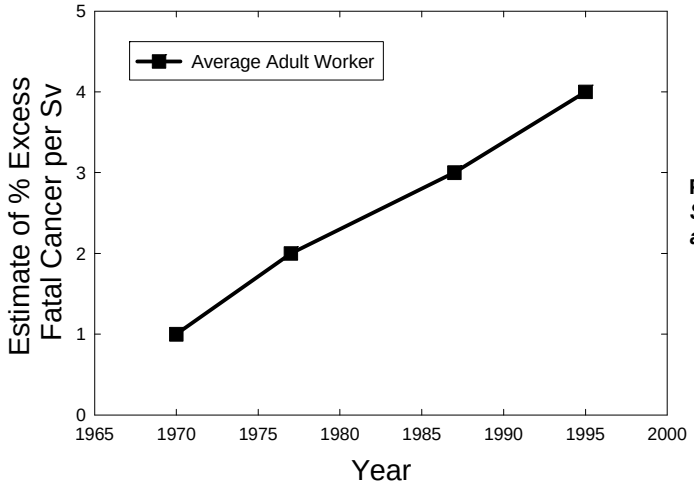


Figure 4-5. ***Estimates of the risk per Sv delivered at low dose-rates for the average adult worker from 1970 to 1997.***

In the 1990s, the additional follow-up and evaluation of atomic-bomb survivor data led to further increases in the estimated cancer risk for a given dose of radiation. Recommendations from the NCRP (NCRP, 2000), while keeping the basic philosophy of risk limitation that had been in the earlier report, advocate significantly lower limits than those that were recommended in 1989 (NCRP, 1989). Table 4-9 provides examples of career radiation limits for a career duration of 10 years, with the doses assumed to be spread evenly over the career. The values from the previous report are also listed for comparison. Both of these reports specify that these limits do not apply to Exploration missions because of the large uncertainties in predicting the risks of late effects from heavy ions.

Table 4-9. ***Career Dose Limits (in Sv) Corresponding to a 3% Excess Cancer Mortality for 10-year Careers as a Function of Age and Sex, as Recommended by the NCRP (NCRP, 1989; 2000)***

Age, year	NCRP Report No. 98		NCRP Report No. 132	
	Male (Sv)	Female (Sv)	Male (Sv)	Female (Sv)
25	1.5	1.00	0.7	0.4
35	2.5	1.75	1.0	0.6
45	3.2	2.50	1.5	0.9
55	4.0	3.00	3.0	1.7

The NCRP Report No. 132 (NCRP, 2000) notes that the use of comparisons to fatalities in the less-safe industries that were advocated by the NCRP in 1989 were no longer viable because of the large improvements that had been made in ground-based occupational safety. Table 4-10, which shows an update to such a comparison, demonstrates that, indeed, the decreased rate of fatalities in the so-called less safe industries (e.g., mining, agriculture) would suggest a limit below the 3% fatality level today as compared to that in 1989. The most recent reviews of the acceptable levels of radiation risk for LEO, including that provided during a 1996 NCPR symposium (NCRP, 1997b) and the recent NCRP Report No. 132 on the LEO dose limits (NCRP, 2000), instead advocate that comparisons to career dose limits for ground-based workers be used. It is also widely

held that the social and scientific benefits of space flight continue to provide justification for the 3% risk level for astronauts who are participating in LEO missions.

In comparison to the limits that have been set by NASA, the U.S. nuclear industry uses age-specific limits that are gender-averaged, which is of sufficient accuracy for the low doses received by nuclear workers. Here career limits are set at a total dose-equivalent that is equal to the individual's age × 0.01 Sv. It is estimated by the NCRP that ground workers who reach their dose limits would have a lifetime risk of about 3%, but note the difference in dose values corresponding to the limit is due to differences in how the radiation doses are accumulated over the worker's career. The short-term (30-day and 1-year) dose limits set by NASA are several times higher than those of terrestrial workers because they are intended to prevent acute risks, while the annual dose limits of 50 mSv (5 rem), which are followed by U.S. terrestrial radiation workers, control the accumulation of career doses.

Table 4-10. ***Occupational Death Rates (National Safety Council) and Lifetime Risks for 40-year Careers for the Less-safe and Safe Industries***

Occupation	Deaths per 10,000 Workers per year			Lifetime Risk (%) of Occupational Death		
	1977	1987	2002	1977	1987	2002
Agriculture	5.4	4.9	2.1	2.2	2.0	0.8
Mining	6.3	3.8	2.9	2.5	1.5	1.2
Construction	5.7	3.5	1.3	2.3	1.4	0.6
Transportation	3.1	2.8	1.0	1.2	1.1	0.5
Manufacturing	0.9	0.6	0.28	0.4	0.2	0.1
Government	1.1	0.8	0.26	0.4	0.3	0.1
All	1.4	1.0	0.36	0.6	0.4	0.2

The exposures that are received by radiation workers in reactors, accelerators, hospitals, etc. rarely approach dose limits with the average annual exposure of 1 to 2 mSv, which is a factor of 25 below the annual exposure limit and significantly less than the average dose for a 6-month ISS mission (100 mSv). Similarly, transcontinental pilots, although they are not characterized as radiation workers in the U.S., receive an annual exposure of about 1 to 5 mSv, and enjoy long careers without approaching the exposure limits that are recommended for terrestrial workers in the U.S. Under these conditions, ground-based radiation workers are estimated to be well below the career limits, even if a 95% CL is applied. As space missions have been of relatively short duration in the past, thereby requiring minimal mitigation, the impact of dose limits when space programs actually approach such boundaries, including the application of the ALARA principle, has been unexplored.

Summary of Approaches for Setting Acceptable Levels of Risk

The various approaches to setting acceptable levels of radiation risk are summarized below.

1. *Unlimited Radiation Risk:* NASA management, the families or loved ones of astronauts, and taxpayers would find this approach unacceptable.

2. *Comparison to Occupational Fatalities in Less-safe Industries*: The life-loss from attributable radiation cancer death is less than that from most other occupational deaths. At this time, this comparison would also be very restrictive on ISS operations because of continued improvements in ground-based occupational safety over the last 20 years.

3. *Comparison to Cancer Rates in General Population:* The number of years of life-loss from radiation-induced cancer deaths can be significantly larger than from cancer deaths in the general population, which often occur late in life (>age 70 years) and with significantly less numbers of years of life-loss.

4. *Doubling Dose for 20 Years Following Exposure:* Provides a roughly equivalent comparison based on life-loss from other occupational risks or background cancer fatalities during a worker's career; however, this approach negates the role of mortality effects later in life.

5. *Use of Ground-based Worker Limits:* Provides a reference point equivalent to the standard that is set on Earth, and recognizes that astronauts face other risks. However, ground workers remain well below dose limits, and are largely exposed to low-LET radiation where the uncertainties of biological effects are much smaller than for space radiation.

A more recent review of cancer and other radiation risks is provided by the NCRP Report No.153 (NCRP, 2006). The stated purpose of this report is to identify and describe the information that is needed to make radiation protection recommendations for space missions beyond LEO. The report contains a comprehensive summary of the current body of evidence for radiation-induced health risks, and makes recommendations on areas requiring future experimentation.

Past space missions

The radiation doses on past space missions have been well characterized using physical and biological dosimetry and radiation transport models (Cucinotta et al., 2001; 2003a; 2008). Phantom torso experiments have been performed on ISS and space shuttle (Badhwar et al., 2000; Yasuda et al., 2000; Cucinotta et al., 2008). Phantom torsos offer good evidence of the accuracy of the NASA radiation transport code, HZETRN (Wilson et al., 1995), nuclear interaction cross sections (Cucinotta et al., 2006). Organ dose and dose-equivalent predictions are shown to agree with measurements to within ±15% in most cases, as shown in Table 4-11(a) and (b) (Cucinotta et al., 2008).

Biodosimetry, which has been performed on all ISS missions as well as for four astronauts on *Mir* missions, offers an alternative evaluation of organ dose-equivalents. Figure 4-6 shows results for the pre- and post-flight frequency of translocations, which are complex aberrations involving more than two chromosomes, and total exchanges. Total exchanges are increased post-flight over pre-flight values in all cases, and translocations increase in all ISS astronauts, but they did not increase for two astronauts: one who was returning from the *Mir* space station, and one who was on a Hubble repair mission. To test whether the overall frequency of complex aberrations was increased by space radiation, Cucinotta et al. (2008) pooled results into two groups: all ISS data, and all ISS data plus results from other NASA missions. The relative frequencies for complex aberrations and translocations were shown to be highly significant ($P<10^{-4}$) (Cucinotta et al., 2008).

Figure 4-7 shows a summary of the crew doses for all NASA missions through the year 2007. The level of accuracy in effective dose determination and in the GCR environments suggests a high level of accuracy in predicting organ dose and dose-equivalencies for both lunar and Mars missions. The cancer projection model of NCRP Report No. 132 (NCRP, 2000), which can be applied to these effective doses, indicates REID values approaching 1% for many astronauts who have flown on ISS or the Russian space station *Mir* (Cucinotta et al., 2001).

Table 4-11(a). ***From Cucinotta et al. (2008): Comparison of Measured Organ Dose-equivalent for the STS-91 Mission by Yasuda et al. (2000) Using the Combined CR-39/TLD Method to HZETRN/QMSFRG Space Transport Model***

Tissue	Organ Dose-equivalent, mSv		
	Measured	HZETRN/QMSFRG	Difference (%)
Skin	4.5 ± 0.05	4.7	4.4
Thyroid	4.0 ± 0.21	4.0	0
Bone surface	5.2 ± 0.22	4.0	–23.1
Esophagus	3.4 ± 0.49	3.7	8.8
Lung	4.4 ± 0.76	3.8	–13.6
Stomach	4.3 ± 0.94	3.6	–16.3
Liver	4.0 ± 0.51	3.7	–7.5
Bone marrow	3.4 ± 0.40	3.9	14.7
Colon	3.6 ± 0.42	3.9	8.3
Bladder	3.6 ± 0.24	3.5	–2.8
Gonad	4.7 ± 0.71	3.9	–17.0
Chest	4.5 ± 0.11	4.5	0
Remainder	4.0 ± 0.57	4.0	0
Effective dose	4.1 ± 0.22	3.9	–4.9

Table 4-11(b). ***From Cucinotta et al. (2008): Comparison of Small Active Dosimetry Data from the ISS Expedition-2 Phantom Torso (July–August 2001) for Absolute Predictions for the HZETRN/QMSFRG Model. [Details on the measurement procedures are given in Badhwar et al. (2000)]***

Organ	Dose from Trapped Radiation, mGy/d		Dose from GCR, mGy/d		Total Dose, mGy/d		Difference (%)
	Expt.	Model	Expt.	Model	Expt.	Model	
Brain	0.051	0.066	0.076	0.077	0.127	0.143	13.3
Thyroid	0.062	0.072	0.074	0.077	0.136	0.148	9.4
Heart	0.054	0.061	0.075	0.076	0.129	0.137	6.7
Stomach	0.050	0.057	0.076	0.077	0.126	0.133	5.5
Colon	0.055	0.056	0.073	0.076	0.128	0.131	2.5

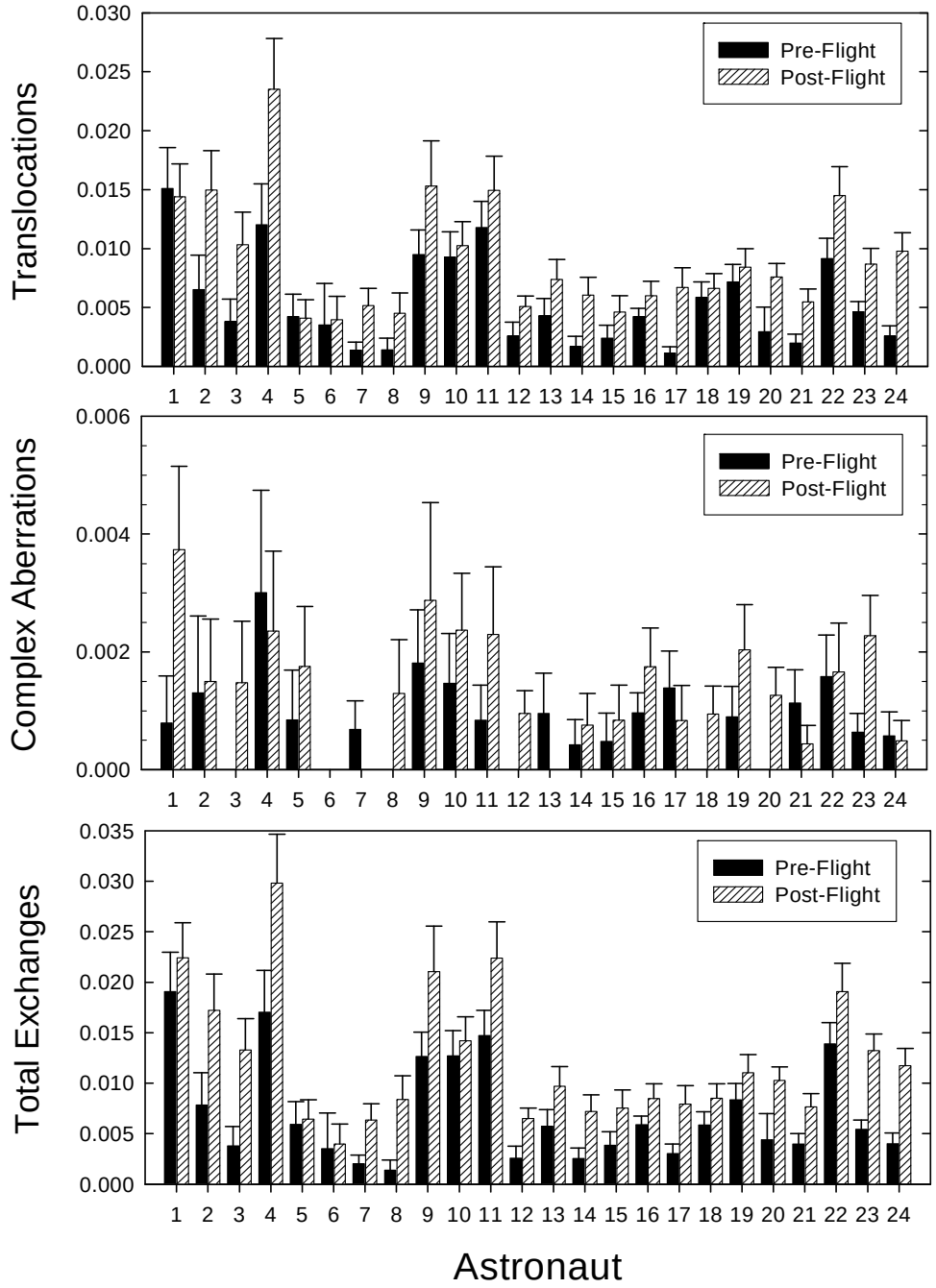


Figure 4-6. ***From Cucinotta et al. (2008): The frequency of translocations, complex aberrations, or total chromosome exchanges that is measured in each astronaut's blood lymphocytes before and after their respective space missions on ISS,*** **Mir,** ***or the space shuttle. An increase in total exchanges was observed for all astronauts. Translocations (22 of 24) and complex aberrations (17 of 24) increased in the majority of astronauts.***

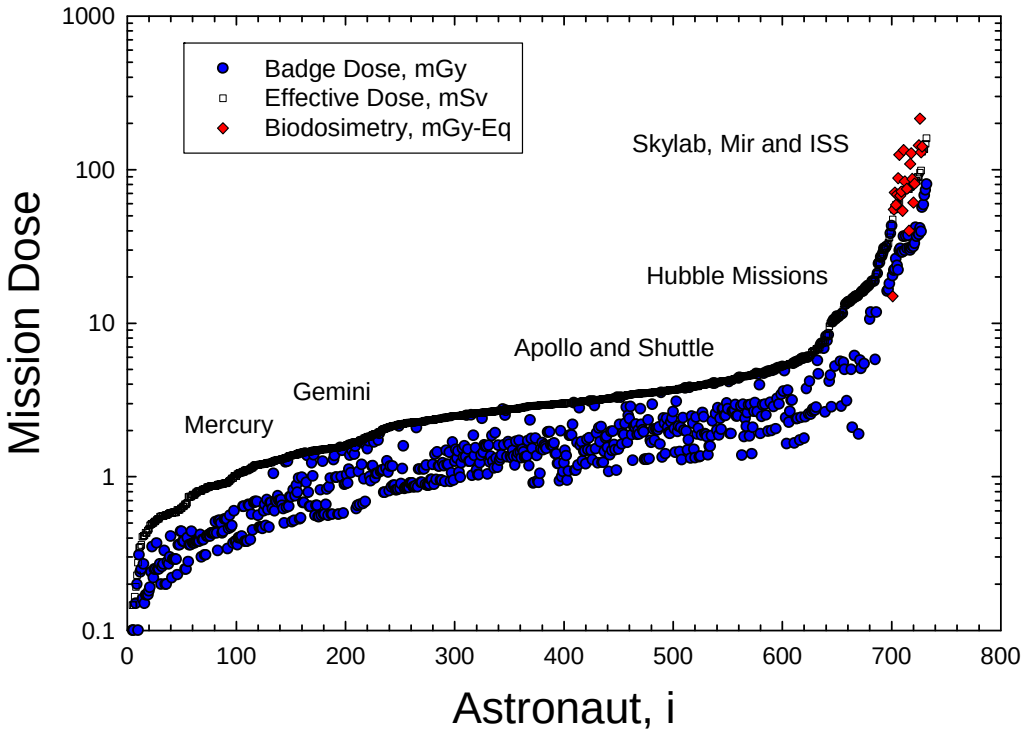


Figure 4-7. ***Summary of mission personnel dosimetry from all past NASA crews (Cucinotta et al., 2008). Effective dose and population average biological dose-equivalent for astronauts on all NASA space missions, including Mercury, Gemini, Apollo, Skylab, Apollo-Soyuz, space shuttle, shuttle-Mir, and ISS missions.***

Radiobiology evidence for protons and HZE nuclei

Studies with protons and HZE nuclei of RBEs for molecular, cellular, and tissue endpoints, including tumor induction, document the higher risk for space radiation components (NAS, 1996; NCRP, 2006; Cucinotta and Durante, 2006). This evidence must be extrapolated to the chronic conditions that are found in space and from the mono-energetic beams that are used at the NSRL and other accelerators to the complex mixed radiation types that are in space. Sufficient proof that experimental models represent cancer processes in humans, including estimating the effectiveness of shielding and biological countermeasures, must be obtained for high-risk missions where acceptable levels of cancer risks are approached or, perhaps, exceeded. Evidence and progress in these areas is described next.

Cancer Induction by Space Radiation

A necessary step for improving space radiation cancer risk assessment is to perform studies on the molecular pathways that are causative of cancer initiation and progression, and to extend these studies to learn how such pathways can be disrupted by HZE ions, including both genetic and epigenetic modifications that are noted as the hallmarks of cancer (figure 4-8). The goal of this research is to establish a more mechanistic approach to estimating risk and to answer questions, including whether HZE effects can be scaled from those of gamma rays, whether risk is linear with low dose-rate, and how individual radiation sensitivity impacts the risks for astronauts, a population that is selected for many factors related to excellence in health.

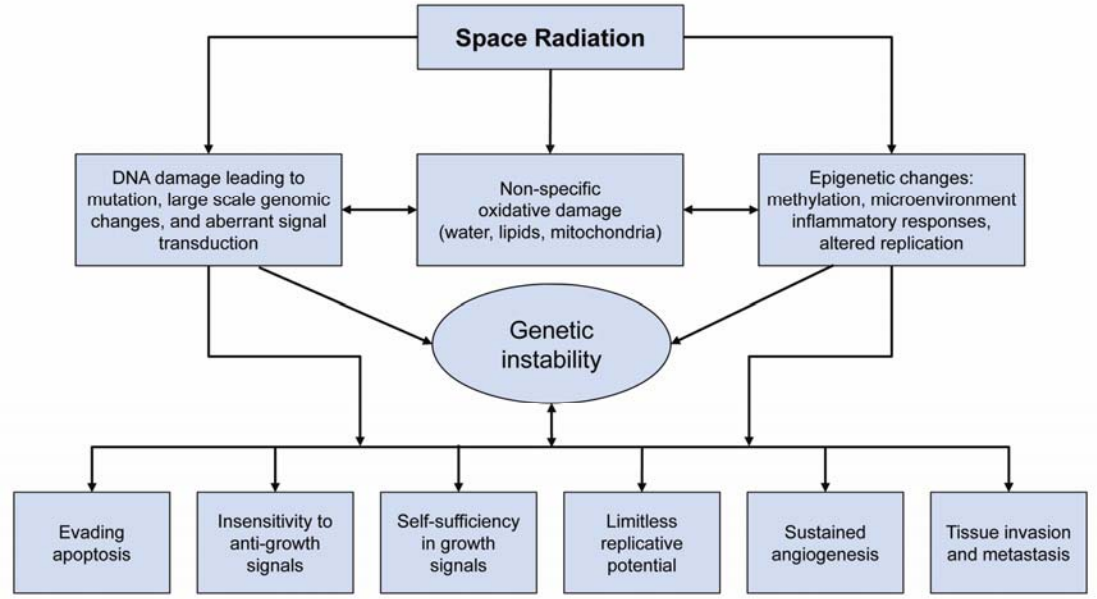


Figure 4-8. ***The hallmarks of cancer (Hanahan and Weinberg, 2000) and possible mechanisms of radiation damage that lead to these changes observed in all human tumors.***

The Initial Biological Events

Energy deposition by HZE ions is highly heterogeneous with a localized contribution along the trajectory of each particle and lateral diffusion of energetic electrons (delta rays) that are many microns from the ions path (Goodhead, 1994; Cucinotta et al., 2000b). These particles are, therefore, characterized by a high LET; however, they contain a low-LET component due to the high-energy electrons that are ejected by ions as they traverse tissue. Biophysical models have shown that the energy deposition events by high-LET radiation produce differential DNA lesions, including complex DNA breaks, and that there are qualitative differences between high- and low-LET radiation, in both the induction and the repair of DNA damage (Prise et al., 1998; Sutherland et al., 2000; Rydberg et al., 2005). The number of DNA single-strand breaks (SSBs) and DSBs that are produced by radiation varies little with radiation type; however, for high-LET radiation, a higher fraction of DNA damages are complex; i.e., clusters containing mixtures of two or more of the various types of damages (SSB, DSB, etc.) within a localized region of DNA. Complex damage is uncommon for endogenous damage or low-LET radiation, and has been associated with the increased RBE of densely ionizing radiation. The repair of DSB is known to occur through direct end-joining and homologous recombination processes. Indications are that (1) for high-LET radiation, where complex DSBs occur with high frequency, little repair occurs, leading to cell death; or (2) the mis-rejoining of unrepairable ends with other radiation-induced DSB leads to large DNA deletions and chromosome aberrations. While the high effectiveness in cell killing provides the rationale for heavy-ion cancer therapy (hadrontherapy), residual damage in surviving cells is of concern for carcinogenesis.

Chromosome damage and mutation

Heavy charged particles are very effective at producing chromosomal exchanges with RBE values exceeding 30 in interphase (as visualized using premature chromosome condensation) and 10 at the first post-irradiation mitosis for energetic Fe-ions (George et al., 2003). The detailed RBE vs. LET relationship that was found for total exchanges is similar to that of earlier studies of mutation (Kiefer et al., 1994; Kiefer, 2002) and in

vitro neoplastic transformation (Yang et al., 1985). For all of these endpoints, RBE peaks at around 100 to 200 keV/µm before it decreases at very high-LET. However, the quality of chromosome damage is different when heavy ions are compared to sparsely ionizing radiation. Large differences in gene expression are observed between X rays and HZE ions, thus reflecting differences in damage response pathways (Ding et al., 2005; Chang et al., 2005). Qualitative differences in the type of gene mutations have also been reported (Kronenberg, 1994; Kronenberg et al., 1995). Novel multicolor fluorescence painting techniques of human chromosomes have clearly demonstrated that high-LET α-particles and Fe-ions induce many more complex types of chromosomal exchanges in human cells than low-LET radiation. Most of these complex chromosomal rearrangements will ultimately lead to cell death. In fact, only a small fraction of the initial damage is transmitted in mice 2 to 4 months after the mice have been exposed to energetic Fe-ions. A low RBE for the induction of late chromosomal damage has also been measured in the progeny of human lymphocytes that were exposed in vitro to energetic Fe-ions, with the interesting exception of terminal deletions, which occurred with much higher frequency in the progeny of cells that were exposed to heavy ions compared to gamma rays (Durante et al., 2002).

Genomic instability

Genomic instability has been observed both in vitro and in vivo in the progeny of cells that are irradiated with heavy ions in several model systems (NCRP, 1997a). The presence of chromosomes that are lacking telomeres in the progeny of cells that were exposed to heavy ions is particularly interesting. Sabatier et al. (1992; 2005) found that rearrangements involving telomere regions are associated with chromosomal instability in human fibroblasts that occur many generations after exposure to accelerated heavy ions. Telomere dysfunction plays a crucial role in initiating or sustaining genomic instability, which is a major step in cancer progression. Heavy-ion-induced effects on telomere stability have also been studied using siRNA (small interfering ribonucleic acid) knockdown for components of DNA-dependent protein kinase (DNA-PK) in human lymphoblasts. Differential results were found for gamma rays and HZE nuclei, with iron nuclei being much more effective in producing DSB-telomere fusions after knockdown of DNA-PK (Zhang et al., 2005). Cells containing telomere-deficient chromosomes will either senesce or undergo breakage-fusion-bridge (B/F/B) cycles, thereby promoting genetic instability. The fate of normal cells that contain a single terminal deletion is unknown, but it has been shown that the loss of a single telomere in cancer cells can result in instability in multiple chromosomes (Feldser et al., 2003; Maser and DePinho, 2002). These recent results suggest that telomere instability could be an important early event in the pathway to cancer induction by HZE nuclei.

Cancer and tissue effects

Animal studies generally demonstrate that HZE nuclei have higher carcinogenic effectiveness than low-LET radiation. The number of studies of animal carcinogenesis with HZE nuclei is extremely limited, as summarized in Table 4-12. Relative biological effectiveness factors comparing gamma rays to HZE ions were measured in mice or rats for tumors of the skin (Burns et al., 1993) and of the Harderian (Fry et al., 1985; Alpen et al., 1993) or mammary gland (Dicello et al., 2004), reaching values as high as 25 to 50 at low doses. However, the risk and detriment of cancer will not be fully characterized until the relationship between radiation quality and latency, where tumors appear earlier after high-LET irradiation, is adequately described. The earlier latency and increasing effectiveness that is found with HZE ions that are similar to those in earlier studies with neutrons (Ullrich, 1984; Fry and Storer, 1987), together with the lack of response of gamma rays that is seen in many low-dose studies, suggests that the scaling concepts that are used in current risk assessment approaches are unable to describe important qualitative effects, and that relative biological effectiveness factors may, in principle, be indefinable or a faulty concept.

Table 4-12. ***Tumor Induction Studies with HZE Nuclei***

Tumor Model	End-point	HZE type	Reference
Mice (B6CF1)	Life-shortening	C, Ar, Fe	Ainsworth (1986)
Mice (B6CF1)	Harderian gland	He, C, Ar, Fe	Fry et al. (1985)
Mice (B6CF1)	Harderian gland	He, Ne, Fe, Nb	Alpen et al. (1993)
Rat (Sprague-Dawley)	Skin tumors	Ne, Ar, Fe	Burns (1992)
Rat (Sprague-Dawley)	Mammary tumors	Fe	Dicello et al. (2004)
Mice (carcinoma-bearing animal (CBA))	Leukemia, liver tumors	Fe, p, Si	Ullrich, in preparation

Recent studies have debated the relative importance of DNA damage and mutation or extracellular matrix remodeling and other non-targeted effects as initiators of carcinogenesis (Barcellos-Hoff et al., 2005). Tissue effects that are independent of DNA damage and that have been associated with cancer initiation or progression include genomic instability (Park et al., 2003), extracellular matrix remodeling, persistent inflammation, and oxidative damage (Mothersill and Seymour, 2004). Other studies are exploring possible relationships between radiation and the activation of dormant tumors and the modulation of angiogenesis (Folkman et al., 1989).

So-called bystander or non-targeted effects may have enormous consequences for space exploration. Non-targeted effects may lead to a supra-linear dose-response curve at low doses, perhaps reducing the effectiveness of spacecraft shielding; but it may also provide protection by removing damaged cells from the organism. Both effects challenge the conventional linear no-threshold risk model assumption, which is currently adopted for radioprotection on Earth and in space. These effects also suggest important targets for biological countermeasures that are likely to be more effective than are countermeasures that target DNA damage.

Results in tissues suggest that differences in biological response between high and low LET differ depending on the model context that is considered (i.e., 2D vs. 3D vs. animal). As a result of the many types of particles, energies, and doses of interest that are in space, extensive animal experimentation has been prohibited by costs in the past. More recently, however, studies in 3D human coculture are proving to be an effective method with which to study cancer risks in a more realistic context (Barcellos-Hoff et al., 2005; Riballo et al., 2004).

Models of Cancer Risks and Uncertainties

Life-table methodology

The double-detriment life-table is the approach that is recommended by the NCRP (NCRP, 2000) to estimate radiation cancer mortality risks. In this approach, the age-specific mortality of a population is followed over its entire life span with competing risks from radiation and all other causes of death described (Bunger et al., 1981). For a homogeneous population receiving an effective dose E at age aE, the probability of dying in the age-interval from a to $a+1$ is described by the background mortality-rate for all causes of death, $M(a)$, and the radiation cancer mortality rate, $m(E,a_E,a)$, as

$$q(E,a_E,a) = \frac{M(a)+m(E,a_E,a)}{1+\frac{1}{2}[M(a)+m(E,a_E,a)]} \quad (7)$$

The survival probability to live to age, *a,* following an exposure, E, at age, a_E, is

$$S(E, a_E, a) = \prod_{u=a_E}^{a-1} [1 - q(E, a_E, u)] \quad (8)$$

The excess lifetime risk (ELR), which is the increased probability that an exposed individual will die from cancer, is defined by the difference in the conditional survival probabilities for the exposed and the unexposed groups as

$$ELR = \sum_{a=a_E}^{\infty} [M(a) + m(E, a_E, a)] S(E, a_E, a) - \sum_{a=a_E}^{\infty} M(a) S(0, a_E, a) \quad (9)$$

A minimum latency-time of 10 years is often used for low-LET radiation (NCRP, 2000); however, alternative assumptions should be considered for high-LET radiation. The REID, which is the lifetime risk that an individual in the population will die from a cancer that is caused by his or her radiation exposure, is defined by

$$REID = \sum_{a=a_E}^{\infty} m(E, a_E, a) S(E, a_E, a) \quad (10)$$

In general, the value of the REID exceeds that of the ELR by about 10% to 20%. Vaeth and Pierce (1990) have discussed cases in which the ELR is ill-defined and suggested that the REID is the preferred quantity for radiation protection. The loss of life-expectancy among exposure-induced-deaths (LLE-REID) is defined by (Vaeth and Pierce, 1990)

$$LLE - REID = \frac{LLE}{REID} \quad (11)$$

where the average loss of life-expectancy, *LLE*, in the population is defined by

$$LLE = \sum_{a=a_E}^{\infty} S(0, a_E, a) - \sum_{a=a_E}^{\infty} S(E, a_E, a) \quad (12)$$

Radiation Carcinogenesis Mortality Rate

For projecting lifetime cancer fatality risks, an age- and gender-dependent mortality rate per unit dose, which is estimated for acute gamma-ray exposures, is multiplied by the radiation quality factor and reduced by the DDREF (NCRP, 2000). The additivity of effects of each component in a radiation field is assumed. Radiation mortality rates are largely modeled using the Japanese atomic-bomb survivor data. For transferring risks from the Japanese to the U.S. population, two models are often considered. A multiplicative transfer model assumes that radiation risks are proportional to spontaneous or background cancer risks. The additive transfer model assumes that radiation risk acts independently of other cancer risks. However, the NCRP (NCRP, 2000) recommends that a mixture model be used that contains fractional contributions from the multiplicative risk model or additive risk model. The radiation mortality rate is

$$m(E, a_E, a) = [\nu ERR(a_E, a) M_c(a) + (1-\nu) EAR(a_E, a)] \frac{\sum_L Q(L) F(L) L}{DDREF} \quad (13)$$

where the *ERR* and *EAR* are the excess relative risk and excess additive risk per Sievert, respectively, $M_c(a)$ is the gender- and age-specific cancer mortality rate in the U.S. population, *F* is the tissue-weighted fluence, and *L* is the LET. In Eq(13), ν is the fractional division between the assumption of the multiplicative and additive risk transfer models. For solid-cancer, it is assumed that ν=1/2; for leukemia, it is assumed that ν=0.

Uncertainties in the Projection Model

Equation (13) consists of a product of several factors: the *ERR* or *EAR*, the background cancer rates, M_c, the effective dose represented by the physical dose, *F(L)*, times the radiation quality factor, *Q(L)*, and the dose and dose-rate reduction factor, *DDREF*. The limiting behavior of the addition of many random variables is well known as the normal distribution. In contrast, the limiting behavior of the multiplication of many random factors will be a log-normal distribution. Equation (7) assumes that each multiplicative factor is independent. This assumption may not be strictly valid, however, because of the possible correlations between factors or non-additivity of different radiation components, since the cells will be traversed by multiple particles and delta rays that are produced by ions passing through adjacent cell layers (Cucinotta et al., 1998b). As the risk for longer-duration missions exceeds a few percent, the upper 95% C.I.s may exceed 10%. In such cases, the Monte-Carlo sampling of mortality rates to estimate uncertainty bands is insufficient, and the expression for the REID that is given by Eq(10) must be used because of competing risks from other causes of death that will reduce the likelihood of very large radiation risks. Therefore, in the sampling approaches that are described below, trials are accumulated for the REID rather than the mortality rate. A criteria that is used to formulate probability distribution functions (PDFs) for various factors is to ensure that the PDFs are peaked at the values that are recommended by the NCRP (NCRP, 2000), such as the DDREF and Q, or in the current physics models of radiation environments and transport that are used in mission projections or spacecraft designs. We next discuss the uncertainties in the projection model.

Uncertainties in Low-LET Epidemiology Data

For Monte-Carlo sampling purposes, the low-LET mortality-rate per Sievert, m_l, is written

$$m_l(E, a_x, a) = \frac{m_0(E, a_x, a)}{DDREF} \frac{x_D x_s x_T x_B}{x_{Dr}} \quad (14)$$

where m_0 is the baseline mortality rate per Sievert (see Eq(13)) and the x_α are quantiles (random variables) whose values are sampled from associated PDFs, $P(x_\alpha)$. Note that the DDREF applies only to the solid cancer risk and not to the leukemia risk under the stated assumptions. The NCRP Report No. 126 (NCRP, 1997a) defines the following subjective PDFs, $P(x_\alpha)$, for each factor that contributes to the acute low-LET risk projection:

1. $P_{dosimetry}$ represents the random and systematic errors in the estimation of the doses received by atomic-bomb blast survivors. It is assumed as a normally distributed PDF for bias correction of random and systematic errors in the dosimetry (DS86) with mean 0.84 and standard deviation 0.11.

2. $P_{statistical}$ represents the distribution in uncertainty in the point estimate of the risk coefficient, r_0. It is assumed as a normally distributed PDF with a mean of 1 and a standard deviation of 0.15.

3. P_{bias} represents any bias resulting for over- or under-reporting cancer deaths. P_{bias} is assumed as a normal distribution with a most probable value of 1.1 and a 90% C.I. from 1.02 to 1.18 corresponding to a standard deviation of 0.05.

4. $P_{transfer}$ represents the uncertainty in the transfer of cancer risk following radiation exposure from the Japanese population to the U.S. population. Both additive and relative risk models were considered by NCRP Report No. 126 (NCPR, 1997a) in assessing the uncertainties in such transfer. $P_{transfer}$ is log-normal with a mean of 1 and a standard deviation of 0.26 (geometric standard deviation (GSD)=1.3).

5. P_{Dr} represents the uncertainty in the knowledge of the extrapolation of risks to low dose and dose-rates, which are embodied in the DDREF. The NCRP assumes P_{Dr} to be a truncated triangle distribution starting at 1 and ending at 5 with a peak at 2 and a relative value of 1/4 or 1/2 at 1 or 5, respectively, compared to the peak values for the DDREF at 2. This PDF is used to scale the low-LET risk coefficient (mortality rates) in our estimates for space radiation.

The NCRP also considered a PDF for bias correction to project cancer risks over a lifetime. It is ignored herein because the astronaut population is generally over age 30 years and the Japanese data are now complete for these ages. We also ignore the assumed "unknown uncertainties" from NCRP Report No. 126 (NCRP, 1997a).

Uncertainties due to Dose-Rate and Protraction Effects for Ions

For a low dose-rate and protracted proton and HZE radiation exposure of more than a few months, new biological factors may influence risk assessments, including redistribution in the cell cycle, repopulation, or promotional effects, especially when particle fluences are sufficiently large to lead to multiple hits of target cells or surrounding cells and tissue environments. Not only are there no human data for protons and HZE ions, there are also very little experimental data at low dose-rates for these particles. Confidence in using radio-epidemiological data for acute (atomic-bomb survivors) or fractionated (patient) data is decreased when it is applied to protracted exposure. Experimental data for protracted proton or heavy ion irradiation in experimental models of carcinogenesis are almost nonexistent. Burns et al. (1994) found that split doses of argon ions that were separated by a few hours up to 1 day increased the risk of skin cancer in rats. Alpen et al. (1994) found that for Harderian gland tumors in mice, using seven 2-week fractions of 0.07 Gy of iron increased risk by 50% as compared to a single acute dose of 0.4 Gy. A study of chromosomal aberrations in human lymphocytes (George et al., 2001), for both acute and low dose-rates (0.08 Gy/hr) with 250 MeV protons, showed less sparring than was found for gamma rays. The Skyhook study (Ainsworth et al. (1986)) considered life-shortening in mice by comparing single acute with weekly fractions of several ions, but the results were unclear with regards to any increase or decrease in risk.

A good number of studies for cancer induction or life-shortening in mice exist for gamma rays and neutrons; these studies show both sparring effects for gamma rays and that neutron effects may be increased due to protraction under certain conditions in some tissues (Ullrich, 1984; NCRP, 1990). Important questions related to the differences in life span, cell turnover rates, or the mechanisms of initiation or promotion in humans and mice make estimates of the effects of protraction on risk difficult. If protraction effects do increase the risk from high-LET radiation, such effects would be more important for a Mars mission than for the shorter lunar missions. In space, each cell will be traversed about every 2 to 3 days by a proton or delta ray that is produced by ions in adjacent cells, and with a decreasing frequency of from weeks to months as the charge of the HZE nuclei increases (Cucinotta et al., 1998b). Studies of mixed-fields of protons and HZE ions are needed to understand the uncertainties in dose-rate and protraction effects from space radiation. Uncertainties that

are related to radiation quality, dose-rate, and protraction could lead to correlations that will be difficult to describe when based on limited experimental data. Methods to treat correlation effects will be needed when the data on protraction effects become available.

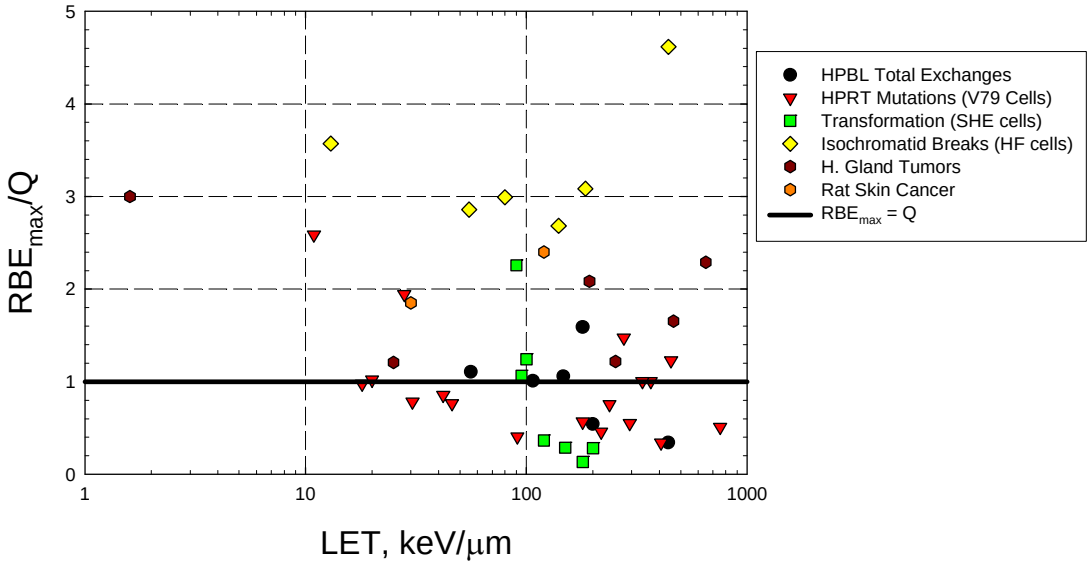
Radiation Quality and Latency or Temporal Patterns of Risk

An additional radiation quality uncertainty is introduced by the scaling assumption that is used in Eq(13) because the time dependence for low- and high-LET radiation is assumed to be identical. Data on tumors or genomic instability in mice with neutrons (Ullrich, 1984; Ulrich and Ponnaiya; NCRP, 1990) and the studies of rat or mammary carcinogenesis with HZE nuclei (Burns et al., 1994; Dicello et al., 2004) suggest that the latency time is appreciably reduced for high-LET radiation compared to low-LET radiation. Sparse data are available to estimate the impact of these differences on uncertainties. A radiation quality-dependent latency is more important in the additive transfer model than in the multiplicative transfer model, especially at younger ages of exposure. We ignore these uncertainties, however, and replace the 10-year minima latency assumption that is made for low LET with the step-in latency model (Pierce et al., 1996) that is used for the leukemia risk. The effects of these assumptions will need to be addressed when data and knowledge on underlying mechanisms become available.

Uncertainties in Quality Factors

Radiation quality factors represent the largest uncertainty when estimating space radiation cancer risks. Past reviews on the relative biological effectiveness of high-LET radiation include International Commission on Radiation Units (ICRU) Report No. 40 (1986), NCRP Report No. 104 (1990), and, more recently, ICRP Report No. 92 (2003). The practice of assigning radiation quality factors that are followed by committees considers an average of the RBE factors at low doses (RBE_{max}) for the most relevant experimental endpoints. Uncertainties in the assignment of RBEs for protons and heavy ions arise for several reasons, including sparseness of data for tumorigenesis in animal models, surrogate tissue, or cellular endpoints; variability in reference radiation and doses and dose-rates employed; and lack of data over the LET range of interest. Linearity at low dose or dose-rates for the reference radiation or ions also is often not sufficiently established in experiments. Statistical limitations frequently hinder studies at the low dose-rates of interest for space radiation protection. For high-LET radiation, a turnover or bending that is found in the dose response for tumor induction and neoplastic transformation is observed at moderate doses, thus presenting further uncertainties in estimating the effectiveness of high-LET radiation at low dose-rates.

Figure 4-9 provides representative examples of the ratio of RBE_{max} to Q for mouse tumors, cell transformation or mutations, or cytogenetic endpoints. The ratio is often two to three times higher or lower than unity, which indicates the expected deviation from Q in available data.



HPBL – human peripheral blood leukocyte; HPRT – hypoxanthine-guanine phosphoribosyltransferase; SHE – Syrian hamster embryo; HF – human fibroblast

Figure 4-9. ***Comparison of ratio of* RBE$_{max}$ *to* Q *for several endpoints found with proton, α-particle, and heavy ion irradiations (reference experiments listed in Table 4-1).***

Table 4-13 shows the LET values at the maximum RBE that was found in past studies that were selected from experiments in which more than five ions were employed. Large deviations from the Q peak at 100 keV/µm are observed in these experiments, with a range from about 50 to 190 keV/µm for the peak. These data are largely derived from the facilities at Berkeley, Calif., Darmstadt, Germany, Chiba, Japan, and the Alternating Gradient Synchrotron (AGS), Brookhaven National Laboratory, Upton, N.Y. The number of past studies and endpoints that were used are limited if they are viewed as surrogate endpoints for human carcinogenesis. Additional data for more appropriate endpoints should become available in the next few years from the NSRL. Track structure models suggest that each ion species would have distinct RBE curves that are of similar shape, with curves for lower-charge ions peaking at a lower LET than for higher-charged ions (Katz et al., 1971; Cucinotta et al., 1996; Nikjoo et al., 1999). Furthermore, above about 1 MeV/u, lower-charged ions have a higher biological effectiveness than higher-charged ions of identical LET. Based on track structure models, we expect that the data sets that consider only a few ions are insufficient for defining the radiation quality dependence of *Q*. LET response curves also are predicted to depend on the target size (e.g., for gene or chromosome region) and intrinsic radiation sensitivity, which includes competition with cell death. These factors likely vary between tissues.

Table 4-13. ***Approximate LET in which Maximum RBE Was Found in Biological Experiments***

Biological System	Endpoint	LET at Peak RBE, keV/µm	LET range (no. of ions studied)	Reference
Human TK6 lymphoblasts cells	TK (triose-kinase) mutants	60	32–190 (6)	Kronenberg (1994)
Human TK6 lymphoblasts cells	HPRT mutants	60	32–190 (6)	Kronenberg (1994)
Human lung fibroblasts	HPRT mutants	90	20–470 (9)	Cox and Masson (1979)
Human skin fibroblasts	HPRT mutants	150	25–920 (7)	Tsuoboi et al. (1992)
V79 Chinese hamster cells	HPRT mutants	90	10–2,000 (16)	Kiefer et al. (1994); Belli et al. (1993)
Caenorhabditis elegans	Recessive lethal mutations	190	0.55–1,110 (14)	Nelson et al. (1989)
Human lymphocyte cells	Chromosomal exchanges	147	0.4–1,000 (10)	George et al. (2003)
Human fibroblast cells	Chromatid breaks	80–185	13-440 (6)	Kawata et al. (2001)
C3H10T1/2 mouse cells	Transformation	140	10–2,000 (10)	Yang et al. (1989)
C3H10T1/2 mouse cells	Transformation	90	20–200 (10)	Miller et al. (1995)
SHE cells	Transformation	90	20–200 (8)	Martin et al. (1995)
Mouse ($B6CF_1$)	H. gland tumors	185*	2–650 (6)	Fry et al. (1985)
Mouse ($B6CF_1$)	H. gland tumors	193	0.4–1,000 (7)	Alpen et al. (1993)
Mouse ($CB6F_1$)	Days life lost	52*	50–500 (6)	Ainsworth (1986)

*Track-segment or spread-out Bragg peak (SOBP) irradiations.

To account for the uncertainties in quality factors, Cucinotta et al (2006) recommend a trial function that has a shape that is guided by both experimental data and biophysical models, and a sample from distributions of parameters that enter into the functional form. The *Q(L)* trial function is defined as

$$Q_{trial}(L) = \begin{cases} 1 & L < L_0 \\ AL - B & L_0 \le L < L_m \\ C / L^p & L \ge L_m \end{cases} \quad (15)$$

The values of L_0, L_m, and p, and the maximum value, $Q_m(L_m)$, which are derived from the PDFs, are described below. Using Eq(15), one can solve for the values of the constants A, B, and C. Often-discussed issues on the definition of *Q(L)*, as embodied in Eq(15), are the value of the slope *p* that controls the decrease in *Q(L)* above a maximum, the maximum value of *Q(L)*, the LET where the maximum occurs, L_m, and the minimum LET where *Q(L)* rises above unity, L_0. We note that the ICRP-60 (ICRP 1991) Q-function corresponds to L_0=10 keV/µm, L_m=100 keV/µm, p = 0.5, and Q_m=30 such that A=0.32, B=2.2, C=300, and the ICRP-26 Q-function, L_0=3.5 keV/µm, L_m=172.5 keV/µm, p = 0, and Q_m = 20.

The parameter samplings are based on the following assumptions for PDFs:

a. L_0: equal probability between 5 and 10 keV/µm, and decreasing to zero at 1 keV/µm, or above 15 keV/µm.
b. L_m: equal probability for LET values between 75 and 150 keV/µm, and decreases to zero at 50 keV/µm or above 250 keV/µ m.
c. p: equal probability between p = 1/2 and 1, and decreasing to zero at p<0 or p>2.
d. Q_m: log-normal distribution with a mean value of 30 and a geometric standard deviation (GSD) of 1.8.

Figure 4-10 shows examples of trial *Q(L)* functions that contribute in the sampling procedures, and figure 4-11 shows the resulting average *Q(L)* and 95% C.I. after 20,000 trials. The resulting range is smaller than in the previous Cucinotta et al. report (2001b); however, it should be a reasonable estimate when the effects of dose protraction are not included in the uncertainty analysis.

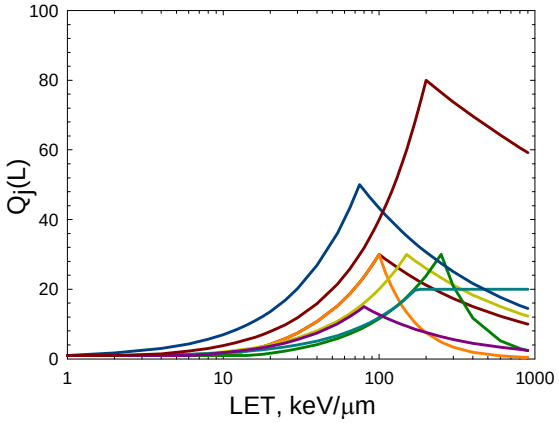


Figure 4-10. ***Examples of trial quality factor functions used in uncertainty calculations. A distinct curve is generated for each trial.***

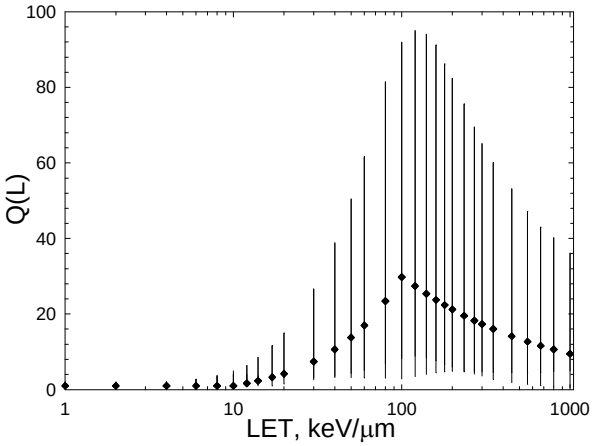


Figure 4-11. ***Average quality factor (circles) and 95% C.I.'s vs. LET that is derived from Monte-Carlo sampling over trial function of Eq(15).***

Uncertainties in Physics: Environments and Transport Codes

Space dosimetry and radiation transport codes have been studied extensively in the past, and although no major scientific questions led to errors in the assessment of space radiation environments, there are uncertainties due to the limitations in the dosimetry that was flown on past space missions. For application of computational models, the level of detail that has been used in transport code comparisons is often limited,

with common simplifications including the use of an aluminum-equivalent shielding approximation, simplified geometries, and no description of orientation effects. Approaches to assess errors in space dosimetry include the inter-comparison of different dosimetry on the same missions and to the results of space radiation transport models. Although statistical errors in the assessment of physical doses are quite small (<5%), the inter-comparisons between laboratories have shown differences on the order of 10% for absorbed dose (Badhwar, 1997). Comparisons of transport calculations to measurements of LET spectra or dose equivalencies should consider the response functions of different detector types to charged particles or neutrons (Nikjoo et al., 2002). Commonly used detectors are TEPCs, silicon detectors, and CR-39 plastic track detectors. Good agreement has been found in the limited number of comparisons that have been made (e.g., Badhwar and Cucinotta, 2000; Kim et al., 2003; Shinn et al., 1998), especially when detector response functions are represented in the comparisons.

Models of the GCR environment rely on the large number of space flight and balloon measurements that have been made, and apply the diffusion theory of Parker (1965) to describe the modulation of the GCR over the solar cycle. The root mean square error for GCR environmental models is less than 7% for the major GCR elements and less than 12% for most minor elements (Badhwar and O'Neill, 1994a; Badhwar et al., 1994b; O'Neill, 2005). Data from the advance composition explorer (ACE) are further improving these models (figure 4-12).

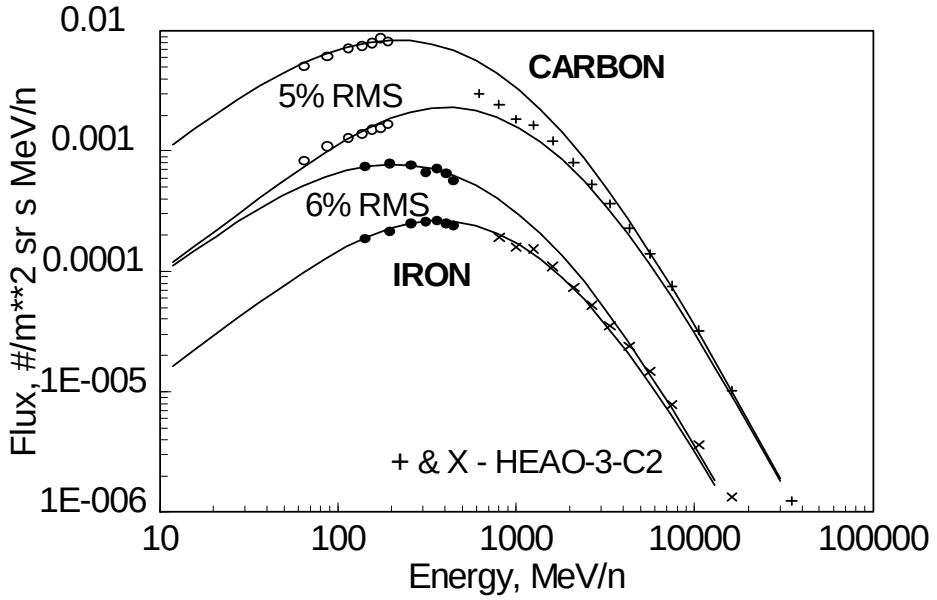


Figure 4-12. ***From O'Neill (2005) Differential flux energy spectra near solar minimum and maximum for two of the more-abundant elements, typical of the better fits. The symbols represent the measured values that are described in O'Neill (2005) and lines in the Badhwar-O'Neill GCR model.***

The isotopic composition of the GCR is also represented in the transport codes (Cucinotta et al., 2003b) that are used in risk calculations. Solar particle event spectra vary from event to event, and there is no method that is available to predict the fluence, energy spectra, or dose-rates of a future event. In this chapter, we discuss calculations for the large SPE of August 1972. Transport codes rely on databases for nuclear interaction cross sections, including inclusive single differential in energy or total fragment production cross sections for projectile

fragments, as well as double differential in energy and angle for lighter mass secondaries (i.e., neutrons, H-ions and He-ions, and mesons). Cross-section data are sparse for some projection-target combinations and in the number of energies, especially above 1,000 MeV/u. Three-dimensional aspects of transport from angular scattering, which is a small correction for high-energy ions, are expected to be an important correction for neutrons and other light mass ions. Computer codes that use multigroup methods or Monte-Carlo simulations to describe angular effects on neutron transport have been developed for GCR shielding applications. The Monte-Carlo codes are limited by the computational times that are needed to describe spacecraft with thousands of parts, and the multigroup methods are limited by the ability to describe complex geometries. However, because flight measurements and the results of the HZETRN code (Wilson et al., 1995) using the Badhwar-O'Neill GCR input spectra (Badhwar and O'Neill, 1994) and QMSFRG (quantum multiple scattering fragmentation) nuclear interaction data base (Cucinotta et al., 2003a) are in good agreement, it is unclear whether such developments will have an important impact on risk assessment.

Differences between transport models and flight dosimetry that account for the response of the detector to different radiation components are generally small, with absolute differences within 10% for the GCR dose and 20% for the GCR dose-equivalent (Badhwar, 1997; Badhwar and Cucinotta, 2000 Cucinotta et al., 2000b; Cucinotta et al., 2003b). However, measurements of dose or dose-equivalent may not provide sufficient information on possible errors in predicting the LET spectra because compensating errors can occur. Neutron spectra also are difficult to assess within complicated spacecraft and tissue geometries. In particular, measurements or calculations of neutron spectra are expected to lead to uncertainties in LET spectra in the LET range from about 30 to 300 keV/μm where recoil nuclei deposit the majority of the energy. Neutrons also cause a low-LET gamma-ray component that is often ignored in calculations. Larger errors are expected at a higher LET, where stopping nuclei, which may be difficult to define due to local tissue variations, dominate. We expect uncertainties to be larger at high-LET values, where the role of local target recoils and stopping GCR primaries are difficult to describe.

The PDFs for the uncertainties in LET spectra should ensure that the resulting dose-equivalent is consistent with the transport code comparisons to past space flight measurements for GCR. A quantile, x_L, which is associated with a normal distribution, $P_F(x_F=F/F_0)$ – where x_F is the ratio of sampled estimate of the fluence, F, to the point estimate, F_0, from the HZETRN code – is used with a standard error that increases with LET to represent the higher uncertainties that are expected for prediction of neutron effects and the difficulty in precisely defining stopping ions in complex geometries. The PDF is given a median of x0F=0.65 to ensure that the resulting dose-equivalent is in agreement with values from prior comparisons between the transport codes and flight measurements that were cited above. Standard deviations for different LET regions are given in Table 4-14 (right).

Table 4-14. ***Standard Deviations for Uncertainties in Model LET Spectra for Several LET Regions***

LET Interval	SD for dF/dL
< 30 keV/μm	1.0
30–300 keV/μm	2.0
> 300 keV/μm	2.5

Figures 4-13 and 4-14 illustrate the errors that are assigned to environmental and physical factors in evaluating LET spectra at tissue sites.

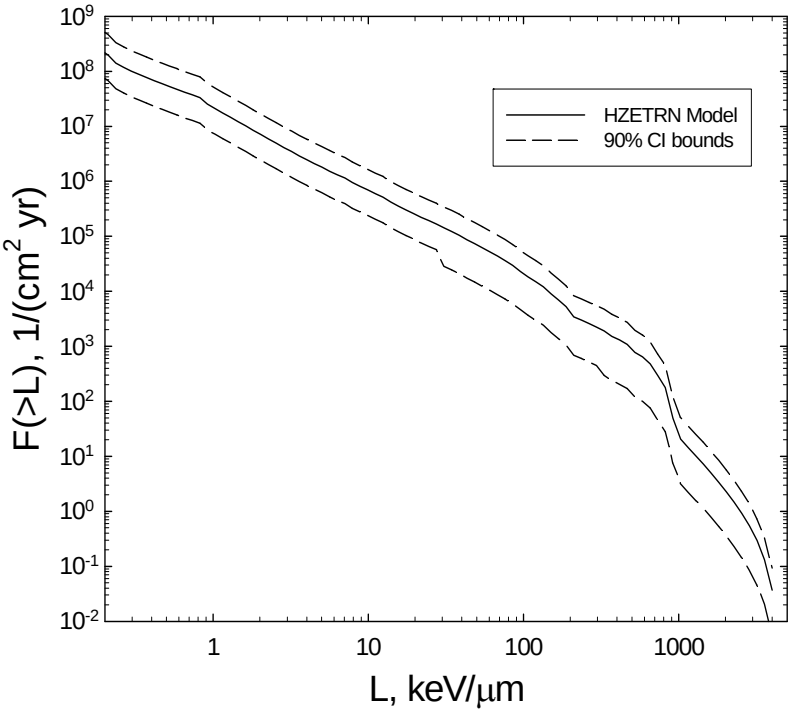


Figure 4-13. ***Calculation of tissue-weighted integral LET spectra and 90% C.I. for space environmental and transport uncertainties for a 20-g/cm^2 aluminum shield for 1 year in deep space.***

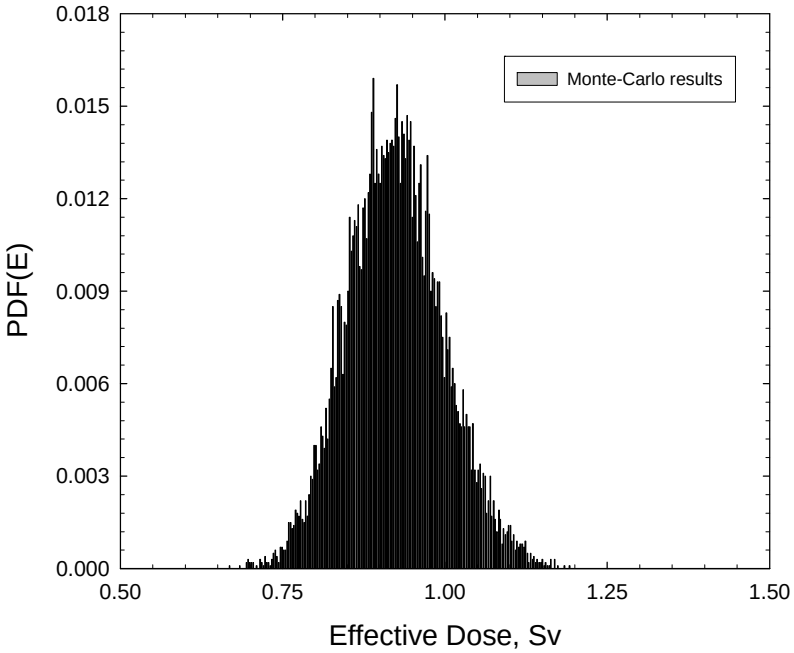


Figure 4-14. ***PDF for GCR effective dose for 20-g/cm^2 aluminum shield for 600-d Mars swing-by mission. The point estimate is 0.86 Sv, and the 95% C.I. for uncertainties in LET distribution at tissue sites is [0.78, 1.08] Sv. Only uncertainties in physics are included.***

Uncertainties due to Life-tables and Population Cancer Rates

Although radiation risk calculations are based on population data, they are used to estimate risks for individuals. Population data reflect gender differences, but also change with calendar year and often are used to make projections far into the future. For the astronaut population, the appropriateness of using the U.S. average population in making projections can be questioned because the so-called "healthy worker" effect is expected for astronauts. In the average U.S. population, females have longer life spans than males, partly due to their overall lower risk of cancer. The formalism of Eq(7) through Eq(13) shows two counteracting effects arising when one attempts to determine whether the use of population rates that are representative of a healthier population compared to the U.S. population would decrease or increase the risk of radiation carcinogenesis.

First the population survival function acts to decrease radiation risks, especially at older ages. An improved survival function that acts alone will, therefore, increase the risk from radiation. However, an improved survival function also suggests lower background cancer rates, which makes up some fraction of the delay in mortality. In the multiplicative transfer model, radiation risks are reduced if a healthy worker effect is due, in part, to a reduced natural incidence of cancer. Thus, the portions of the risk transfer that are assigned to multiplicative and additive transfer act in opposition if a healthy worker effect is present.

In a model where a geometric average of these two models is used, we expect a minor change if an improved life-table and background cancer rates are assumed. The role of the survival function is also reduced if solid cancers would display a plateau at long times after exposure (>30 years), as has been suggested in some studies (Preston et al., 2003). This discussion points to the need for better understanding of the biological basis for risk transfer models and dependence of risk after long follow-up times. Cucinotta et al. (2006) considered projections of life expectancy that were made by the Social Security Administration (SSA, 2006) and differences in rates between males and females to estimate errors in the life-table formalism. Uncertainties, which can be on the order of 25%, will increase if healthy worker effects are estimated. As these uncertainties are greater than those of the space environmental models and are at about the same level of uncertainty that was estimated for radiation transport codes, they should not be ignored.

Risk in Context of Exploration Mission Operational Scenarios

The accuracy of GCR environmental models, transport codes, and nuclear interaction cross sections, as described above, allow NASA to make predictions of the space environments and organ exposures that will be encountered on missions to the moon or Mars. However, major questions arise due to the lack of knowledge on biological effects. For cancer risk projections, propagating individual uncertainties in factors that enter risk model calculations is used to place reasonable bounds on the cancer risks that will be encountered.

Figure 4-15 shows predictions for the Mars surface. In this figure, the upward neutron flux, which is not included, is judged to carry the largest uncertainty in physics models for exploration. The variation in doses is due to the variation in atmospheric height at different geographic locations (Saganti et al., 2004).

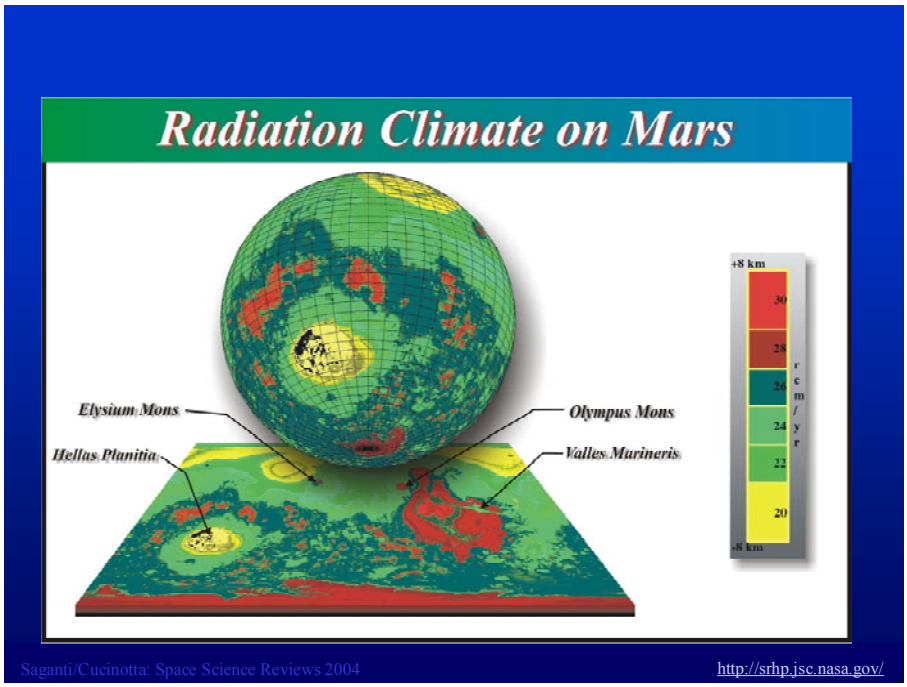


Figure 4-15. ***From Saganti et al. (2004) Predictions of skin dose-equivalent as a function of position on the Mars surface. Atmospheric data are taken from the MOLA [Mars orbiter laser altimeter] experiment.***

PDFs for space exploration missions

The cancer risk projection for space missions is found by folding predictions of the tissue-weighted LET spectra behind spacecraft shielding, dF/dL, with the radiation cancer mortality rate to form a rate for a trial J.

$$m_J(E,a_E,a) = m_{IJ}(E,a_E,a)\int dL\frac{dF}{dL}LQ_{trial-J}(L)x_{L-J} \tag{16}$$

(Not shown are the quantiles that are associated with the low-LET mortality rate.) Alternatively, particle-specific energy spectra, $F_j(E)$, for each ion, j, can be used.

$$m_J(E,a_E,a) = m_{IJ}(E,a_E,a)\sum_j\int dEF_j(E)L(E)Q_{trial-J}(L(E))x_{L-J} \tag{17}$$

The result of Eq(16) or Eq(17) is then inserted into the expression for the REID of Eq(10). In implementing a numerical procedure, we group the PDFs that are related to the risk coefficient of the normal form, which consist of the dosimetry, bias, and statistical uncertainties, into a combined PDF, P_{cmb}(x). After accumulating sufficient trials (~10^5), the results for the REID estimates are binned, and the median values and confidence intervals are found.

We use the χ^2 test for determining whether the PDFs for two distinct shielding configurations or materials are significantly different. We denote the calculated PDFs for a REID of R_i for two configurations or materials as

$p_1(R_i)$ and $p_2(R_i)$, respectively. Each $p(R_i)$ follows a Poisson distribution with variance, $\sqrt{p(R_i)}$. The chi-squared, χ^2 test for n-degrees of freedom characterizing the dispersion between the two distributions is then

$$\chi^2 = \sum_n \frac{[p_1(R_n) - p_2(R_n)]^2}{\sqrt{p_1^2(R_n) + p_2^2(R_n)}} \quad (18)$$

Once χ^2 is determined, the probability P(n, χ^2) that the two distributions are the same is calculated. If χ^2 is sufficiently large such that P(n, χ^2) is less than about 20%, this indicates that we can conclude that the two distributions lead to distinct cancer risks from GCR and/or SPEs, with the material with the lowest mean and upper 95% CL values preferred for radiation protection. However, the opposite result indicates that either the materials are approximately the same, or that the uncertainties in risk models prevent us from concluding that either configuration or material is superior in radiation protection properties. We therefore evaluate χ^2 for the LET-dependent parts of the uncertainties (i.e., quality factors and physics) separately, as only these contributions explicitly depend on the modification of radiation fields by shielding. Tables 4-15 and 4-16 show fatal cancer risk projections at solar minimum for males and females of age 40 years at the time of the mission. Cancer morbidity risks that are about 50% higher than mortality risks are described here. Calculations are made for minimally shielded spacecraft of 5-g/cm^2 aluminum and a heavily shielded spacecraft of 20 g/cm^2. Similar calculations that are near solar maximum are shown in Tables 4-17 and 4-18; an SPE fluence that is equivalent to the August 1972 SPE is assumed to have occurred. At solar minimum, it is seen that a four-fold addition of mass reduces the cancer risk by only about 15%.

Table 4-15. ***Calculations of Effective Doses, REID, and 95% C.I. for Lunar or Mars Missions. Calculations Are at Solar Minimum for a 5-g/cm^2 Aluminum Shield***

Exploration Mission	D, Gy	E, Sv	REID(%)	95% C.I.
	Males (40 years)			
Lunar-long	0.06	0.017	0.68	[0.20, 2.4]
Mars swing-by	0.37	1.03	4.0	[1.0, 10.5]
Mars surface	0.42	1.07	4.2	[1.3, 13.6]
	Females (40 years)			
Lunar-long	0.06	0.17	0.82	[0.23, 3.1]
Mars swing-by	0.37	1.03	4.9	[1.4, 16.2]
Mars surface	0.42	1.07	5.1	[1.6, 16.4]

Table 4-16. ***Calculations of Effective Doses, REID, and 95% C.I. for Lunar or Mars Missions. Calculations Are at Solar Minimum for a 20-g/cm^2 Aluminum Shield***

Exploration Mission	D, Gy	E, Sv	REID(%)	95% C.I.
	Males (40 years)			
Lunar-long	0.06	0.14	0.57	[0.18, 1.9]
Mars swing-by	0.36	0.87	3.2	[1.0, 10.4]
Mars surface	0.41	0.96	3.4	[1.1, 10.8]
	Females (40 years)			
Lunar-long	0.06	0.14	0.68	[0.22, 2.4]
Mars swing-by	0.36	0.87	3.9	[1.2, 12.7]
Mars surface	0.41	0.96	4.1	[1.3, 13.3]

Results differ at solar maximum, where a four-fold increase in shielding mass leads to a more than two-fold reduction in cancer risk and solar protons (Tables 4-17 and 4-18), which are less penetrating than GCR, are effectively mitigated by shielding. However, for heavy shielding ($\geq$ 20 g/cm^2), GCR dominates over SPEs and the further addition of shielding provides marginal reductions. Each SPE is unique in that it has distinct fluence, energy spectra, and dose-rates; the shielding thickness where GCR doses exceed SPE doses therefore varies from event to event. Cancer incidence projections (not shown) are about 60% higher than those listed in these tables. Tables 4-17 and 4-18 show that cancer risk estimates still exceed the PELs for many Exploration mission scenarios and will remain as such until the uncertainties are reduced.

Table 4-17. ***Calculations of Effective Doses, REID, and 95% C.I. for Lunar or Mars Missions. Calculations Are Near Solar Maximum, Assuming 1972 SPE in the Deep Space Segment of the Mission with a 5-g/cm^2 Aluminum Shield***

Exploration Mission	D, Gy	E, Sv	REID(%)	95% C.I.
	Males (40 years)			
Lunar-long	0.49	0.74	3.0	[0.95, 7.9]
Mars swing-by	0.62	1.21	4.4	[1.5, 13.1]
Mars surface	0.66	1.24	4.8	[1.6, 14.2]
	Females (40 years)			
Lunar-long	0.49	0.74	3.6	[1.1, 9.6]
Mars swing-by	0.62	1.21	5.7	[1.8, 17.1]
Mars surface	0.66	1.24	5.8	[2.0, 17.3]

Table 4-18. ***Calculations of Effective Doses, REID, and 95% C.I. for Lunar or Mars Missions. Calculations Are Near Solar Maximum, Assuming 1972 SPE in the Deep Space Segment of the Mission with a 20-g/cm^2 Aluminum Shield***

Exploration Mission	D, Gy	E, Sv	REID(%)	95% C.I.
	Males (40 years)			
Lunar-long	0.08	0.18	0.72	[0.24, 2.4]
Mars swing-by	0.22	0.54	2.0	[0.60, 6.8]
Mars surface	0.25	0.60	2.4	[0.76, 7.8]
	Females (40 years)			
Lunar-long	0.08	0.18	0.86	[0.26, 2.8]
Mars swing-by	0.22	0.54	2.5	[0.76, 8.3]
Mars surface	0.25	0.60	2.9	[0.89, 9.5]

Biological and physical countermeasures

Identifying effective countermeasures with which to reduce the biological damage that is produced by radiation remains a long-term goal of space research. As noted by Durante and Cucinotta (2008), such countermeasures may not be needed for a lunar base, but they probably will be for the Mars mission and definitely will be needed for exploring Jupiter, the Saturn moon Titan, or the nearby satellites. In all of the basic radioprotection textbooks, the authors have stated that there are three means to reduce exposure to ionizing radiation: increasing the *distance* from the radiation source, reducing the exposure *time*, and through use of *shielding*. Distance plays no role in space, as space radiation is omnidirectional. The time that will be spent in space by human crews is likely to be increased rather than decreased, given the plans for exploration and colonization. Shielding remains a plausible countermeasure, albeit a prohibitively costly one in light of current launch mass capabilities. Furthermore, the present uncertainties in risk projection prevent us from determining the true benefit of shielding. Other strategies can be effective in reducing exposure, or the effects of the irradiation, in space. These strategies include the choice of an appropriate time of flight, administration of drugs or dietary supplements to reduce the radiation effects, and crew selection.

Radioprotective Agents

The search for efficient radioprotectors is a major goal of research in radiation protection and therapy. Both radiation injury and oxygen poisoning occur through the formation of reactive oxygen species; therefore, antioxidants can be efficiently used to prevent the damage (Weiss and Landauer, 2003).

As summarized by Durante and Cucinotta (2008),

> "Phosphorothioates and other aminothiols, which are usually administered shortly before irradiation, are so effective in tissue protection against ionizing radiation that one specific compound (Ethyol, also known as amifostine or WR-2721) is approved in many countries for clinical use during chemotherapy and radiotherapy cancer treatments (Sasse et al., 2006). Unfortunately, amifostine (WR-2721) and other thiols have significant side effects, including nausea, vomiting, vasodilatation, and hypotension (Boccia et al., [sic] 2002), precluding their use in spaceflights. Natural occurring antioxidants are less effective than phosphorothioate agents in protection against high-dose acute radiation burden. However, nutritional antioxidants have a low toxicity, can be used for prolonged time, and they seem to play a key role in the prevention of cancer (Halliwell, 2000; Bingham and Riboli, 2004). A diet rich in fruit and vegetables significantly reduced the risk of cancer in the A-bomb survivor

cohort (Sauvaget et al., 2004). Retinoids and vitamins (A, C, and E) are probably the most well-known and studied natural radioprotectors, but hormones (e.g. melatonin), gluthatione, superoxide dismutase, phytochemicals from plant extracts (including green tea and cruciferous vegetables), and metals (especially selenium, zinc, and copper salts) are also under study as dietary supplements for individuals overexposed to radiation (Weiss and Landauer, 2000), including astronauts. In addition, there is evidence of a reduced antioxidant capacity during spaceflight, as shown by reduced superoxide dismutase (SOD) and total antioxidant activity in some astronauts returning from missions on the International Space Station (Smith et al., 2005).

"Understanding the effectiveness of antioxidants in space is complicated by the presence of HZE particles. In principle, antioxidants should provide reduced or no protection against the initial damage from densely ionizing radiation, because the direct effect is more important than free radical-mediated indirect radiation damage at high LET. However, there is an expectation that some benefits should occur for persistent oxidative damage related to inflammation and immune responses. Some recent experiments suggest at least for acute high dose irradiation that an efficient radioprotection by dietary supplements can be achieved even in case of exposure to high-LET radiation. Ascorbate reduces the frequency of mutations in human-hamster hybrid cells exposed to high-LET C-ions (Waldren et al., 2004). Vitamin A strongly reduces the induction of fibroma in rats exposed to swift Fe-ions (Burns et al., 2007). Dietary supplementation with Bowan-Birk protease inhibitors (Guan et al., 2006), L-selenomethionine or a combination of selected antioxidant agents (Kennedy et al., 2007) could partially or completely prevent the decrease in the total antioxidant status in the plasma of mice exposed to proton or HZE particle radiation, and neoplastic transformation of human thyroid cells in vitro. However, because the mechanisms of biological effects are different for low dose-rate compared to acute irradiation, new studies for protracted exposures will be needed to understand the potential benefits of biological countermeasures."

Even if antioxidants can act as radioprotectors, this does not necessarily translate as an advantage for cancer risk. If antioxidants protect cells by rescuing them from apoptosis, this may allow the survival of damaged cells, which eventually can initiate tumor progression. Concern about this possibility is sustained by a recent meta-study of the effects of antioxidant supplements in the diet of normal subjects (Bjelakovic et al., 2007). The authors of this study did not find statistically significant evidence that antioxidant supplements have beneficial effects on mortality. On the contrary, these authors concluded that β-carotene, vitamin A, and vitamin E seem to increase the risk of death. Concerns not only include rescuing cells that still sustain DNA mutations, but also the altered methylation patterns that can result in genomic instability (Kovalchuk et al., 2004). An approach to target damaged cells for apoptosis may be advantageous for chronic exposures to galactic cosmic radiation. Radioprotectors tested for acute exposures at high doses should be used with care – rescuing cells may make the problem worse in the long term.

Shielding

For terrestrial radiation workers, additional protection against radiation exposure is usually provided through increased shielding. Unfortunately, shielding in space is problematic, especially when GCRs are considered. High-energy radiation is very penetrating: a thin or moderate shielding is generally efficient in reducing the equivalent dose, but, as the thickness increases, shield effectiveness drops. This is the result of the production of a large number of secondary particles, including neutrons, that are caused by nuclear interactions of the GCR with the shield. These particles have generally lower energy, but they can have higher quality factors than incident cosmic primary particle. Radiation shielding effectiveness depends on the atomic constituents of the material that is used. Shielding effectiveness per unit mass, which is the highest for hydrogen, decreases with increasing atomic number (Wilson et al. 1995). Liquid hydrogen would display the maximum performance as shield material, but it is not practical since it is a low-temperature liquid. Instead, polyethylene could be a good compromise. Secondary neutron production increases with the mass number of the atomic constituents of the

material and can grow to be large values for materials such as aluminum or the regolith on the martian surface, or for heavier materials such as lead. Unfortunately, most of the biologically dangerous secondary radiation is produced in tissue by very-high-energy GCR nuclei, even behind hydrogen shielding.

For SPE shielding, the situation is much better, and the majority of events on record can be reduced to reasonable dose levels (< 100 mSv) with localized shielding of polyethylene inside a lightly shielded vehicle or habitat (figure 4-16).

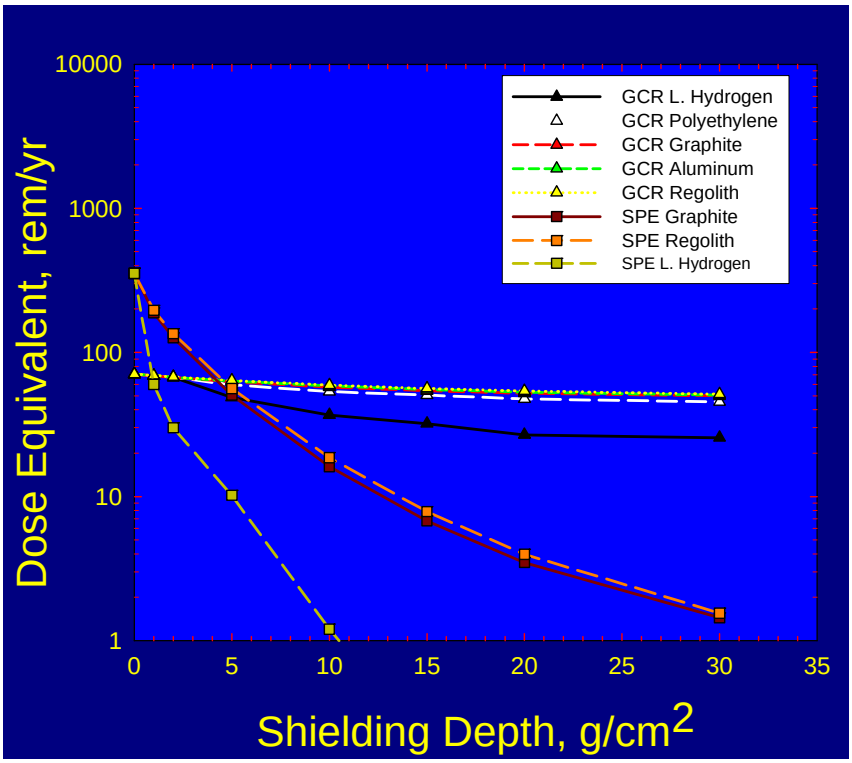


Figure 4-16. ***Effective doses vs. depth in several materials for GCR at solar minimum and the 1972 SPE (Cucinotta et al., 2006).***

Conclusion

The evidence for cancer risks from humans who are exposed to low-LET radiation is extensive for doses above 100 mSv. There are important uncertainties for low-LET radiation at lower doses (<100 mSv), for low dose-rates, and in transferring risks among populations that have different genetic, dietary, etc. attributes. Although human epidemiology can be applied to space exposures, additional uncertainties are related to the quality of radiation in space that is known to produce both qualitative and quantitative differences compared to low-LET radiation in experimental models. The doses that are to be expected on space missions, and the nuclear type and energies, are well understood. NASA has existing models that quite accurately determine radiation physics parameters in space. Reducing the uncertainties in risk assessment, which is required before a mission to Mars can be undertaken, has led to a number of investigations that are guided by molecular and genetic research on carcinogenesis and degenerative diseases. The large uncertainties in risk projection models will only be reduced by improving our basic understanding of the underlying biological processes and their disruption by space radiation. There are unique aspects involved in this approach due to the specific challenges to biological systems that are presented by space radiation, especially HZE ions. It is unlikely that the radiation risk problem for space exploration will be solved by a simple countermeasure, such as shielding or radioprotective drugs. Rather, the risk will be understood and controlled only with more basic research in the field of cancer induction by charged particles (Cucinotta and Durante, 2006).

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Chapter 5:
Risk of Acute Radiation Syndromes Due to Solar Particle Events

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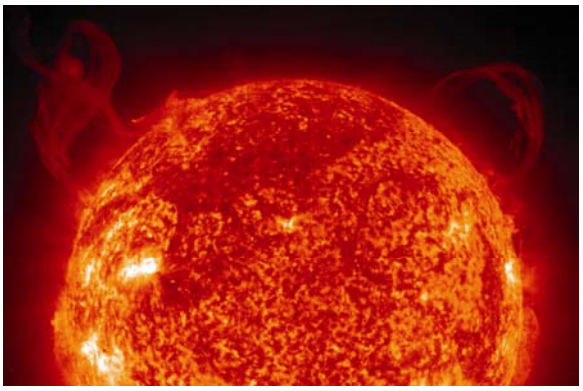
Radiation and synergistic effects of radiation may place the crew at significant risk for acute radiation sickness from a major solar event or artificial event, such that the mission or crew survival may be placed in jeopardy. Crew health and performance may be impacted by acute solar events. Beyond Low Earth Orbit, the protection of the Earth's atmosphere is no longer available, such that increased shielding and protective mechanisms are necessary in order to prevent acute radiation sickness and impacts to mission success or crew survival. The primary data available at present are derived from analysis of medical patients and persons accidentally exposed to high doses of radiation. Data more specific to the spaceflight environment must be compiled to quantify the magnitude of increase of this risk and to develop appropriate protection strategies. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.



Research to improve estimates of the risk of acute radiation syndrome resulting from exposure to solar particle events (as pictured here) will help ensure that the risk is sufficiently mitigated through shielding protection, monitoring, and alert systems.

Executive Summary

The foundation of evidence for acute radiation syndrome (ARS) is ground-based observations for humans who were exposed to ionizing radiation, and well-defined dose projections for space explorations missions. Scenarios in which ARS is likely to have a major health impact entail nuclear power plant workers in the event of a nuclear accident; military personnel, in the event of nuclear war; and the general population, should a terrorist attack occur that involves nuclear devices (Waselenko et al., 2004; Pellmar et al., 2005). ARS has been documented in humans who were exposed to gamma or X rays, and these data have been summarized in the literature and in numerous committee reports (e.g., NAS/NRC, 1967; NCRP, 1982; NCRP, 1989; Baum et al., 1984; Evans et al., 1985; ICRP, 2000; ICRP, 2002). NASA has funded several reports from the NAS and the NCRP that provided evidence for the radiation risks in space. Of note, the NCRP is chartered by the United States Congress to guide federal agencies such as NASA on the risk from radiation exposures to their workers. Reports from the NCRP and the NRC on space radiation risks are the foundation of the evidence that is used at NASA for research and operational radiation protection methods and plans.

The risk of ARS from exposure to large SPEs during space missions was identified in the early days of the human space program (NAS/NRC, 1967). The ARS symptoms that appear in the prodromal phase post-exposure (i.e., nausea, vomiting, anorexia, and fatigue) could potentially more significantly affect space mission success because of the lower threshold dose with which these occur compared to other acute risks, as well as the likely dose ranges from SPEs. While ARS has been well defined for gamma- and X-ray exposures, less is known about the acute effects from whole-body exposures to SPE protons, which are characterized by dynamic changes in energy distribution and dose-rates at specific locations in the human body. Protons dominate the dose inside the spacecraft. During EVAs, however, the helium and heavy-ion component of SPEs is also of biological importance. Protons with energies that are above 10 MeV are characterized as low-LET radiation. Inside tissue, a fraction of SPE doses is from high-LET radiation due to the slowing down of higher energy protons, and nuclear reactions producing neutrons and heavy ions. RBE factors for these radiation types are poorly defined. There have also been few investigations of the effectiveness of medical countermeasures for proton, microgravity, or reduced-gravity environments. Improvements in SPE forecasting and alert systems are needed to minimize operational constraints, especially for EVA. While radiation shielding is an effective mitigation to ARS, the high cost of shielding requires precise estimates of the risk to ensure that sufficient protection is provided without overesti-mating shielding requirements, especially in light of the existence of a dose threshold for many ARS components.

Introduction

Description of acute risks of concern to NASA

During an SPE, the sun releases a large amount of energetic particles. Although the composition of the particle type varies slightly from event to event, on average these particles consist of 96% protons, 4% helium-ions, and a small fraction of heavier ions (NCRP, 1989; Cucinotta et al., 1994; Townsend et al., 1994; Kim et al., 1999). The intensity and the energy spectrum of an SPE varies throughout the course of the event, which lasts from a few hours to several days. The intensity of the event can be described by particle fluence, F>E, which is the number of ions per unit area with energy greater than E, expressed as mega electron volts per nucleon (MeV/n). The energies of the protons are important because the range of penetration of these protons increases with energy. Protons with energies above 30 MeV have sufficient range to penetrate an EVA spacesuit, and are used as a simple scaling parameter to compare different SPEs. Each event has distinct temporal and energy characteris-tics, however. The majority of SPEs are relatively harmless to human health, with doses below 10 mGy for

minimal shielding protection; but the SPEs that have the highest fluence of particle of energies above 30 MeV are a major concern for future missions outside the protection of the magnetic field of the Earth.

Figure 5-1 shows data that were collected in the modern era for the F>30 MeV proton fluence (bottom panel) from large SPEs and the solar modulation parameter (Φ) (upper panel). The solar modulation parameter describes the strength of the sun's magnetic field with solar maximum where Φ>1,000 MV. The various SPEs shown in figure 5-1, which are characterized as large SPEs (F>30 MeV > 108 per cm^2), would contribute doses of 10 to 500 mGy for average shielding conditions. Although the dose resulting from the majority of SPEs is small, SPEs nonetheless pose significant operational challenges because the eventual size of an event cannot be predicted until several hours after the particles are initially detected. Extraordinarily large SPEs were recorded in November 1960, August 1972, and October 1989. In general, SPEs occur more often near solar maximum, but, as figure 5-1 shows, the correlation between event frequency and solar conditions is not precise. To date, accurate short- or long-term prediction of SPEs has not been possible.

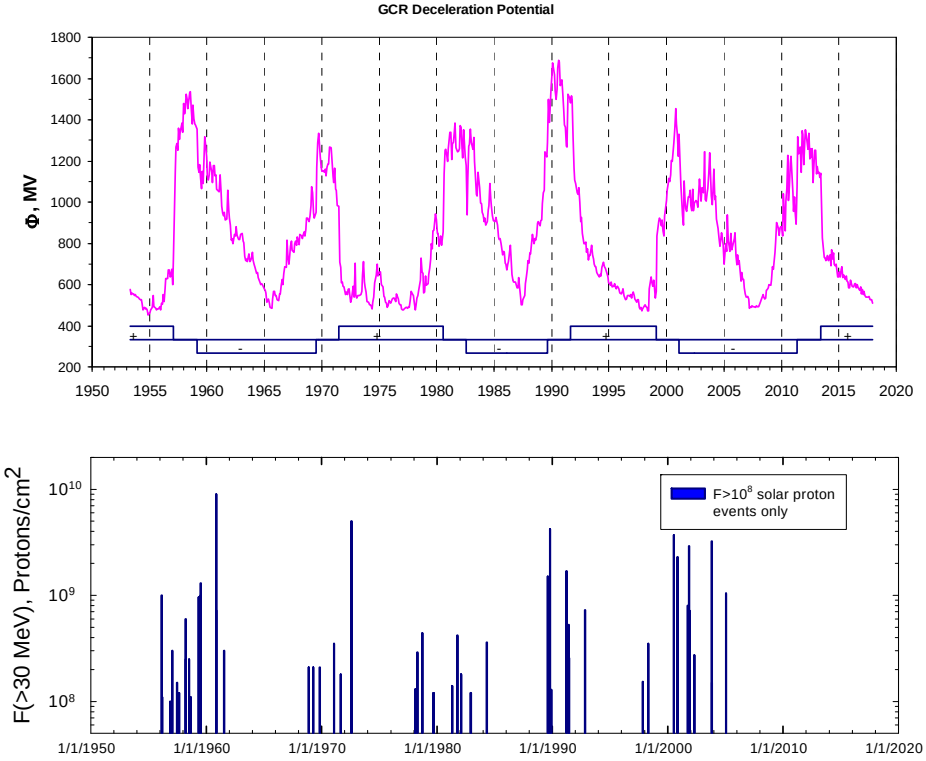


Figure 5-1. ***Historical data on fluence of protons above 30 MeV per cm^2 (F(>30 MeV) from large SPEs relative to solar modulation parameter (Φ). Only events with $F_{>30\ MeV}$ >10^8 particles per cm^2 are shown.***

In contrast to the constant presence of GCRs in space, SPE exposures are sporadic and occur with little warning. Without sufficient shielding protection, a large SPE may result in a whole-body dose of over 0.5 Gy (500 mGy) received over a period of several hours. Humans who are exposed to gamma or X rays at doses above 0.5 Gy are known to experience ARS (Anno et al., 1989). ARS can be classified clinically as hematopoietic syndrome, GI syndrome, and neurovascular syndrome. Based on the time of appearance, ARS can be divided into prodromal phase (0–24 hr), latent phase, manifest illness phase, and recovery phase. The most probable ARS effects from

SPE exposure in space flight that can potentially affect mission success include prodromal effects (nausea, vomiting, anorexia, and fatigue), skin injury, and depletion of the blood-forming organs (BFOs), possibly leading to death. SPEs are of much lower energy than are GCRs and occur at modest dose-rates. Shielding is an effective countermeasure to SPEs inside spacecraft, making ARS extremely unlikely except in EVA or combined EVA and intravehicular activity (IVA) scenarios. The magnitude of ARS risks on the moon has been hypothesized to be increased significantly due to a possible synergistic effect of reduced gravity (Todd et al., 1999) or the background GCR exposure. The operational impacts of ARS on space flight crew members could affect crew performance and lead to the possibility of mission failure. Recovery of ARS can also be hindered by changes of the immune status, including from combined skin burns and blood system depletion, and a slower wound-healing process.

NASA, in past reviews, has included the risks of hereditary, fertility, and sterility effects as part of the collection of risks embodied in the acute radiation effects category. There is no perfect match of these effects with any of the four major identified NASA HRP radiation risks, and, based on past reviews of these effects (NCRP, 1989; 2000), they alone are not likely to rise to the level of a major concern. As SPEs would be the primary cause of fertility and sterility effects, these items are included as part of the acute category of risks.

Current NASA permissible exposure limits

PELs for short-term and career astronaut exposures to space radiation have been approved by the NASA Chief Health and Medical Officer. These PELs provide the basis for setting requirements and standards for mission design and crew selection. Short-term dose limits (i.e., PELs) are imposed to prevent clinically significant deterministic health effects, including performance degradation in flight. Dose limits for deterministic effects, which are given in units of Gray-equivalent, are listed in Table 5-1. The unit of Gray-equivalent is distinct from the unit of Sievert that is used to project cancer risk because distinct radiation quality functions occur for ARS and cancer. The Gray-equivalent is calculated using the RBE values that are described in NCRP Report No. 132 (2000) and Sievert using the LET-dependent radiation quality function. For mission planning, these limits should be applied with a P>0.99 success criteria for a worst-case radiation environment and available mitigation procedures. The basis for the PELs originated in prior reports and recommendations to NASA by the NAS Space Science Board (NAS/NRC, 1967; 1970) and the NCRP (NCRP, 1989; 2000). These reports are summarized below.

Table 5-1. ***Dose Limits (in mGy-Eq or mGy) for Non-cancer Radiation Effects (BFO Refers to the Blood-forming Organs and CNS to the Central Nervous System)***

Organ	30-day limit	1-year limit	Career
Lens*	1,000 mGy-Eq	2,000 mGy-Eq	4,000 mGy-Eq
Skin	1,500 mGy-Eq	3,000 mGy-Eq	6,000 mGy-Eq
BFO	250 mGy-Eq	500 mGy-Eq	Not applicable
Heart**	250 mGy-Eq	500 mGy-Eq	1,000 mGy-Eq
CNS***	500 mGy-Eq	1,000 mGy-Eq	1,500 mGy-Eq
CNS*** (Z≥10)	–	100 mGy	250 mGy

*Lens limits are intended to prevent early (<5 years) severe cataracts (e.g., from an SPE). An additional cataract risk exists at lower doses from cosmic rays for subclinical cataracts, which may progress to severe types after long latency (>5 years) and are not preventable by existing mitigation measures; they are deemed an acceptable risk to the program, however.

**Heart doses calculated as average over heart muscle and adjacent arteries.

***CNS limits should be calculated at the hippocampus.

Evidence

Reviews of human data in patients and accident victims

Evidence of ARS in humans from low-LET radiation, such as gamma- or X-ray exposures, has been thoroughly reviewed and documented in the reports that have been generated by regulatory institutes such as NAS, NCRP, the ICRP, and the U.S. Nuclear Regulatory Commission. Data accumulated from the last half-century that were used in the construction of the dose threshold for ARS include: studies on the Japanese atomic-bomb survivors (Ishida and Matsubayashi, 1948; Ohkita, 1975; Oughterson and Warren, 1956); case studies of nuclear accident victims (Blakely, 1968; Vodopick and Andrews, 1974; Gilberti, 1980); and records of total-body therapy patients for cancer and other diseases (Adelstein and Dealy, 1965; Brown, 1953; Warren and Grahn, 1973). More recent events include the Chernobyl accident in 1986 (Bouville et al., 2006); an accident that occurred in Tokai-mura, Japan, in 1999 (Hirama et al., 2003); and the death of a Russian citizen after a possible internal overdose of radioactive materials that was reported in the popular media in 2006.

ARS appears in various forms and has different threshold onset doses for the possible effects. The threshold whole-body dose for ARS is about 0.1 to 0.2 Gy for radiation that is delivered under acute conditions where dose-rates are more than 1 Gy/hr occur. At lower dose-rates, a reduction in effects occur, as described below. At doses that are slightly above this threshold, decreases in sperm counts occur that cause temporary sterility in males (NAS/NRC, 1967; Paulsen, 1973; NCRP, 1989). The dose range and associated patho-physiological events have been summarized previously (Anno et al., 1989). Doses that are in the range of 0.5 to 1 Gy cause minor acute damage to the hemopoietic system and mild prodromal effects (nausea, vomiting, anorexia, and fatigue) in a small number of irradiated persons (Anno et al., 1989). In the dose range of 1 to 2 Gy acute, prodromal effects and injury to the hemopoietic system increase significantly. Most victims will probably survive, however, with only 5% lethality in a population after doses of about 2 Gy (NAS/NRC, 1967; McFarland and Pearson, 1963). Survival is possible within the dose range of 2 to 3.5 Gy; however, prodromal effects become more pronounced, decreasing in latency and increasing in severity. As the dose reaches about 3.25 Gy, 50% may die within 60 days if appropriate medical care is not administered (Lushbaugh, 1969). From 3.5 to 5.5 Gy, symptoms are more severe, affecting nearly all who are exposed. If untreated, 50% to 99% of those who are affected may die primarily because of extensive injury to the hemopoietic system that is manifested by overwhelming infections and bleeding (NAS/NRC, 1967; Lushbaugh, 1969; Messerschmidt, 1979). At this dose range, permanent sterility results in both males and females (Paulsen, 1973; NCRP, 1989).

Responses to doses between 5.5 and 7.5 Gy begin to reflect the combined effects of GI and hemopoietic damage. Survival is almost impossible, short of a compatible bone marrow transplant and/or extensive medical care. Nearly everyone who is irradiated at this level suffers severe prodromal effects during the first day after exposure. When doses range between 7.5 and 10 Gy, injuries are much more severe due to a greater depletion of bone marrow stem cells (Adelstein and Dealy, 1965; Lushbaugh, 1962), increased GI damage, and systemic complications from bacterial endotoxins entering the blood system.

Doses that are between 10 and 20 Gy produce early post-exposure renal failure (Lushbaugh, 1974). Death results in fewer than 2 weeks from septicemia due to severe GI injury, which is complicated by complete bone marrow damage and the cessation of granulocyte production (Lushbaugh 1962). Above approximately 13 Gy, death may occur sooner from electrolyte imbalance and dehydration due to vomiting and diarrhea, especially in hot and humid conditions. Extremely severe GI and cardiovascular damage causes death within 2 to 5 days after doses of 20 to 23 Gy (Lushbaugh, 1969).

Prodromal Effects

Prodromal effects, which have a threshold dose of about 0.5 Gy, are the most likely acute effect to be experienced by crew members after exposure to SPE based on the historical record of SPE fluence and likely shielding conditions. Dose and onset of sickness are inversely correlated, with higher doses producing the shortest time for sickness to occur. The prodromal phase comprises the clinical symptoms (nausea, vomiting, and anorexia) and signs that appear in the first 48 hours after exposure. Prodromal vomiting is of particular importance because it could have catastrophic consequences in space, especially to helmeted individuals (NCRP, 1989), and other symptoms can seriously impair mission success in space. Several sets of data on humans, who are mostly cancer patients, are available to make initial estimates of the likelihood and types of effects (e.g., Lushbaugh et al., 1967; Lushbaugh, 1974). In general, symptoms develop within a few hours of radiation exposure and rarely exceed 24 hours with low-LET radiation (Fajardo et al., 2001). Exposure to higher doses results in greater severity, early onset, and longer duration of the symptoms (Anno et al., 1996). Prodromal effects are not noted below low-LET radiation doses of 0.5 Gy (Mettler and Upton, 1995).

Significantly smaller amounts of data are available for prodromal effects from continuous exposure at lower dose-rates. The current knowledge that has been collected from studies on victims who were exposed to radioactive fallout following the testing of nuclear devices and to other sources (Kumatori et al., 1980; Cronkite et al., 1956) is that dose-rates of perhaps less than a few tens of mGy/h are probably not sufficient to cause ARS. However, continuous dose-rates of around 100 mGy/h are probably high enough to cause significant vomiting within a period of 1 day or so. Accordingly, between a few tens of mGy/h to approximately 100 mGy/h, a considerable amount of uncertainty exists concerning the human response to continuous radiation exposure, which is likely due to variations in the sensitivity of individuals as well as the quality of the very limited amount of existing data.

Skin Damage

The skin may receive a dose that is up to a magnitude greater than that of internal organs from an SPE during an EVA, when minimal protection is available (Kim et al., 2006a). Risks of concern include erythema, moist desquamation, and epilation (NCRP, 1989). The ED10 (a dose in which 10% of a population receives the effect) has been estimated to be 4 Gy for erythema and 14 Gy for the more serious moist desquamation (Strom, 2003; Haskin et al., 1997). Protraction of exposure increases the dose that is required for a given degree of severity by a factor of about 3. The response of the skin depends on the number of exposures, the total dose, the dose per exposure, and the volume of tissue that is irradiated (Turesson and Notter, 1984). It has been noted that deterministic radiogenic skin injury complicates the treatment of many of the high-dose casualties at Chernobyl (Strom, 2003). Skin doses during an SPE can vary more than five-fold for different regions of the bodydue to the varying energies of solar protons and body self-shielding(Kim et al., 2006a).

Reviews of space flight issues

Past reviews of evidence by the NAS and the NCRP form the basis for the NASA PELs. NAS first reviewed space flight issues in 1967 (NAS, 1967) and conducted a further review in 1970 (NAS, 1970) that led to the dose limits that were used at NASA until 1989. Extensive reviews of humans and experimental radiobiology data for ARS were provided to NASA by reports of the NCRP in 1989, 2000, and 2006 (NCRP, 1989; 2000; 2006). The report of the NAS in 1970 is the basis for the BFO limits that are used at NASA. The rationale for this limit is to protect the hematopoietic system from depletion below a critical limit. Dose limits for the prodromal risks were not advocated by the NAS or the NCRP for NASA missions in the past. The BFO limit likely occurs at doses below that of the threshold for prodromal effects, however.

Acute Risks for Protons, Neutrons, and High-Z High-energy Nuclei

RBE and dose-rate studies in mice, rats, ferrets, and larger species

The data of ARS for high-LET radiation – e.g., neutrons and heavy ions – are collected primarily in animal studies. As mice and rats do not display the prodromal effects such as vomiting, limited research on this particular ARS has been performed on ferrets for particle types of radiation. Rabin et al. (1992; 1994) have studied the dose response of 600 MeV/n ^{56}Fe-ion-induced emesis in ferrets and compared it with the dose response from other radiation types. Over the dose range of 0.2 to 0.5 Gy, fission spectrum neutrons and ^{56}Fe-ions were more effective than Co-60 gamma rays in inducing emesis, and the effects of the ^{56}Fe-ions and fission neutrons could not be distinguished from each other. Co-60 gamma rays were significantly more effective in producing emesis than high-energy electrons or 200-MeV protons. The dose-rates ranged from 0.1 to 1 Gy/min. The relatively large difference in LET between ^{56}Fe-ions and fission neutrons was not associated with any difference in the effectiveness with which the two types of radiation produced emesis.

Relative biological effectiveness and dose-rate studies in cell inactivation

Since some of the ARS effects are related to cell killing or tissue damage, the RBE and dose-rate data for cell inactivation by protons are insightful for ARS that is induced from SPE exposures (Cucinotta, 1999; Yang, 1999). Early results of cell inactivation by charged particles over a wide range of LET have been reviewed by Ainsworth (1986). In general, the RBE for cell inactivation in vitro peaked at LET around 100 keV/micron, and the peak RBE value varied between 1.5 and 5 for different cell types. The maximum RBE for in vivo responses tended to be lower and occurred at a lower LET value in comparison to the in vitro data. The reported RBE-LET relationship for in vitro cell killing showed similar trends as in the early in vivo data (Furusawa et al., 2000).

Factors that determine the dose-rate dependence of ARS include: the kinetics of DNA repair, apoptosis, cell-repopulation and proliferation, and dose distributions across critical organs. Irradiation at reduced dose-rates is known to reduce the probability of lethality of ARS that is induced by low-LET radiation compared to acute irradiation, as illustrated in figure 5-2. Differences between dose-rate effects for protons and X rays or gamma rays may occur due to the heterogeneous dose contribution from slowing protons or recoil nuclei in SPE organ doses. The heterogeneous dose distribution across the bone marrow for protons should lead to a sparing effect that complicates comparisons to gamma rays, where doses are more uniform. The dose distribution across the stomach and other organs in the GI-tract also varies several-fold for SPEs, which complicates the use of gamma-ray data to predict prodromal risks from SPE.

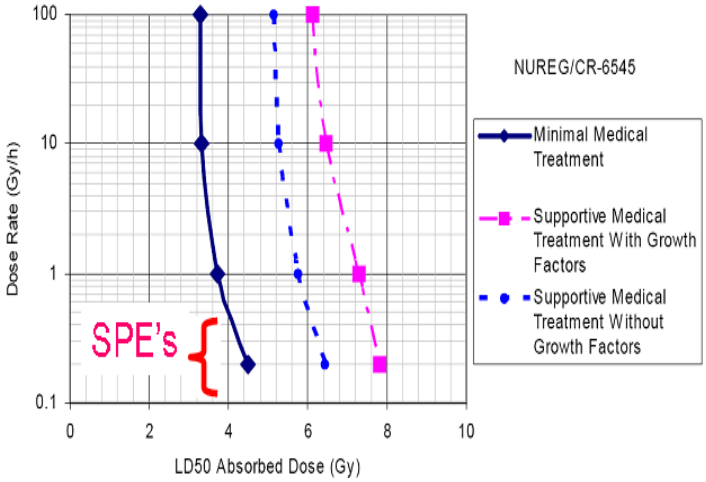


Figure 5-2. ***Effects of medical treatment and dose-rate on the LD50 for gamma radiation; also shows expected region of dose-rates for SPEs during EVA (adapted from Haskin, 1997).***

Models of acute risks

Department of Defense and Nuclear Regulatory Commission Models

The radiation-induced performance decrement from ARS is one of the major concerns for military personnel in a nuclear war scenario. The Defense Nuclear Agency has developed a computer model to calculate the dose and time-dependent human response to ionizing radiation for acute and protracted exposure conditions (Anno et al., 1996). A set of differential equations was mathematically developed to model the ARS for a given dose and the bodily repair and recovery process when the exposure takes place over a period of time. Most of the parameters in the equations were determined from human accident data or data of patients who were receiving whole-body radiation in medical treatment; limited data came from ferrets and other animals for protracted exposures.

Two models were developed separately for upper gastrointestinal distress (UGID) and for fatigue/weakness (FW); these models were based on the postulated pathways. For UGID, the severity of the signs and symptoms was classified in five categories ranging from no noticeable effect (Severity Level 1) to vomiting and retching several times (Severity Level 5). For FW, Severity Level 5 is defined as exhaustion with almost no strength. Outputs of the computer codes are the probability of occurrence of specific symptoms as a function of input dose, dose-rate, and time after exposure. These radiation effects were also related to performance decrement for infantry tasks such as engaging a target with a rifle or walking up a rocky hill. Similar issues will be faced by NASA when astronauts are exposed to SPE on the surface of the moon. The mathematical model applies to gamma- or X-ray exposures only, but it has been adapted to proton effects at NASA (Hu et al., 2009).

Cell Kinetics Models

Cell kinetics models of the relevant cell lineages in the blood system are of interest for describing dose-rate effects. A group at Oak Ridge National Laboratory developed models of the blood system using a linear kinetics formula of cell damage, repair, and repopulation (Morris et al., 1993). The model has been fit to data for mice and larger species. This model, which was applied to study the risk of acute mortality following a large SPE (Wilson et al., 1999), indicates a very small probability for acute death for the largest SPEs, as in the Defense Nuclear Agency model that is described above. In addition, a nonlinear cell population kinetics model of ARS was developed that provides a more realistic simulation of the underlying biology of ARS

(Smirnova and Yonezawa, 2004), including an adaptive response due to simulation of the immune defense mechanisms.

Risk in Context of Exploration Mission Operational Scenarios

Solar particle event environment models and doses

Estimates of likely SPE cumulative doses and dose-rates at critical organs are important for assessing the probability of ARS for specific mission scenarios. Detailed spectra and temporal information are available for most of the SPEs that have occurred since 1955. Analysis of nitrate concentrations in Arctic ice-core samples provides data on integral fluences that are above 30 MeV for SPEs dating back to the 15th century (McKracken et al., 2001). The nitrate core samples indicate that several SPEs that are larger than the August 1972 event, which is considered to be the largest in modern times, have occurred in the past. The nitrate core sample data also allow researchers to estimate their frequency. The prediction of SPEs on Mars, taken from Earth observations, will require improved observational capabilities. Improved knowledge of the physics of these processes can be used to improve the radiation protection of crews.

An understanding of the physical characteristics of solar disturbances is important for protecting the crews that are on Exploration missions. Thus, a summary from the book *Safety design for space systems* (Musgrave et al., 2009, pp. 53–58), is provided here. The solar wind is a plasma that contains both positive and negative particles that are trapped in a magnetic field emanating from the sun. The solar wind is an extension of the solar corona for at least several astronomical units (AUs) from the sun (1 AU $\approx 1.5 \times 10^8$ km). It is composed mostly of protons and persists through variable parts of the sun's output during less active solar phases. The solar wind protons have thermal energies of approximately 1 to 10 keV. Except when the sun is active, the solar wind constitutes the most important particulate solar radiation.

A solar flare is an intense local brightening on the face of the sun close to a sunspot. This solar abnormality results in an alteration of the general outflow of solar plasma at moderate energies and local solar magnetic fields that are carried by that plasma. As the solar plasma envelops the Earth, the magnetic screening effects that are inherent in plasmas act to shield the Earth from GCRs, a process that is known as a Forbush decrease (Forbush, 1937). When the solar plasma interacts with the geomagnetic field, a disturbance or storm occurs. During an intense magnetic disturbance, the magnetic field of the Earth is compressed into the atmosphere in the polar regions of the Earth, and electrons that are trapped in the belt are lost. These auroral electrons, which are observed only in the polar regions, are associated with the coronal mass ejection (CME) that occurs after solar flares.

In association with many of the optical flares that occur from time to time on the solar surface, large fluxes of solar energetic particles are sometimes accelerated and emitted; these emissions of solar cosmic radiation are designated as SPEs. SPEs, with periods of several hours to days, represent one of several short-lived manifestations of the active sun. The solar wind and SPEs are composed of the same types of particles, primarily protons with the next significant component being α-particles. These two groups of particles are distinguished by their numbers as well as their speed or energy. Heavier nuclei, which are mostly in the carbon, nitrogen, and oxygen group (NCRP, 2006), and even heavier particles (atomic charge number, Z, between 22 and 30) have also been observed in major SPEs. Rare clusters of events of high intensity (i.e., of several orders of magnitude) with large numbers of high-energy particles are critical to space flight and EVA because the large events alone determine the yearly fluences of solar particles, and there is a much higher dose-rate effect during the short period of peak intensity (Kim et al., 2006b).

For recent solar cycles 19 through 21 (1955–1986), a list of major SPEs and associated proton fluences has been assembled by Shea and Smart (1990), who place all of the available flux and fluence data in a useful continuous database. From 1986 to the present (solar cycles 22 and 23), both an SPE list and the geostationary operational environmental satellite (GOES) spacecraft measurements of the 5-minute-average integral proton flux can be obtained through direct access to the National Oceanographic and Atmospheric Agency (NOAA) National Geophysical Data Center. Table 5-2 lists the large SPEs that occurred in the past five solar cycles for which the omnidirectional proton fluence with energy above 30 MeV, Φ_{30}, exceeded 10^9 protons/cm^2.

Table 5-2. ***Large SPEs during Solar Cycles 19 through 23 Corresponding to $\Phi_{30} > 10^9$ protons/cm^2***

Solar Cycle	SPE	$\Phi_{>30}$ protons/cm^2
19	11/12/1960	9.00×10^9
20	08/02/1972	5.00×10^9
22	10/19/1989	4.23×10^9
23	07/14/2000	3.74×10^9
23	10/26/2003	3.25×10^9
23	11/04/2001	2.92×10^9
19	07/10/1959	2.30×10^9
23	11/08/2000	2.27×10^9
22	03/23/1991	1.74×10^9
22	08/12/1989	1.51×10^9
22	09/29/1989	1.35×10^9
23	01/16/2005	1.04×10^9
19	02/23/1956	1.00×10^9

In Figure 5-3, the frequency of SPE occurrence that was recorded by the NOAA GOESs for solar cycle 23 is shown for 3-month periods. The monthly mean number of sunspots is included in the figure to show the association between SPE occurrence and solar activity. The times at which the five largest SPEs with $\Phi_{30} > 10^9$ protons/cm^2 occurred are marked with arrows. It is expected that an increase in SPEs occurs with increasing solar activity; however, no recognizable pattern has been identified. Large events have occurred during solar active years, but have not always occurred during months of solar maximal activity. Moreover, large events are more likely to occur in the ascending or declining phases of a solar cycle. This sporadic behavior of SPE occurrence is a major operational problem in planning for missions to the moon and Mars.

The shapes of the energy spectra, as well as the total fluence, vary considerably from event to event. Figure 5-4 shows the energy spectra of the January 16, 2005 SPE, which is one of the more recent large events. At that time, there was a sudden increase in proton flux, especially in particles with energies that were greater than 50 MeV. Protons with energies that were greater than 100 MeV increased by as much as four orders of magnitude after they declined following the major pulse. During this sharp commencement, the fluence did not reach the value that was obtained at the major peak intensities; however, this type of sudden increase in high-energy particles may pose a greater threat than the major particle intensities. Total fluence of an SPE is the representative indicator of a large SPE, and the detailed energy spectra for a large SPE – especially at high energies – is the important parameter for assessing the risk of radiation exposure (Kim et al., 2006b).

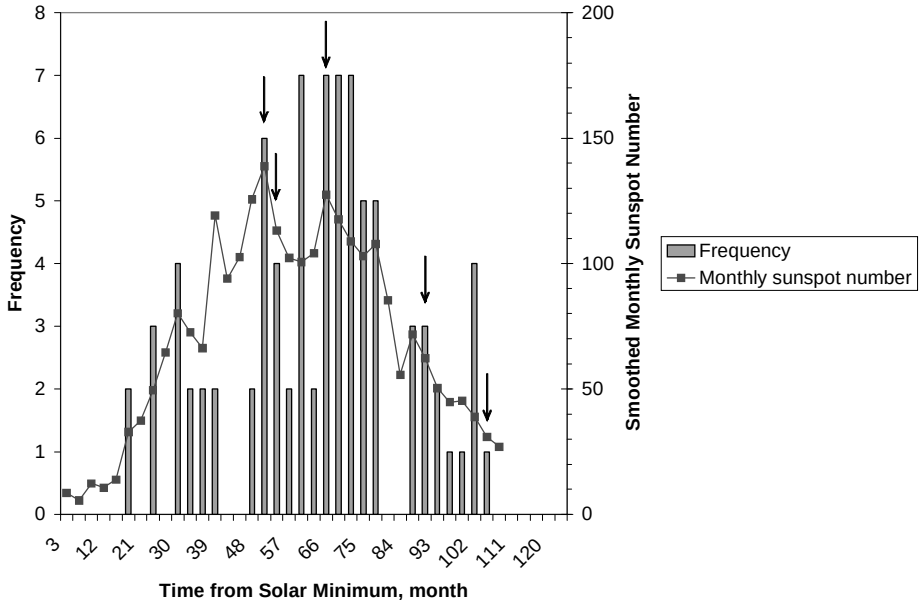


Figure 5-3. ***Frequency of SPE occurrence in 3-month periods of solar cycle 23. The arrows indicate the times at which large SPEs with $\Phi_{30}>10^9$ protons/cm^2 occurred.***

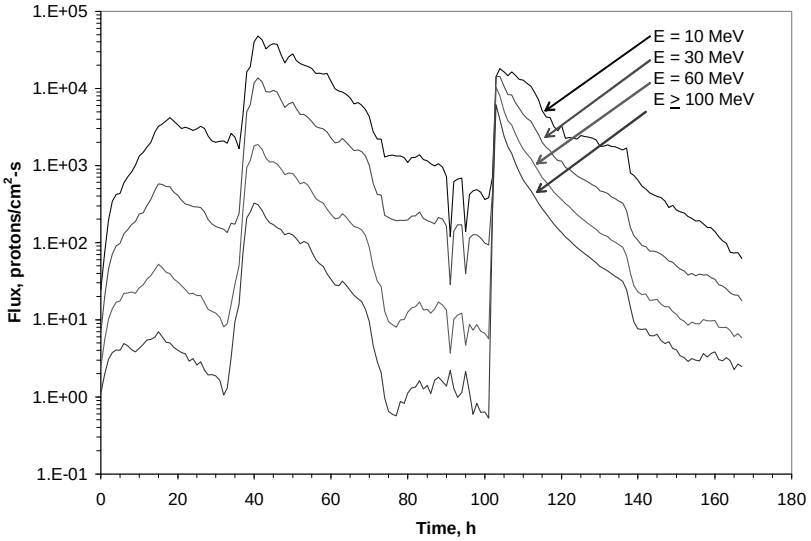


Figure 5-4. ***Hourly-average proton flux from GOES measurements during the SPE of January 16–22, 2005.***

A detailed temporal analysis of dose-rate at the BFOs for the August 1972 SPE is illustrated in figure 5-5. This event, which was one of the largest SPEs in the modern era, had the highest dose-rate at its peak. The temporal behavior that is shown in figure 5-5 suggests that significant biological damage would occur in a crew if adequate shielding is not provided. Figure 5-6 shows the SPE doses during this same event. Estimates for the Φ>30 MeV flux, which were determined from nitrate samples and then scaled to the August 1972 energy

spectra, are also shown. Biological effects are expected to increase significantly for dose-rates that are above 0.05 Gy/h. For an extended EVA, the current recommended 30-day exposure limit for the BFOs, which is 0.25 Gy-Eq (NCRP, 2000), is easily exceeded. The early effects from acute exposure may not be avoided when only a conventional amount of spacecraft material is provided to protect the BFOs from this class of SPE. To avoid placing unrealistic mass on a space vehicle while at the same time increasing safety factors for the astronauts, one solution for shielding against SPEs would be to select optimal materials for the vehicle structure and shielding. To this end it has been shown that materials that have lower atomic mass constituents have better shielding effectiveness (Wilson et al., 1999, Cucinotta, 1999). Overall exposure levels from this specific event have been estimated to be greater than 100 mSv (10 rem) at sensitive sites, while those from other large SPEs that have been recorded in the modern era can be reduced to below 0.1 Sv when heavily shielded "storm shelters" are added to a typical spacecraft (Kim et al., 2006b). Interpretation of this result, however, should be made while keeping in mind the caveat that significant uncertainties are inherent in determining the source spectra of protons (Musgrave et al., 2009.)

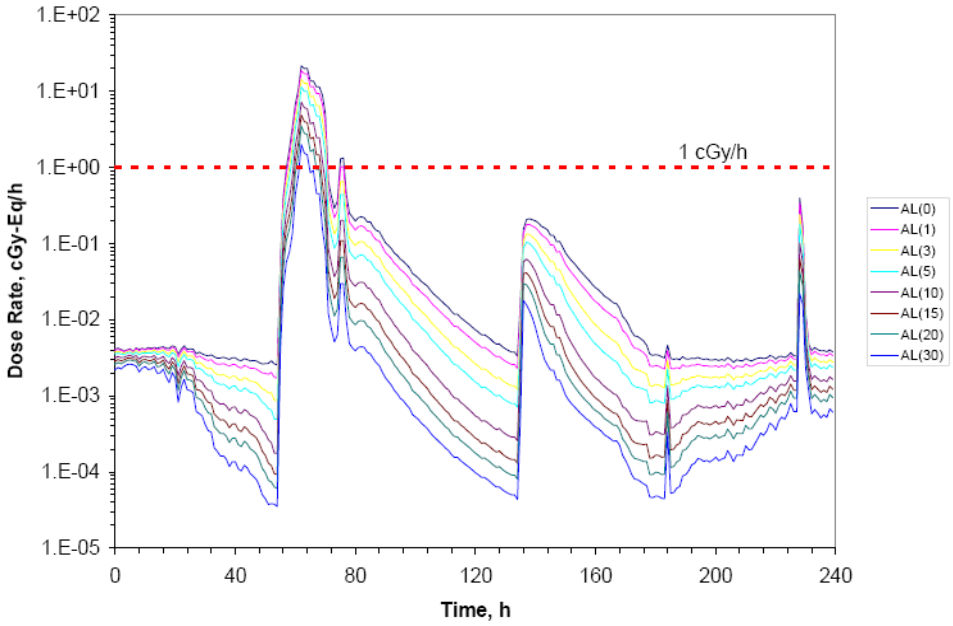


Figure 5-5. Dose-rate to the BFO for increasing levels of aluminum shielding for the large SPE of August 1972 (Kim et al., 2006a).

Solar alert and monitoring

An effective operational procedure requires an SPE warning or alert system. This system, which would be activated at the onset of proton exposure, would include pertinent information concerning the event, such as the fluence or flux and the energy distribution. These capabilities do not exist at the current time, and forecasts from NOAA are limited. New capabilities for deep-space mission forecasting will be needed prior to the Mars mission because the alignment of the Earth and Mars does not allow all SPEs on Mars to be observed from Earth. A recent report by the NRC discussed research approaches in space science that should lead to improved forecasting and alert capabilities for SPEs (NAS/NRC, 2006), including a status of approaches supported by the NASA Science Mission Directorate.

The most likely outcome of an SPE is mission disruption with little or no harm to the crew because, despite the occurrence of some very large SPEs such as the 1972 event described previously, more than 90% of SPEs result in very small radiation doses to critical organs (<10cGy-Eq), as shown in figure 5-6. Mission disruption is likely because the size of the SPE cannot be determined until several hours after its initial onset. Reliable radiation dosimeters that can transmit to Mission Control and provide a self-alert to astronauts are required. Such instrumentation has been available for many years, including during the Apollo missions (NCRP, 1989).

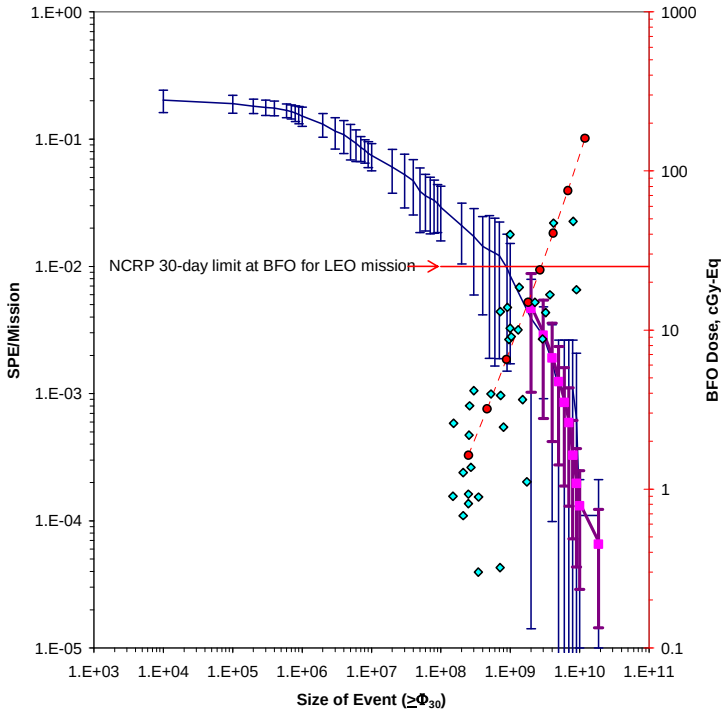


Figure 5-6. ***Probability of SPE in a 1-week mission (thin line: average probability of SPE and statistical fluctuation during space era; thick line: extended average probability including impulsive nitrate events; ■ impulsive nitrate events data) and BFO dose (--●-- BFO dose of the worst-case SPE model scaled by Φ>30 flux to August 1972 SPE; ♦ BFO dose of 34 large SPEs during space era using actual spectra).***

A recent publication (Posner, 2007) provides evidence that detection of relativistic solar electrons may enable as much as a 1-hour warning of proton events as well as prediction of the integral number of protons that can be expected, as illustrated in figure 5-7. The color matrix that is shown provides a code to predict future proton intensity, 1 hour ahead of time, as predicted by relativistic electron measurements. The parameter space is given by the current maximum electron increase parameter, which goes back in time at least 5 minutes and up to 60 minutes, and current relativistic electron intensity. The matrix is derived from the aggregate of all 1998 to 2002 relativistic electron observations and their corresponding 30- to 50-MeV proton intensities that occurred 1 hour later. Data was obtained from the comprehensive suprathermal and energetic particle analyzer (COSTEP) instrument on the solar and heliospheric observatory (SOHO) satellite. The color shows the average for the proton intensity in each locus. Statistical considerations limit the utility of the matrix at the bottom and upper-right ranges. The importance of the findings of Posner (2007) cannot be overestimated as they not only provide up to a 1-hour early detection capability, but also may allow astronauts and Mission Control personnel to predict whether an event will likely be of insignificant size, which is the most likely outcome. Long-term forecasting from hours to days before the onset of an SPE at this time is inherently inaccurate, with a large number of false alarms predicted and many events not predicted at all (NCRP, 2006).

Mechanisms of radiation-induced vomiting

The mechanisms by which radiation induces nausea and vomiting are not well understood. It is known that radiation induces the secretion of serotonin in the GI-tract. In turn, the binding of serotonin to receptors in the brain mediates vomiting. The physiological effects of high-dose radiation are also mediated, in part, by inflammatory responses. Increased secretion of inflammatory cytokines IL-12 and IL-18 was reported in mouse macrophages after irradiation (Shan et al., 2007). Increased production of IL-6 and TNF-α, which are also pro-inflammatory cytokines, has been observed in the lungs of irradiated mice (Fedorocko et al., 2002). Pro-inflammatory cytokines mediate symptoms of nausea, vomiting, anorexia, and cachexia in instances of cancer and other diseases as well as pregnancy. In addition, ionizing radiation directly generates numerous reactive oxygen species. Additional reactive oxygen species are indirectly generated by cellular responses to radiation, initiating long-lasting cascades of inflammatory events. How these molecules interact to induce the symptoms of prodromal syndrome is unknown.

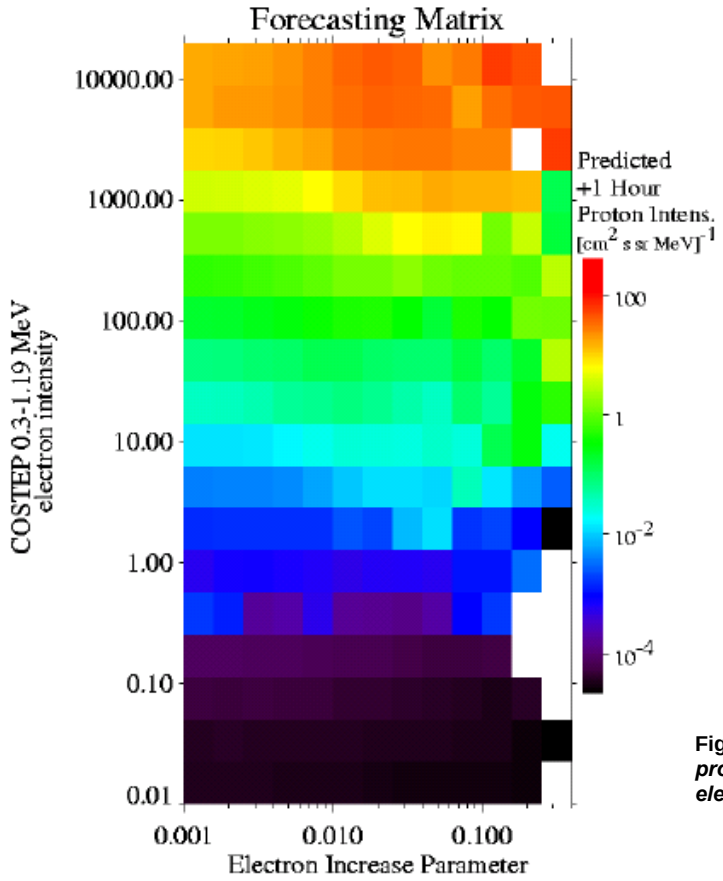


Figure 5-7. ***One-hour lead time prediction of proton spectra that are generated from real-time electron measurements (Posner, 2007).***

Potential for biological countermeasures

Radioprotectors, such as antioxidants, are agents that reduce the damage to various organs by radiation (Gudkow and Komarova, 2005). The likelihood that SPE will produce doses that are above 1 Gy is small, while the occurrence of doses that can induce prodromal risks are quite possible. Although prodromal syndrome may seem more innocuous than the other symptoms of ARS, biological countermeasures for the prodromal risks are a major consideration. Many radioprotectors, including antioxidants and WR-2721, are not expected to coun-

teract prodromal risks such as vomiting or nausea (Harding, 1988). Several classes of drugs have been used to treat the nausea and vomiting that are experienced by patients who are undergoing whole-body radiotherapy (Harding, 1988). While the molecules that regulate vomiting are not well understood, the inhibitors or antagonists of serotonin, dopamine, histamine, and substance P suppress vomiting. Clinical trials have demonstrated that serotonin antagonists were more effective than prochlorperazine or metoclopramide (Franzen et al., 1996; Priestman et al., 1993). Of the 5-HT_3 class drugs, ondansetron has been best studied (Licitra et al., 2002). Studies of the efficacy of combinations of drugs of different classes, such as palonosetron and aprepitant when used with olanzapine or gabapentin, are under way to prevent acute and delayed chemotherapy-induced nausea and vomiting (Navari and Province, 2006). These treatments need to be investigated to determine the efficacy and tolerability for SPE-induced prodromal effects. Cannabinoids, anticholinergics, steroids, benzodiazepides, and plant extracts are also currently being evaluated for their antiemetic properties. Thus, the mechanisms of SPE-induced prodromal symptoms are unclear, but a broad spectrum of potential countermeasures is available for testing.

Conclusion

The biological effects of space radiation, including ARS, are a significant concern. High doses of radiation can induce profound radiation sickness and death. Lower doses of radiation induce symptoms that are much milder physiologically, but that pose operational risks that are equally serious. Both scenarios have the potential to seriously affect crew health and/or prevent the completion of mission objectives. Radiation protection must be provided in the form of predictive models, shielding, and biological countermeasures when traveling outside of the protective magnetosphere of the Earth. Unfortunately, the development of these tools is hindered by a lack of relevant space radiation research. Most radiation studies focus on radiation species and doses that are unlike the radiation that is encountered in space. There is therefore a pressing need for research that accurately reflects the radiation risks that are native to the space environment and that facilitate the development of both improved risk assessment and effective radioprotective strategies.

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Chapter 6:
Risk of Acute or Late Central Nervous System Effects from Radiation Exposure

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Acute and late radiation damage to the central nervous system (CNS) may lead to changes in motor function and behavior, or neurological disorders. Radiation and synergistic effects of radiation with other space flight factors may affect neural tissues, which in turn may lead to changes in function or behavior. Data specific to the spaceflight environment must be compiled to quantify the magnitude of this risk. If this is identified as a risk of high enough magnitude then appropriate protection strategies should be employed. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

Acute and late radiation damage to the central nervous system (CNS) may lead to changes in motor function and behavioral or neurological disorders. A vigorous ground-based cellular and animal model research program will help quantify the risk to the CNS from space radiation exposure on future long distance space missions and promote the development of optimized countermeasures.

Executive Summary

Possible acute and late risks to the CNS from GCRs and SPEs are a documented concern for human exploration of our solar system (NAS, 1973; NAS/NRC, 1996, NCRP, 2006). In the past, the risks to the CNS of adults who were exposed to low to moderate doses of ionizing radiation ((0 to 2 Gy (1 Gray) (Gy = 100 rad)) have not been a major consideration. However, the heavy ion component of space radiation presents distinct biophysical challenges to cells and tissues as compared to the physical challenges that are presented by terrestrial forms of radiation. Soon after the discovery of cosmic rays, the concern for CNS risks originated with the prediction of the light flash phenomenon from single HZE nuclei traversals of the retina (Tobias, 1952); this phenomenon was confirmed by the Apollo astronauts in 1970 and 1973. HZE nuclei are capable of producing a column of heavily damaged cells, or a microlesion, along their path through tissues, thereby raising concern over serious impacts on the CNS (Todd, 1989). In recent years, other concerns have arisen with the discovery of neurogenesis and its impact by HZE nuclei, which have been observed in experimental models of the CNS.

Human epidemiology is used as a basis for risk estimation for cancer, acute radiation risks, and cataracts. This approach is not viable for estimating CNS risks from space radiation, however. At doses above a few Gy, detrimental CNS changes occur in humans who are treated with radiation (e.g., gamma rays and protons) for cancer. Treatment doses of 50 Gy are typical, which is well above the exposures in space even if a large SPE were to occur. Thus, of the four categories of space radiation risks (cancer, CNS, degenerative, and acute radiation syndromes), the CNS risk relies most extensively on experimental data with animals for its evidence base. Understanding and mitigating CNS risks requires a vigorous research program that will draw on the basic understanding that is gained from cellular and animal models, and on the development of approaches to extrapolate risks and the potential benefits of countermeasures for astronauts.

Several experimental studies, which use heavy ion beams simulating space radiation, provide constructive evidence of the CNS risks from space radiation. First, exposure to HZE nuclei at low doses (<50 cGy) significantly induces neurocognitive deficits, such as learning and behavioral changes as well as operant reactions in the mouse and rat. Exposures to equal or higher doses of low-LET radiation (e.g., gamma or X rays) do not show similar effects. The threshold of performance deficit following exposure to HZE nuclei depends on both the physical characteristics of the particles, such as LET, and the animal age at exposure. A performance deficit has been shown to occur at doses that are similar to the ones that will occur on a Mars mission (<0.5 Gy). The neurocognitive deficits with the dopaminergic nervous system are similar to aging and appear to be unique to space radiation. Second, exposure to HZE disrupts neurogenesis in mice at low doses (<1 Gy), showing a significant dose-related reduction of new neurons and oligodendrocytes in the subgranular zone (SGZ) of the hippocampal dentate gyrus. Third, reactive oxygen species (ROS) in neuronal precursor cells arise following exposure to HZE nuclei and protons at low dose, and can persist for several months. Antioxidants and anti-inflammatory agents can possibly reduce these changes. Fourth, neuroinflammation arises from the CNS following exposure to HZE nuclei and protons. In addition, age-related genetic changes increase the sensitivity of the CNS to radiation.

Research with animal models that are irradiated with HZE nuclei has shown that important changes to the CNS occur with the dose levels that are of concern to NASA. However, the significance of these results on the morbidity to astronauts has not been elucidated. One model of late tissue effects (Rubin and Casarett, 1968) suggests that significant effects will occur at lower doses, but with increased latency. It is to be noted that the studies that have been conducted to date have been carried out with relatively small numbers of animals (<10 per dose group); therefore, testing of dose threshold effects at lower doses (<0.5 Gy) has not been carried out sufficiently at this time. As the problem of extrapolating space radiation effects in animals to humans will be a challenge for space radiation research, such research could become limited by the population size that is used in animal

studies. Furthermore, the role of dose protraction has not been studied to date. An approach to extrapolate existing observations to possible cognitive changes, performance degradation, or late CNS effects in astronauts has not been discovered. New approaches in systems biology offer an exciting tool to tackle this challenge. Recently, eight gaps were identified for projecting CNS risks. Research on new approaches to risk assessment may be needed to provide the necessary data and knowledge to develop risk projection models of the CNS from space radiation.

Introduction

Both GCRs and SPEs are of concern for CNS risks. The major GCRs are composed of protons, α-particles, and particles of HZE nuclei with a broad energy spectra ranging from a few tens to above 10,000 MeV/u. In interplanetary space, GCR organ dose and dose-equivalent of more than 0.2 Gy or 0.6 Sv per year, respectively, are expected (Cucinotta et al., 2003; Cucinotta and Durante, 2006). The high energies of GCRs allow them to penetrate to hundreds of centimeters of any material, thus precluding radiation shielding as a plausible mitigation measure to GCR risks on the CNS. For SPEs, the possibility exists for an absorbed dose of over 1 Gy from an SPE if crew members are in a thinly shielded spacecraft or performing a spacewalk (Kim et al., 2007). The energies of SPEs, although substantial (tens to hundreds of MeV), do not preclude radiation shielding as a potential countermeasure. However, the costs of shielding may be high to protect against the largest events.

The fluence of charged particles hitting the brain of an astronaut has been estimated several times in the past (Craven and Rycroft, 1994; Curtis et al., 1989; Cucinotta et al., 1998). One estimate is that during a 3-year mission to Mars at solar minimum (assuming the 1972 spectrum of GCR), 20 million out of 43 million hippocampus cells and 230 thousand out of 1.3 million thalamus cell nuclei will be directly hit by one or more particles with charge Z>15 (Curtis et al., 1998; 2000). These numbers do not include the additional cell hits by energetic electrons (delta rays) that are produced along the track of HZE nuclei (Cucinotta et al., 1998) or correlated cellular damage (Cucinotta et al., 1999; Ponomarev and Cucinotta, 2006). The contributions of delta rays from GCR and correlated cellular damage increase the number of damaged cells two- to three-fold from estimates of the primary track alone and present the possibility of heterogeneously damaged regions, respectively. The importance of such additional damage is poorly understood.

At this time, the possible detrimental effects to an astronaut's CNS from the HZE component of GCR have yet to be identified. This is largely due to the lack of a human epidemiological basis with which to estimate risks and the relatively small number of published experimental studies with animals. RBE factors are combined with human data to estimate cancer risks for low-LET radiation exposure. Since this approach is not possible for CNS risks, new approaches to risk estimation will be needed. Thus, biological research is required to establish risk levels and risk projection models and, if the risk levels are found to be significant, to design countermeasures.

Description of central nervous system risks of concern to NASA

Acute and late CNS risks from space radiation are of concern for Exploration missions to the moon or Mars. Acute CNS risks include: altered cognitive function, reduced motor function, and behavioral changes, all of which may affect performance and human health. Late CNS risks are possible neurological disorders such as Alzheimer's disease, dementia, or premature aging. The effect of the protracted exposure of the CNS to the low dose-rate (< 50 mGy h^{-1}) of proton, HZE particles, and neutrons of the relevant energies for doses up to 2 Gy is of concern.

Current NASA permissible exposure limits

PELs for short-term and career astronaut exposure to space radiation have been approved by the NASA Chief Health and Medical Officer. The PELs set requirements and standards for mission design and crew selection as recommended in NASA-STD-3001, Volume 1. NASA has used dose limits for cancer risks and the non-cancer risks to the BFOs, skin, and lens since 1970. For Exploration mission planning, preliminary dose limits for the CNS risks are based largely on experimental results with animal models. Further research is needed to validate and quantify these risks, however, and to refine the values for dose limits. The CNS PELs, which correspond to the doses at the region of the brain called the hippocampus, are set for time periods of 30 days or 1 year, or for a career with values of 500, 1,000, and 1,500 mGy-Eq, respectively. Although the unit mGy-Eq is used, the RBE for CNS effects is largely unknown; therefore, the use of the quality factor function for cancer risk estimates is advocated. For particles with charge Z>10, an addition PEL requirement limits the physical dose (mGy) for 1 year and the career to 100 and 250 mGy, respectively. NASA uses computerized anatomical geometry models to estimate the body self-shielding at the hippocampus.

Evidence

Review of human data

Evidence of the effects of terrestrial forms of ionizing radiation on the CNS has been documented from radiotherapy patients, although the dose is higher for these patients than would be experienced by astronauts in the space environment. CNS behavioral changes such as chronic fatigue and depression occur in patients who are undergoing irradiation for cancer therapy (Tolifon and Fike, 2000). Neurocognitive effects, especially in children, are observed at lower radiation doses (Schultheiss et al., 1995; BEIR-V, 1990). A recent review on intelligence and the academic achievement of children after treatment for brain tumors indicates that radiation exposure is related to a decline in intelligence and academic achievement, including low intelligence quotient (IQ) scores, verbal abilities, and performance IQ; academic achievement in reading, spelling, and mathematics; and attention functioning (Butler and Haser, 2006). Mental retardation was observed in the children of the atomic-bomb survivors in Japan who were exposed to radiation prenatally at moderate doses (<2 Gy) at 8 to 15 weeks post-conception, but not at earlier or later prenatal times (BEIR-V, 1990).

Radiotherapy for the treatment of several tumors with protons and other charged particle beams provides ancillary data for considering radiation effects for the CNS. NCRP Report No. 153 (NCRP, 2006) notes charge particle usage "for treatment of pituitary tumors (Kjellberg and Kliman, 1979; Linfoot, 1979), hormone-responsive metastatic mammary carcinoma (Tobias, 1979), brain tumors (Castro et al., 1985; Suit et al., 1982), and intracranial arteriovenous malformations and other cerebrovascular diseases (Fabrikant et al., 1989; Fabrikant et al., 1985; Fabrikant et al., 1984; Kjellberg et al., 1983; Levy et al., 1989; Steinberg et al., 1990)." In these studies are found associations with neurological complications such as impairments in cognitive functioning, language acquisition, visual spatial ability, and memory and executive functioning, as well as changes in social behaviors. Similar effects did not appear in patients who were treated with chemotherapy. In all of these examples, the patients were treated with extremely high doses that were below the threshold for necrosis (Goldberg et al., 1982; Keime-Guibert et al., 1998). Since cognitive functioning and memory are closely associated with the cerebral white volume of the prefrontal/frontal lobe and cingulate gyrus, defects in neurogenesis may play a critical role in neurocognitive problems in irradiated patients (NCRP, 2006).

Review of space flight issues

The first proposal concerning the effect of space radiation on the CNS was made by Cornelius Tobias in his 1952 description of light flash phenomenon caused by single HZE nuclei traversals of the retina (Tobias et al., 1952). Light flashes, such as those described by Tobias, were observed by the astronauts during the early Apollo missions as well as in dedicated experiments that were subsequently performed on Apollo and Skylab missions (Pinsky et al., 1974). More recently, studies of light flashes were made on the Russian *Mir* space station and the ISS (Sannita et al., 2004). A 1973 report by the NAS considered these effects in detail. This phenomenon, which is known as a phosphene, is the visual perception of flickering light. It is considered a subjective sensation of light since it can be caused by simply applying pressure on the eyeball (NCRP, 2006). The traversal of a single, highly charged particle through the occipital cortex or the retina was estimated to be able to cause a light flash. Possible mechanisms for HZE-induced light flashes include direction ionization and Cerenkov radiation within the retina (NAS, 1973).

The observation of light flashes by the astronauts brought attention to the possible effects of HZE nuclei on brain function. The microlesion concept, which considered the effects of the column of damaged cells surrounding the path of an HZE nucleus traversing critical regions of the brain, originated at this time (NAS, 1973; Todd, 1989). An important task that still remains is to determine whether and to what extent such particle traversals contribute to functional degradation within the CNS.

The possible observation of CNS effects in astronauts who were participating in past NASA missions is highly unlikely for several reasons. First, the lengths of past missions are relatively short and the population sizes of astronauts are small. Second, when astronauts are traveling in LEO, they are partially protected by the magnetic field and the solid body of the Earth, which together reduce the GCR dose-rate by about two-thirds from its free space values. Furthermore, the GCR in LEO has lower LET components compared to the GCR that will be encountered in transit to Mars or on the lunar surface because the magnetic field of the Earth repels nuclei with energies that are below about 1,000 MeV/u, which are of higher LET. For these reasons, the CNS risks are a greater concern for long-duration lunar missions or for a Mars mission than for missions on the ISS.

Radiobiology studies of central nervous system risks for protons, neutrons, and high-Z high-energy nuclei

Both GCR and SPE could possibly contribute to acute and late CNS risks to astronaut health and performance. This section presents a description of the studies that have been performed on the effects of space radiation in cell, tissue, and animal models.

Effects in Neuronal Cells and the Central Nervous System

Neurogenesis

The CNS consists of neurons, astrocytes, and oligodendrocytes that are generated from multipotent stem cells. NCRP Report No. 153 provides the following excellent and short introduction to the composition and cell types of interest for radiation studies of the CNS (NCRP, 2006): “The CNS consists of neurons differing markedly in size and number per unit area. There are several nuclei or centers that consist of closely packed neuron cell bodies (e.g., the respiratory and cardiac centers in the floor of the fourth ventricle). In the cerebral cortex the large neuron cell bodies, such as Betz cells, are separated by a considerable distance. Of additional importance are the neuroglia which are the supporting cells and consist of astrocytes, oligodendroglia, and microglia. These cells permeate and support the nervous tissue of the CNS, binding it together like a scaffold that also supports the vasculature. The most numerous of the neuroglia are Type I astrocytes, which make up about half the brain, greatly outnumbering the neurons. Neuroglia retain the capability of cell

division in contrast to neurons and, therefore, the responses to radiation differ between the cell types. A third type of tissue in the brain is the vasculature which exhibits a comparable vulnerability for radiation damage to that found elsewhere in the body (Reinhold and Hopewell, 1980). Radiation-induced damage to oligodendrocytes and endothelial cells of the vasculature accounts for major aspects of the pathogenesis of brain damage that can occur after high doses of low-LET radiation." Based on studies with low-LET radiation, the CNS is considered a radioresistant tissue. For example: in radiotherapy, early brain complications in adults usually do not develop if daily fractions of 2 Gy or less are administered with a total dose of up to 50 Gy (NCRP, 2006). The tolerance dose in the CNS, as with other tissues, depends on the volume and the specific anatomical location in the human brain that is irradiated (Schultheiss et al., 1995).

In recent years, studies with stem cells uncovered that neurogenesis still occurs in the adult hippocampus, where cognitive actions such as memory and learning are determined (Squire, 1992; Eisch, 2002). This discovery provides an approach to understand mechanistically the CNS risk of space radiation. Accumulating data indicate that radiation not only affects differentiated neural cells, but also the proliferation and differentiation of neuronal precursor cells and even adult stem cells. Recent evidence points out that neuronal progenitor cells are sensitive to radiation (Mizumatsu et al., 2003; Monje et al., 2002; Tofilon and Fike, 2000). Studies on low-LET radiation show that radiation stops not only the generation of neuronal progenitor cells, but also their differentiation into neurons and other neural cells. NCRP Report No. 153 (NCRP, 2006) notes that cells in the SGZ of the dentate gyrus undergo dose-dependent apoptosis above 2 Gy of X-ray irradiation, and the production of new neurons in young adult male mice is significantly reduced by relatively low (>2 Gy) doses of X rays. NCRP Report No. 153 (NCRP, 2006) also notes that: "These changes are observed to be dose dependent. In contrast there were no apparent effects on the production of new astrocytes or oligodendrocytes. Measurements of activated microglia indicated that changes in neurogenesis were associated with a significant dose-dependent inflammatory response even 2 months after irradiation. This suggests that the pathogenesis of long-recognized radiation-induced cognitive injury may involve loss of neural precursor cells from the SGZ of the hippocampal dentate gyrus and alterations in neurogenesis."

Recent studies provide evidence of the pathogenesis of HZE nuclei in the CNS (Casadesus et al., 2004; 2005; Rola et al., 2004; 2005). The authors of one of these studies (Casadesus et al., 2005) were the first to suggest neurodegeneration with HZE nuclei, as shown in figure 6-1(a). These studies demonstrate that HZE radiation led to the progressive loss of neuronal progenitor cells in the SGZ at doses of 1 to 3 Gy in a dose-dependent manner. NCRP Report No. 153 (NCRP, 2006) notes that "Mice were irradiated with 1 to 3 Gy of ^{12}C or ^{56}Fe-ions and 9 months later proliferating cells and immature neurons in the dentate SGZ were quantified. The results showed that reductions in these cells were dependent on the dose and LET. Loss of precursor cells was also associated with altered neurogenesis and a robust inflammatory response, as shown in figures 6-1(a) and 6-1(b). These results indicate that high-LET radiation has a significant and long-lasting effect on the neurogenic population in the hippocampus that involves cell loss and changes in the microenvironment. The work has been confirmed by other studies (Casadesus et al., 2004; Casadesus et al., 2005). These investigators noted that these changes are consistent with those found in aged subjects, indicating that heavy-particle irradiation is a possible model for the study of aging."

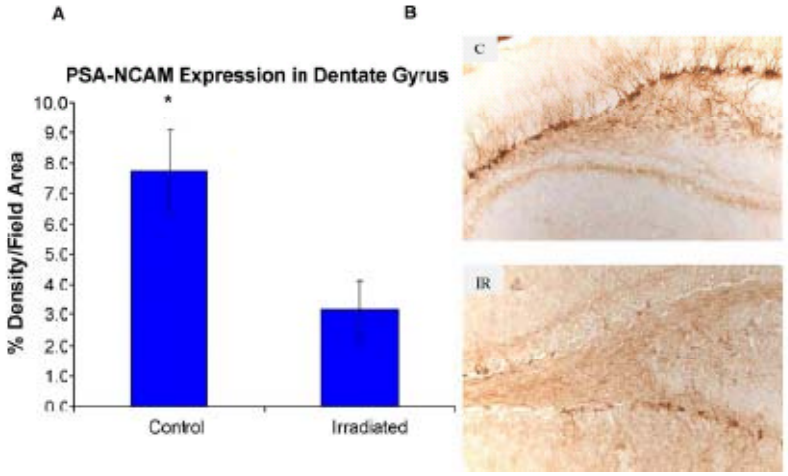

Figure 6-1(a). (Panel A) ***Expression of polysialic acid form of neural cell adhesion molecule (PSA-NCAM) in the hippocampus of rats that were irradiated (IR) with 2.5 Gy of ^{56}Fe high-energy radiation and control subjects as measured by % density/field area measured.*** **(Panel B)** ***PSA-NCAM staining in the dentate gyrus of representative irradiated (IR) and control (C) subjects at 5× magnification (Casadesus et al., 2005).***

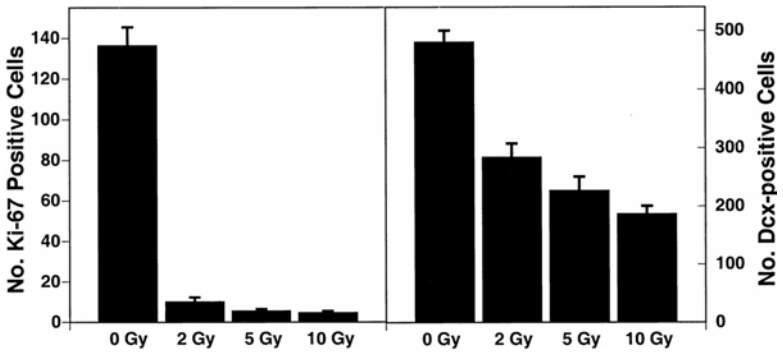

Figure 6-1(b). ***Numbers of proliferating cells (left panel) and immature neurons (right panel) in the dentate SGZ are significantly decreased 48 hours after irradiation. Antibodies against Ki-67 and doublecortin (Dcx) were used to detect proliferating cells and immature neurons, respectively. Doses from 2 to 10 Gy significantly ($p < 0.05$) reduced the numbers of proliferating cells. Immature neurons were also reduced in a dose-dependent fashion ($p<0.001$). Each bar represents an average of four animals; error bars, and standard error (Mizumatsu et al., 2003).***

Oxidative damage

Recent studies indicate that adult rat neural precursor cells from the hippocampus show an acute, dose-dependent apoptotic response that was accompanied by an increase in ROS Limoli et al., 2004). Low-LET protons are also used in clinical proton beam radiation therapy, at an RBE of 1.1 relative to megavoltage X rays at a high dose. NCRP Report No. 153 (NCRP, 2006) notes that: "Relative ROS levels were increased at nearly all doses (1 to 10 Gy) of Bragg-peak 250 MeV protons at post-irradiation times (6 to 24 hours) compared to unirradiated controls (Giedzinski et al., 2005). The increase in ROS after proton irradiation was

more rapid than that observed with X rays and showed a well-defined dose response at 6 and 24 hours, increasing about 10-fold over controls at a rate of 3% per Gy. However, by 48 hours post-irradiation, ROS levels fell below controls and coincided with minor reductions in mitochondrial content. Use of the antioxidant alpha-lipoic acid (before or after irradiation) was shown to eliminate the radiation-induced rise in ROS levels. These results corroborate the earlier studies using X rays and provide further evidence that elevated ROS are integral to the radioresponse of neural precursor cells." Furthermore, high-LET radiation led to significantly higher levels of oxidative stress in hippocampal precursor cells as compared to lower-LET radiations (X rays, protons) at lower doses (≤1 Gy) (figure 6-2). The use of the antioxidant lipoic acid was able to reduce ROS levels below background levels when added before or after ^{56}Fe-ion irradiation. These results conclusively show that low doses of ^{56}Fe-ions can elicit significant levels of oxidative stress in neural precursor cells at a low dose.

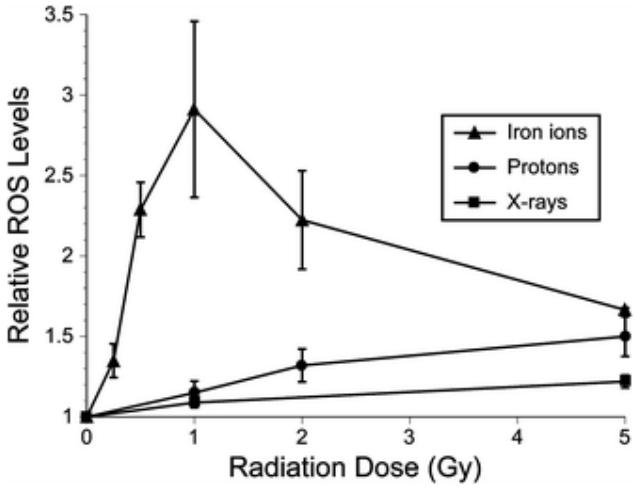

Figure 6-2. ***Dose response for oxidative stress after ^{56}Fe-ion irradiation. Hippocampal precursors that are subjected to ^{56}Fe-ion irradiation were analyzed for oxidative stress 6 hours after exposure. At doses ≤1 Gy a linear dose response for the induction of oxidative stress was observed. At higher ^{56}Fe doses, oxidative stress fell to values that were found using lower-LET irradiations (X rays, protons). Experiments, which represent a minimum of three independent measurements (±SE), were normalized against unirradiated controls set to unity. ROS levels induced after ^{56}Fe irradiation were significantly (P < 0.05) higher than controls (Limoli et al., 2007).***

Neuroinflammation

Neuroinflammation, which is a fundamental reaction to brain injury, is characterized by the activation of resident microglia and astrocytes and local expression of a wide range of inflammatory mediators. Acute and chronic neuroinflammation has been studied in the mouse brain following exposure to HZE. The acute effect of HZE is detectable at 6 and 9 Gy; no studies are available at lower doses. Myeloid cell recruitment appears by 6 months following exposure. The estimated RBE value of HZE irradiation for induction of an acute neuroinflammatory response is three compared to that of gamma irradiation (Rola et al., 2005). COX-2 pathways are implicated in neuroinflammatory processes that are caused by low-LET radiation. COX-2 up-regulation in irradiated microglia cells leads to prostaglandin E2 production, which appears to be responsible for radiation-induced gliosis (overproliferation of astrocytes in damaged areas of the CNS) (Kyrkanides et al., 2002; Moore et al., 2005; Hwang et al., 2006).

Behavioral Effects

As behavioral effects are difficult to quantitate, they consequently are one of the most uncertain of the space radiation risks. NCRP Report No. 153 (NCRP, 2006) notes that: "The behavioral neurosciences literature is replete with examples of major differences in behavioral outcome depending on the animal species, strain, or measurement method used. For example, compared to unirradiated controls, X-irradiated mice show hippocampal-dependent spatial learning and memory impairments in the Barnes maze, but not in

the Morris water maze (Raber et al., 2004) which, however, can be used to demonstrate deficits in rats (Shukitt-Hale et al., 2003; Shukitt-Hale et al., 2000). Particle radiation studies of behavior have been accomplished with rats and mice, but with some differences in the outcome depending on the endpoint measured."

The following studies provide evidence that space radiation affects the CNS behavior of animals in a somewhat dose- and LET-dependent manner.

Sensorimotor effects

Sensorimotor deficits and neurochemical changes were observed in rats that were exposed to low doses of ^{56}Fe-ions (Joseph et al., 1992; 1993). Doses that are below 1 Gy reduce performance, as tested by the wire suspension test. Behavioral changes were observed as early as 3 days after radiation exposure and lasted up to 8 months. Biochemical studies showed that the K^+-evoked release of dopamine was significantly reduced in the irradiated group, together with an alteration of the nerve signaling pathways (Joseph and Cutler, 1994). A negative result was reported by Pecaut et al. (2004), in which no behavioral effects were seen in female C57/BL6 mice in a 2- to 8-week period following their exposure to 0, 0.1, 0.5 or 2 Gy accelerated ^{56}Fe-ions (1 GeV/u ^{56}Fe) as measured by open-field, rotorod, or acoustic startle habituation.

Radiation-induced changes in conditioned taste aversion

There is evidence that deficits in conditioned taste aversion (CTA) are induced by low doses of heavy ions (Hunt et al., 1989; Rabin et al., 1989; 1991; 1994; 2000). The CTA test is a classical conditioning paradigm that assesses the avoidance behavior that occurs when the ingestion of a normally acceptable food item is associated with illness. This is considered a standard behavioral test of drug toxicity (Riley and Tuck, 1985). NCRP Report No. 153 (NCRP, 2006) notes that: "The role of the dopaminergic system in radiation-induced changes in CTA is suggested by the fact that amphetamine-induced CTA, which depends on the dopaminergic system, is affected by radiation, whereas lithium chloride-induced CTA, which does not involve the dopaminergic system, is not affected by radiation. It was established that the degree of CTA due to radiation is LET-dependent ([figure 6-3]) and that ^{56}Fe-ions are the most effective of the various low and high LET radiation types that have been tested (Rabin et al., 1989; Rabin et al., 1991). Doses as low as ~0.2 Gy of ^{56}Fe-ions appear to have an effect on CTA."

The RBE of different types of heavy particles on CNS function and cognitive/behavioral performance was studied in Sprague-Dawley rats (Rabin et al., 2007). The relationship between the thresholds for the HZE particle-induced disruption of amphetamine-induced CTA learning is shown in figure 6-4; and for the disruption of operant responding is shown in figure 6-5. These figures show a similar pattern of responsiveness to the disruptive effects of exposure to either ^{56}Fe or ^{28}Si particles on both CTA learning and operant responding. These results suggest that the RBE of different particles for neurobehavioral dysfunction cannot be predicted solely on the basis of the LET of the specific particle.

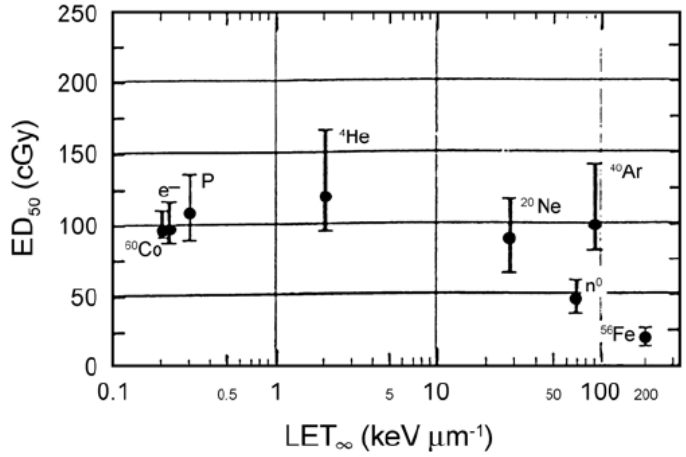

Figure 6-3. ***ED_{50} for CTA as a function of LET for the following radiation sources: ^{40}Ar = argon ions, ^{60}Co = cobalt-60 gamma rays, e^- =electrons, ^{56}Fe = iron ions, ^{4}He = helium ions, n^0 = neutrons, ^{20}Ne = neon ions (Rabin et al., 1991).***

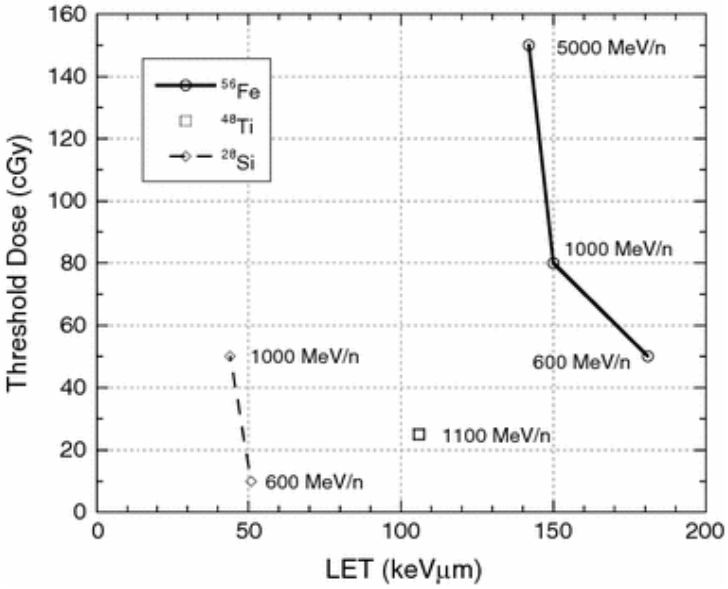

Figure 6-4. ***Radiation-induced disruption in CTA. This figure shows the relationship between exposure to different energies of ^{56}Fe and ^{28}Si particles and the threshold dose for the disruption of amphetamine-induced CTA learning. Only a single energy of ^{48}Ti particles was tested. The threshold dose (cGy) for the disruption of the response is plotted against particle LET (keV/μm (Rabin et al., 2007).***

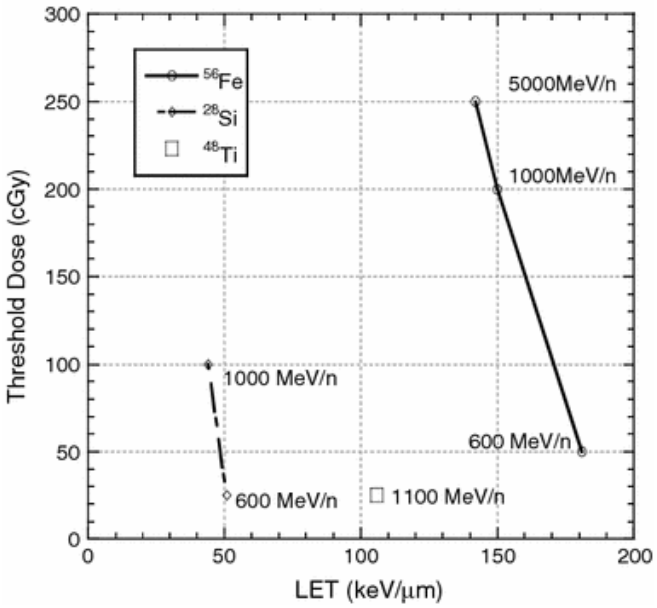

Figure 6-5. ***High-LET radiation effects on operant response. This figure shows the relationship between the exposure to different energies of ^{56}Fe and ^{28}Si particles and the threshold dose for the disruption of performance on a food-reinforced operant response. Only a single energy of ^{48}Ti particles was tested. The threshold dose (cGy) for the disruption of the response is plotted against particle LET (keV/µm) (Rabin et al., 2007).***

Radiation affect on operant conditioning

Operant conditioning uses several consequences to modify a voluntary behavior. Recent studies by Rabin et al. (2003) have examined the ability of rats to perform an operant order to obtain food reinforcement using an ascending fixed-ratio (FR) schedule. They found that ^{56}Fe-ion doses that are above 2 Gy affect the appropriate responses of rats to increasing work requirements. NCRP Report No. 153 (NCRP, 2006) notes that "The disruption of operant response in rats was tested 5 and 8 months after exposure, but maintaining the rats on a diet containing strawberry, but not blueberry, extract were shown to prevent the disruption (Rabin et al., 2005). When tested 13 and 18 months after irradiation, there were no differences in performance between the irradiated rats maintained on control, strawberry or blueberry diets. These observations suggest that the beneficial effects of antioxidant diets may be age dependent."

Spatial learning and memory

The effects of exposure to HZE nuclei on spatial learning, memory behavior, and neuronal signaling have been tested, and threshold doses have also been considered for such effects. It will be important to understand the mechanisms that are involved in these deficits to extrapolate the results to other dose regimes, particle types, and, eventually, astronauts. Studies on rats were performed using the Morris water maze test 1 month after whole-body irradiation with 1.5 Gy of 1 GeV/u ^{56}Fe-ions. Irradiated rats demonstrated cognitive impairment that was similar to that seen in aged rates. This leads to the possibility that an increase in the amount of ROS may be responsible for the induction of both radiation- and age-related cognitive deficits (Shukitt-Hale et al., 2000).

NCRP Report No. 153 (NCRP, 2006) notes that: "Denisova *et al*. exposed rats to 1.5 Gy of 1 GeV/u ^{56}Fe-ions and tested their spatial memory in an eight-arm radial maze. Radiation exposure impaired the rats' cognitive behavior, since they committed more errors than control rats in the radial maze and were unable to adopt a spatial strategy to solve the maze (Denisova et al., 2000). To determine whether these findings related to brain-region specific alterations in sensitivity to oxidative stress, inflammation or neuronal plasticity, three regions of the brain, the striatum, hippocampus and frontal cortex that are linked to behavior, were isolated and compared to controls. Those that were irradiated were adversely affected as reflected through the levels of dichlorofluorescein, heat shock, and synaptic proteins (for example, synaptobrevin and synaptophysin). Changes in these factors consequently altered cellular signaling (for example, calcium-dependent protein kinase C and protein kinase A). These changes in brain responses significantly correlated with working memory errors in the radial maze. The results show differential brain-region-specific sensitivity induced by ^{56}Fe irradiation ([figure 6-6]). These findings are similar to those seen in aged rats, suggesting that increased oxidative stress and inflammation may be responsible for the induction of both radiation and age-related cognitive deficits."

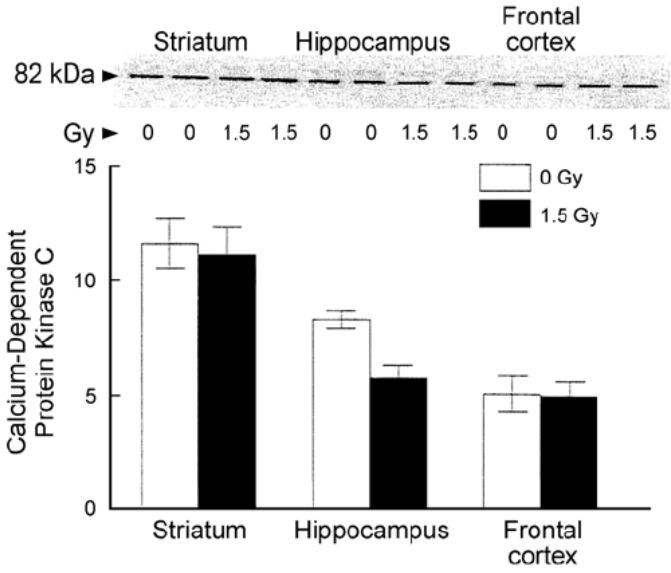

Figure 6-6. ***Brain-region-specific calcium-dependent protein kinase C expression was assessed in control and irradiated rats using standard Western blotting procedures. Values are means ± SEM (standard error of mean) (Denisova et al., 2002).***

Acute Central Nervous System Risks

In addition to the possible in-flight performance and motor skill changes that were described above, the immediate CNS effects (i.e., within 24 hours following exposure to low-LET radiation) are anorexia and nausea (Fajardo et al., 2001). These prodromal risks are dose-dependent and, as such, can provide an indicator of the exposure dose. Estimates are ED_{50} = 1.08 Gy for anorexia, ED_{50} = 1.58 Gy for nausea, and ED_{50}=2.40 Gy for emesis. The relative effectiveness of different radiation types in producing emesis was studied in ferrets and is illustrated in figure 6-7. High-LET radiation at doses that are below 0.5 Gy show greater relative biological effectiveness compared to low-LET radiation (Rabin et al., 1994). The acute effects on the CNS, which are associated with increases in cytokines and chemokines, may lead to disruption in the proliferation of stem cells or memory loss that may contribute to other degenerative diseases.

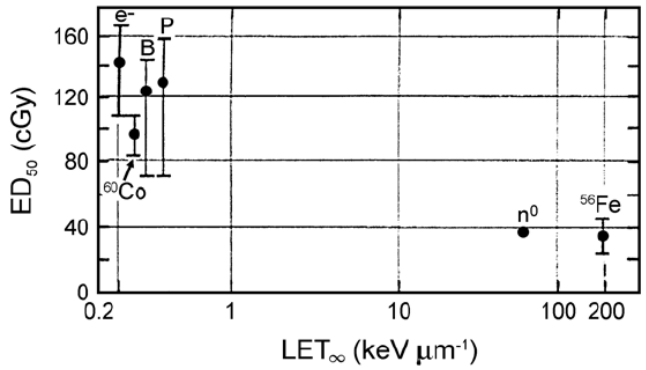

Figure 6-7. ***LET dependence of RBE of radiation in producing emesis or retching in a ferret. B = bremstrahlung; e^- = electrons; P = protons; ^{60}Co = cobalt gamma rays; n^o = neutrons; and ^{56}Fe = iron***

Computer Models and Systems Biology Analysis of Central Nervous System Risks

Since human epidemiology and experimental data for CNS risks from space radiation are limited, mammalian models are essential tools for understanding the uncertainties of human risks. Cellular, tissue, and genetic animal models have been used in biological studies on the CNS using simulated space radiation. New technologies, such as three-dimensional cell cultures, microarrays, proteomics, and brain imaging, are used in systematic studies on CNS risks from different radiation types. According to biological data, mathematical models can be used to estimate the risks from space radiation.

Systems biology approaches to Alzheimer's disease that consider the biochemical pathways that are important in CNS disease evolution have been developed by research that was funded outside of NASA. Figure 6-8 shows a schematic of the biochemical pathways that are important in the development of Alzheimer's disease. The description of the interaction of space radiation within these pathways would be one approach to developing predictive models of space radiation risks. For example, if the pathways that were studied in animal models could be correlated with studies in humans who are suffering from Alzheimer's disease, an approach to describe risk that uses biochemical degrees-of-freedom could be pursued. Edelstein-Keshet and Spiros (2002) have developed an *in silico* model of senile plaques that are related to Alzheimer's disease. In this model, the biochemical interactions among TNF, IL-1B, and IL-6 are described within several important cell populations, including astrocytes, microglia, and neurons. Further, in this model soluble amyloid causes microglial chemotaxis and activates IL-1B secretion. Figure 6-9 shows the results of the Edelstein-Keshet and Spiros model simulating plaque formation and neuronal death. Establishing links between space radiation-induced changes to the changes that are described in this approach can be pursued to develop an *in silico* model of Alzheimer's disease that results from space radiation.

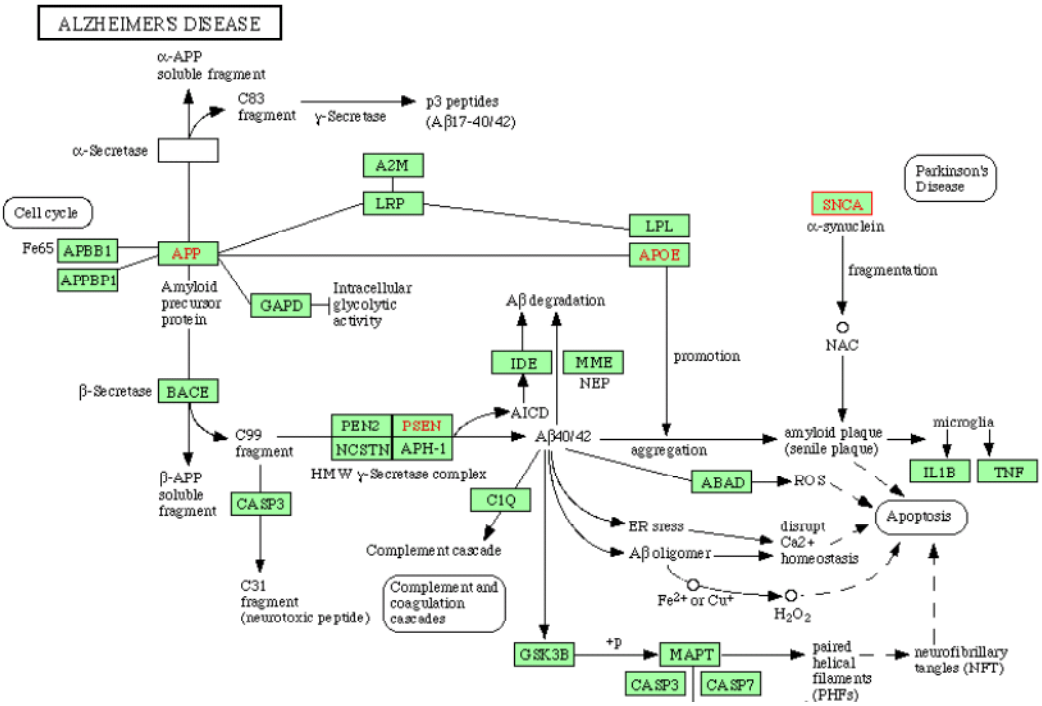

Figure 6-8. ***Molecular pathways important in Alzheimer's disease. From*** **Kyoto Encyclopedia of Genes and Genomes (*http://www.genome.ad.jp/kegg/pathway/hsa/hsa05010.html*).**

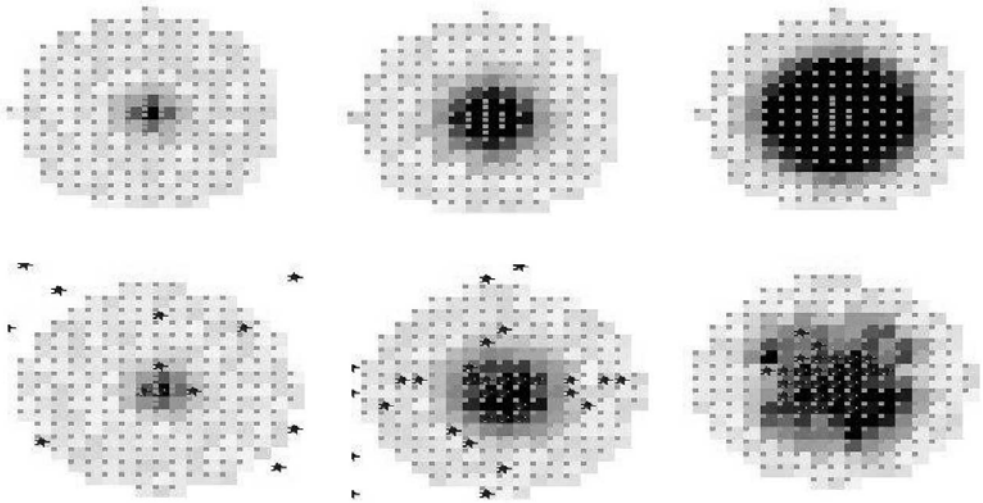

Figure 6-9. ***Model of plaque formation and neuronal death in Alzheimer's disease. From Edelstein-Keshet and Spiros, 2002*****: Top row:** ***Formation of a plaque and death of neurons in the absence of glial cells, when fibrous amyloid is the only injurious influence. The simulation was run with no astrocytes or microglia, and the health of neurons was determined solely by the local fibrous amyloid. Shown above is a time sequence (left to right) of three stages in plaque development, at early, intermediate, and advanced stages. Density of fibrous deposit is represented by small dots and neuronal health by shading from white (healthy) to black (dead). Note radial symmetry due to simple diffusion.*** **Bottom row:** ***Effect of microglial removal of amyloid on plaque morphology. Note that microglia (small star-like shapes) are seen approaching the plaque (via chemotaxis to soluble amyloid, not shown). At a later stage, they have congregated at the plaque center, where they adhere to fibers. As a result of the removal of soluble and fibrous amyloid, the microglia lead to irregular plaque morphology.*** **Size scale:** ***In this figure, the distance between the small single dots (representing low-fiber deposits) is 10 mm. Similar results were obtained for a 10-fold scaling in the time scale of neuronal health dynamics.***

Other interesting candidate pathways that may be important in the regulation of radiation-induced degenerative CNS changes are signal transduction pathways that are regulated by Cdk5. Cdk5 is a kinase that plays a key role in neural development; its aberrant expression and activation are associated with neurodegenerative processes, including Alzheimer's disease (Catania et al., 2001; Muyllaert et al., 2008). This kinase is up-regulated in neural cells following ionizing radiation exposure (Cruz et al., 2003)

Risks in Context of Exploration Mission Operational Scenarios

Projections for space missions

Reliable projections of CNS risks for space missions cannot be made from the available data. Animal behavior studies indicate that high-HZE radiation has a high RBE, but the data are not consistent. Other uncertainties include: age at exposure, radiation quality, and dose-rate effects, as well as issues regarding genetic susceptibility to CNS risk from space radiation exposure. More research is required before CNS risk can be estimated.

Potential for biological countermeasures

The goal of space radiation research is to estimate and reduce uncertainties in risk projection models and, if necessary, develop countermeasures and technologies to monitor and treat adverse outcomes to human health and performance that are relevant to space radiation for short-term and career exposures, including acute or late CNS effects from radiation exposure. The need for the development of countermeasures to CNS risks is dependent on further understanding of CNS risks, especially issues that are related to a possible dose threshold, and if so, which NASA missions would likely exceed threshold doses. As a result of animal experimental studies, antioxidant and anti-inflammation are expected to be effective countermeasures for CNS risks from space radiation (Rabin et al., 2005). Diets of blueberries and strawberries were shown to reduce CNS risks after heavy-ion exposure. Estimating the effects of diet and nutritional supplementation will be a primary goal of CNS research on countermeasures.

A diet that is rich in fruit and vegetables significantly reduces the risk of several diseases. Retinoids and vitamins A, C, and E are probably the most well-known and studied natural radioprotectors, but hormones (e.g., melatonin), glutathione, superoxide dismutase, and phytochemicals from plant extracts (including green tea and cruciferous vegetables), as well as metals (especially selenium, zinc, and copper salts) are also under study as dietary supplements for individuals, including astronauts, who have been overexposed to radiation (Durante and Cucinotta, 2008). Antioxidants should provide reduced or no protection against the initial damage from densely ionizing radiation such as HZE nuclei, because the direct effect is more important than the free-radical-mediated indirect radiation damage at high LET. However, there is an expectation that some benefits should occur for persistent oxidative damage that is related to inflammation and immune responses (Barcellos-Hoff et al., 2005). Some recent experiments suggest that, at least for acute high-dose irradiation, an efficient radioprotection by dietary supplements can be achieved, even in the case of exposure to high-LET radiation. Although there is evidence that dietary antioxidants (especially strawberries) can protect the CNS from the deleterious effects of high doses of HZE particles (Rabin et al. 2005), because the mechanisms of biological effects are different at low dose-rates compared to those of acute irradiation, new studies for protracted exposures will be needed to understand the potential benefits of biological countermeasures.

Concern about the potential detrimental effects of antioxidants was raised by a recent meta-study of the effects of antioxidant supplements in the diet of normal subjects (Bjelakovic et al., 2007). The authors of this study did

not find statistically significant evidence that antioxidant supplements have beneficial effects on mortality. On the contrary, they concluded that β-carotene, vitamin A, and vitamin E seem to increase the risk of death. Concerns are that the antioxidants may allow rescue of cells that still sustain DNA mutations or altered genomic methylation patterns following radiation damage to DNA, which can result in genomic instability. An approach to target damaged cells for apoptosis may be advantageous for chronic exposures to GCR.

Individual risk factors

Individual factors of potential importance are genetic factors, prior radiation exposure, and previous head injury, such as concussion. Apolipoprotein E (ApoE) has been shown to be an important and common factor in CNS responses. ApoE controls the redistribution of lipids among cells and is expressed at high levels in the brain (Raber et al., 1998). New studies are considering the effects of space radiation for the major isoforms of ApoE, which are encoded by distinct alleles (ε2, ε3, and ε4). The isoform ApoE ε4 has been shown to increase the risk of cognitive impairments and to lower the age for Alzheimer's disease. It is not known whether the interaction of radiation sensitivity or other individual risks factors is the same for high- and low-LET radiation. Other isoforms of ApoE confer a higher risk for other diseases. People who carry at least one copy of the ApoE ε4 allele are at increased risk for atherosclerosis, which is also suspected to be a risk increased by radiation. People who carry two copies of the ApoE ε2 allele are at risk for a condition that is known as hyperlipoproteinemia type III. It will therefore be extremely challenging to consider genetic factors in a multiple-radiation-risk paradigm

Conclusion

Reliable projections for CNS risks from space radiation exposure cannot be made at this time due to a paucity of data on the subject. Existing animal and cellular data do suggest that space radiation can produce neurological and behavioral effects; therefore, it is possible that mission operations will be impacted. The significance of these results on the morbidity to astronauts has not been elucidated, however. It is to be noted that studies, to date, have been carried out with relatively small numbers of animals (<10 per dose group); this means that testing of dose threshold effects at lower doses (<0.5 Gy) has not yet been carried out to a sufficient extent. As the problem of extrapolating space radiation effects in animals to humans will be a challenge for space radiation research, such research could become limited by the population size that is typically used in animal studies. Furthermore, the role of dose protraction has not been studied to date. An approach has not been discovered to extrapolate existing observations to possible cognitive changes, performance degradation, or late CNS effects in astronauts. Research on new approaches to risk assessment may be needed to provide the data and knowledge that will be necessary to develop risk projection models of the CNS from space radiation. A vigorous research program, which will be required to solve these problems, must rely on new approaches to risk assessment and countermeasure validation because of the absence of useful human radio-epidemiology data in this area.

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Chapter 7:
Risk of Degenerative Tissue or Other Health Effects from Radiation Exposure

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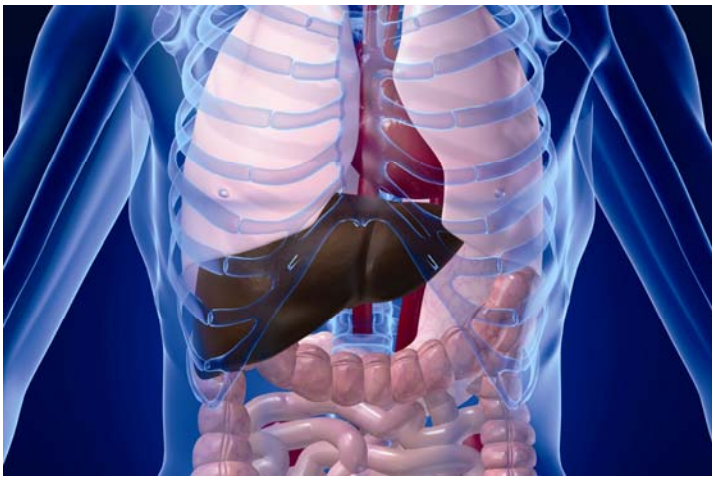
Occupational radiation exposure from the space environment may result in degenerative tissue diseases (non-cancer or non-CNS) such as cardiac, circulatory, or digestive diseases, as well as cataracts, although the mechanisms and the magnitude of influence of radiation leading to these diseases are not well characterized. Radiation and synergistic effects of radiation cause increased DNA strand and tissue degeneration, which may lead to acute or chronic disease of susceptible organ tissues. Data specific to the spaceflight environment must be compiled to quantify the magnitude of this risk to determine if additional protection strategies are required. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.



Exposure to space radiation may result in non-cancer or non-CNS degenerative tissue diseases, including cardiac, circulatory and digestive disorders, as well as cataracts. NASA's research program in this area currently focuses on determining the risks for these diseases from low dose-rate exposures and for HZE nuclei so that appropriate countermeasures can be developed to mitigate these risks.

Executive Summary

Human epidemiology studies of people who are exposed to various doses of ionizing radiation provide strong evidence that degenerative diseases are to be expected from exposures during long-duration space travel to GCRs or large SPEs in which fluences of more than 10^7 protons per cm^2 with energies that are above 30 MeV occur. The RBE factors for most degenerative diseases that are caused by space radiation are unknown. However, the range of doses that have been observed in human studies is sufficient to make the probability of degenerative disease risks from GCR and SPE exposure during space flight a major concern. The types of radiation that are in space present additional uncertainties in risk estimates for degenerative diseases, and the results of several studies suggest that both quantitative and qualitative differences may occur when comparing LET radiation on Earth, such as X rays and gamma rays, to high-LET radiation in space, such as heavy ions and recoil nuclei and neutrons that are produced in nuclear reactions. A shortened latency is expected for high-LET radiation in space, which increases the detriment above that of identical diseases in the U.S. population. Therefore, the greater likelihood of degenerative diseases presents a risk that is competitive with the already well-documented risks of mortality and morbidity with respect to cancer. As the focus for NASA is on understanding and mitigating risk, space radiation is a large obstacle to mission success. It is unknown at this time whether radiation shielding approaches that are distinct from those needed for the other radiation risks are needed for degenerative risks. Research on individual sensitivity to and biological countermeasures for degenerative risks, except for cataracts, is nonexistent.

Introduction

The environment outside of the shield-like atmosphere and magnetosphere of the Earth contains several types of radiation. Most of the particles in interplanetary space are derived from the solar wind, which produces a constant flux of low-energy particles. Dangerous and intermittent SPEs can produce large quantities of highly energetic protons and heavy ions. An additional constituent of space radiation, GCRs, emanate from outside our solar system and comprise mostly highly energetic protons with a small component of HZE nuclei. Researchers have predicted that an astronaut will receive a total body dose of approximately 1 to 2 mSv each day in interplanetary space and approximately 0.5 to 1 mSv each day on the surface of Mars, and these numbers will increase in the event of an SPE (Cucinotta and Durante, 2006; Saganti et al., 2004).

Exposure to ionizing radiation affects cells and tissues either by directly damaging cellular components or by producing highly reactive free radicals from water and other constituents of cells. Both of these mechanisms can produce sufficient damage to cause cell death, DNA mutation, or abnormal cell function. The extent of damage is generally believed to depend on the dose and the type of particle, and to follow a linear response to radiation dose for initial induction of damage. This is true for high and moderate radiation doses, but it is extremely difficult to measure for lower doses because of the challenges in distinguishing the effects of radiation exposure from those of normal cellular oxidative stress.

As HZE nuclei are the components of space radiation that have the highest biological effectiveness, they are a large concern for astronaut safety. HZE nuclei produce highly ionizing tracks as they pass through matter. In addition, they leave columns of damage at the molecular level when they traverse a biological system – damage that is fundamentally different from the damage that is left by low-LET radiation sources such as gamma and X rays. HZE nuclei impart damage through the primary energetic particle and secondary delta-ray electrons as well as from fragmentation events that produce a spectrum of other energetic nuclei, protons, neutrons, and heavy fragments (Wilson et al., 1995). Therefore, a large penumbra of energy deposition extends outward from the

primary particle track (Cucinotta et al., 2000). The lack of epidemiological data and sparse radiobiological data on the effects of these HZE nuclei leads to a high level of uncertainty in risk estimates for long-term health effects after exposure to GCRs and SPEs.

NASA has funded several previous reports from the NAS and the NCRP that provided evidence for the radiation risks in space. The NCRP is chartered by the U.S. Congress to guide federal agencies such as NASA on the risk from radiation exposures to their workers. Reports from the NCRP and the NRC on space radiation risks are the foundation of how NASA views the wide scientific body of evidence that is used for its research and operational radiation protection methods and plans.

Description of degenerative risks of concern to NASA

The major degenerative conditions of concern that could potentially result from space radiation exposure are as follows:

- Cataract formation
- Degenerative changes in the heart and vasculature (e.g., atherosclerosis and cardiomyopathy)
- Other diseases that are related to aging, including digestive and respiratory disease
- Other aging effects, including premature senescence and endocrine and immune system dysfunction

Note that risks to the CNS may also involve degenerative conditions, but they are treated as a stand-alone risk category by NASA and are described in Chapter 6 of this document.

Current NASA permissible exposure limits

PELs for short-term and career exposures to space radiation have been approved by the NASA Chief Health and Medical Officer, who also sets the requirements and standards for mission design and crew selection. Table 7-1, which is taken directly from NASA-STD-3001, Volume 1 (Table 4, p. 67), lists the current short- and long-term PELs for non-cancer effects (in mGy-Eq. or mGy). The lifetime limits for cataracts and heart disease are imposed to limit or prevent risks of degenerative tissue diseases. The approach here, which uses an estimate of threshold doses for heart and cataracts risk, is quite distinct from that of cancer risk limits, in which a probabilistic assessment of the risk is made using a projection model. Such an approach will likely be needed in the future for the degenerative risks. Career limits for the heart are intended to limit the REID as a result of heart disease, so, those limits fall below the current estimate of a threshold dose (NCRP, 2000); however, exposure would lead to some risk if a linear dose response with no threshold model were established.

Table 7-1. ***Short- and Long-term Dose Limits for Non-cancer Effects***

Organ	30-day limit	1-year Limit	Career
Lens*	1,000 mGy-Eq	2,000 mGy-Eq	4,000 mGy-Eq
Skin	1,500 mGy-Eq	3,000 mGy-Eq	4,000 mGy-Eq
BFO	250 mGy-Eq	500 mGy-Eq	Not applicable
Heart**	250 mGy-Eq	500 mGy-Eq	1,000 mGy-Eq
CNS***	500 mGy-Eq	1,000 mGy-Eq	1,500 mGy-Eq
CNS*** (Z≥10)	–	100 mGy	250 mGy

*Lens limits are intended to prevent early (<5 years) severe cataracts (e.g., from an SPE). An additional cataract risk – sub-clinical cataracts – exists at lower doses from cosmic rays, which may progress to severe types after long latency (>5 years). Although these cataract risks are not preventable by existing mitigation measures, they are deemed an acceptable risk to the program.
**Heart doses calculated as average over heart muscle and adjacent arteries.
***CNS limits should be calculated at the hippocampus.

Evidence

Review of human data

Cataracts

The development of ocular cataracts, which is a degenerative opacification of the crystalline lens, is a well-recognized late effect of exposure to ionizing radiation. The first reports of radiation-induced cataracts appeared early in the 20th century, shortly after the first X-ray machines were developed (Rollins, 1903). It is now clear that radiation-induced cataracts exhibit relationships between radiation dose and disease severity as well as between dose and latency. Evidence for this link comes, most notably, from survivors of radiotherapy who received high doses (>5 Gy) of ionizing radiation using X rays, gamma rays, and proton beams for ocular tumors (Ferrufino-Ponce and Henderson, 2006; Blakely et al., 1994; Gragoudas et al., 1995) and from individuals who received whole-body therapeutic radiation (Belkacemi et al., 1996; Dunn et al., 1993; Frisk et al., 2000).

Evidence of cataract risk (moderate- to low-dose gamma-ray exposures) comes from epidemiological data from atomic-bomb survivors who were followed in the life span study, which is a longitudinal study of Japanese survivors of the bombings of both Hiroshima and Nagasaki, which remains one of the most valuable and informative epidemiological studies for evaluating long-term health effects of radiation exposure (Preston et al., 2003).

Among the atomic-bomb survivors, the frequency and the severity of cataracts are dose-dependent. Severity refers to the size and loss of visual acuity of the cataract, or the presence of conditions requiring lens implants to prevent blindness. Symptoms appeared as soon as several months after exposure for severe cases and several years after exposure for less-severe cases. The frequency of appearance was related to the proximity of the subject to the hypocenter of the atomic bomb. A possible threshold dose was originally estimated to be in the range 0.6 to 1.5 Gy (Junk et al., 1998; Otake and Schull, 1982; 1991), but a non-threshold dose model has been proposed in more recent reports (Neriishi et al., 2007). In a prospective study that follows the development of radiation-induced cataracts in workers who were exposed to radiation during the efforts to clean up after the Chernobyl nuclear power plant disaster, it was found that posterior subcapsular or cortical cataracts were present in 25% of the examined individuals. The investigators estimated that the dose-effect threshold for cataract formation in exposures is less than 1 Gy (Worgul et al., 2007).

As noted by Blakely and Chang (2007a), published data on radiation-induced human cataracts are limited in predicting the risk from chronic exposure to low doses of protons or low fluence of heavy ions, such as that encountered in space, because of the possible qualitative differences in effect.

Cardiovascular Diseases and Other Degenerative Changes

A clear link has been established between exposure to high doses of ionizing radiation and the long-term development of cardiovascular disease and degenerative heart changes. Like the evidence described for cataractogenesis, the major evidence that proves a link between ionizing radiation exposure and the development of degenerative heart and vasculature changes comes from prospective studies that follow the long-term, treatment-related effects in cancer survivors. These patients received relatively high therapeutic doses (~5–50 Gy) of low-LET thoracic radiation exposure in the course of therapy for cancers of the head, neck, and chest, such as Hodgkin's lymphoma and breast cancer (Prosnitz et al., 2005; Darby et al., 2005; Carver et al., 2007; Swerdlow et al., 2007). There is a dose-dependent increase in the development of a wide variety of cardiovascular diseases, including acute and chronic pericarditis, coronary artery disease (CAD), cardiomyopathy, valvular disease, and conduction abnormalities, that lead to arrhythmia in these individuals. A commonality in each of these disorders seems to be damage to the microvasculature and small coronary arteries that result from acute inflammation and ischemia and is followed by progressive degenerative fibrotic changes (Little et al., 2008). Impairment in nitric oxide signal transduction may contribute to degenerative vascular changes (Soloviev et al., 2003). Atherosclerosis that is caused in this manner, as a secondary effect to radiation treatment, looks pathologically similar to atherosclerosis that is caused by other factors. A paucity of data exists on doses and dose-rates that cause atherosclerosis in humans.

Other evidence that supports a link between the occurrence of cardiovascular disease and radiation exposure is derived from prospective studies of atomic-bomb survivors who received moderate doses of radiation (0–2 Gy) as well as from occupationally exposed workers who received continuous low-dose exposure (Darby et al., 2005; Yamada et al., 2004; Preston et al., 2003; Hayashi et al., 2003). In atomic-bomb survivors who are enrolled in the life-span study, the development of health effects has been extensively studied through continuous longitudinal health assessments. The average doses that were received by the atomic-bomb survivors (Preston, 2003) are similar to the effective doses for an ISS mission and somewhat lower than the effective dose that is expected for a Mars mission. A significant dose-response relationship exists for hypertension, stroke, and heart attack in survivors who were exposed at less than 40 years of age; their ERR is estimated to be 14% per Sievert (Sv); but the existence of a threshold dose cannot be excluded for risks that are associated with doses that are less than 0.25 Sv (Table 7-2).

For occupationally exposed workers, such as employees of nuclear power facilities, data are less convincing. A recent study of U.S. workers who were exposed to radiation with doses that were below 1 Sv in nuclear power plants showed a significant correlation between radiation dose and death from cardiovascular disease (Howe et al, 2004). However, similar studies (Table 7-3) have shown risks that are more similar to those of the atomic-bomb survivors, or no increased risk. Further studies are warranted, as evidence at doses that are below 0.5 Sv is suggestive at best (Vrijheid et al., 2007). Finally, follow-up studies of the health risks in Chernobyl recovery workers also show an increased risk for cardiovascular diseases; however, the contribution of lifestyle factors to this risk estimate cannot be eliminated at this point, and further analysis is needed (Ivanov et al., 2006; McGale and Darby, 2005).

Table 7-2. ***Estimates of Excess Relative Risk per Sievert for Non-cancer deaths from Life-span Study of the Atomic-bomb Survivors (Preston et al., 2003). Life-Span Study Cause-Specific, Non-cancer Disease ERR Estimates 1968–1997***

Cause	ERR per Sv	Deaths[a]	Estimated number of radiation-associated deaths
All non-cancer diseases (0–139, 240–279, 290–799)	0.14 (0.08; 0.2)[b]	14,459	273 (176; 375)[b]
Heart disease (390–429)	0.17 (0.08; 0.26)	4,477	101 (47; 161)
Stroke (430–438)	0.12 (0.02; 0.22)	3,954	64 (14; 118)
Respiratory disease (640–519)	0.18 (0.06; 0.32)	2,266	57 (19; 98)
Pneumonia (480–487)	0.16 (0.00; 0.32)	1,528	33 (4; 67)
Digestive disease (520–579)	0.15 (0.00; 0.32)	1,292	27 (0; 58)
Cirrhosis (571)	0.19 (–0.05; 0.5)	567	16 (–2; 37)
Infectious disease (000–139)	–0.02 (< –0.2; 0.25)	397	–1 (–14; 15)
Tuberculosis (010–018)	–0.01 (< –0.2; 0.4)	237	–0.5 (–2; 13)
Other diseases[c] (240–279; 319–389; 580–799)	0.08 (–0.04; 0.23)	2,073	24 (–12; 64)
Urinary diseases (589–629)	0.25 (–0.01; 0.6)	515	17 (–1; 39)

[a]Deaths among potential survivors between 1968 and 1997; [b]90% C.I.; [c]Excluding diseases of the blood and BFOs.

Table 7-3. ***Occupational Studies and Circulatory Disease Mortality (Hoel, 2006)***

Occupationally Exposed Persons			
Study	**Workers (Circulatory deaths)**	**ERR per Sv**	**Comments**
U.K. radiologists (Berrington, 2001)	2,698 (514)	< 0	Time trend in cancer but not in CVD
U.S. radiologists (Matanoski, 1975)	30,084	0.2	Time trend in cancer but not in CVD
U.S. radiology techs (Hauptmann, 2003)	90,284 (1,070)	0.01–0.42	Time trend in both stroke and CHD
Nuclear workers study IARC 3 country study (Cardis, 1995)	95,673 (7,885)	0.26	5% works > 0.2 Sv 2% workers > 0.4 Sv
U.S. power reactors (Howe et al., 2004)	53,698 (350)	8.3	95% C.I.: (2.3, 18.2)
Mayak workers (Bolotnikova, 1994)	9,373 (749)	0.01	
Chernobyl emergency (Ivanov, 2001)	65,095 (1,728	0.79	Exposures 0 to 0.35 Sv

CHD = coronary heart disease; CVD = cardiovascular disease; IARC = International Agency for Research on Cancer.

Digestive and Respiratory Diseases

Figures 7-1 and 7-2 show results from Preston et al. (2003) for the ERR for death vs. dose for several diseases, including digestive and respiratory diseases. Significant risks are observed for doses that are above 1 Sv for the acute gamma-ray exposures that were received by the atomic-bomb survivors. As dose-rates in space are below 5 mSv/hour for GCR and, in most cases, are below 50 mSv/hour for SPE, respiratory and digestive diseases have not been considered a risk for ISS missions. However, for missions to Mars or lunar missions incurring a large SPE, doses that are above 1 Sv are likely. Average years of life-loss for these diseases is about 9 years in the atomic-bomb survivors. Absolute probabilities for disease morbidity will, of course, be higher than those for mortality risks.

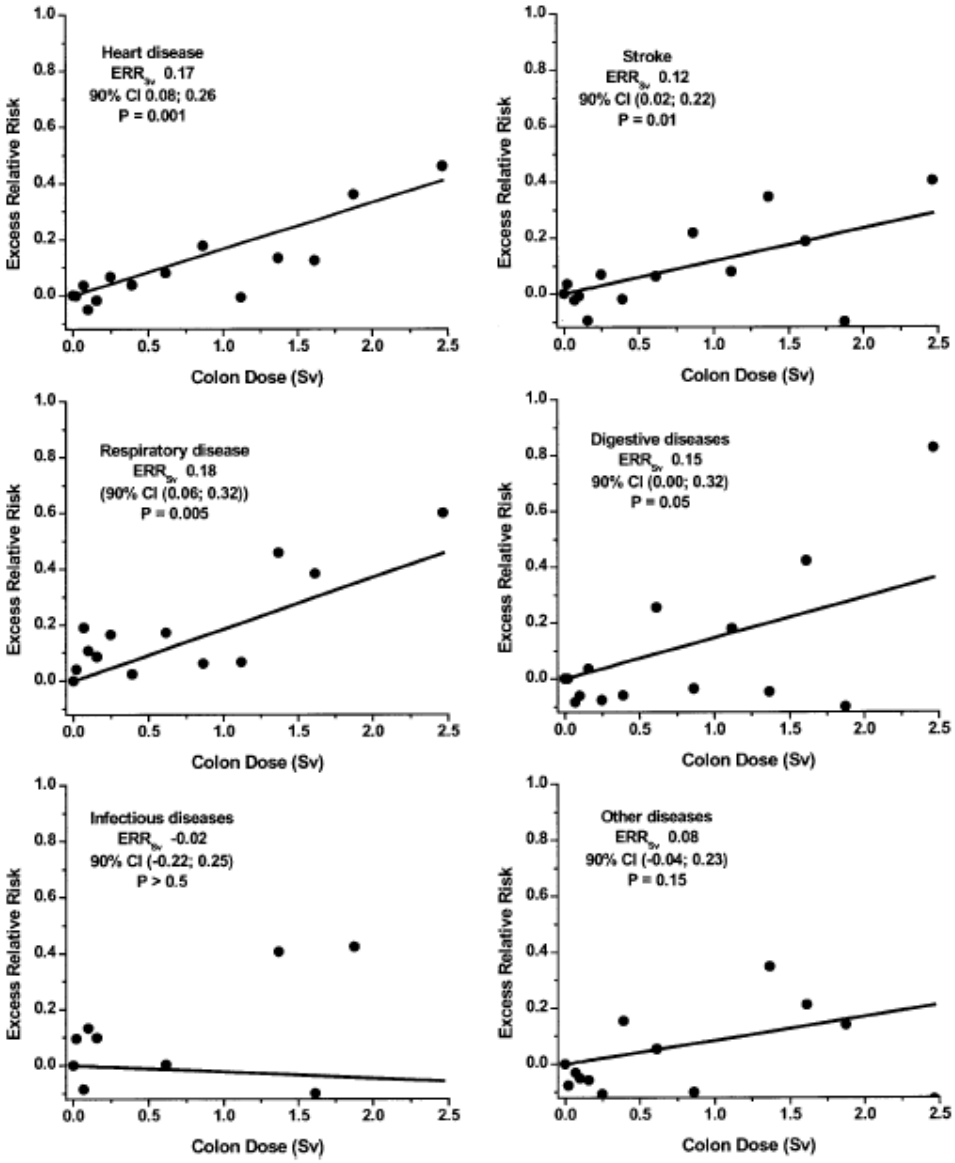


Figure 7-1. ***Preston et al. (2003): Cause-specific dose-response functions for non-cancer deaths. The plots display the best-fitting ERR models together with nonparametric ERR estimates for 20 dose categories.***

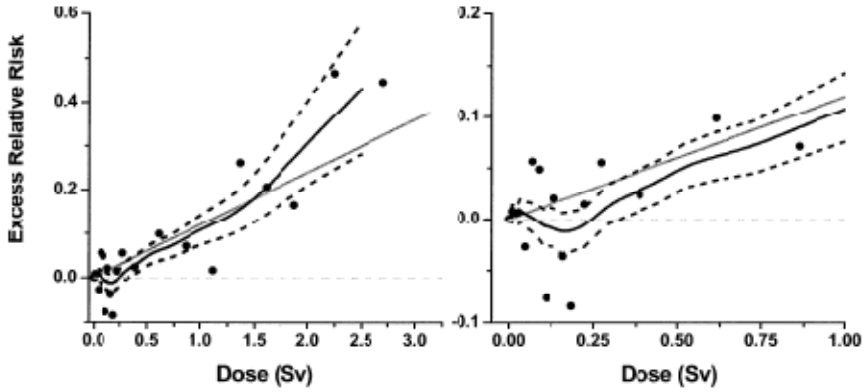


Figure 7-2. ***Preston et al. (2003): Non-cancer dose-response function for the period 1968–1997. The solid line indicates the fitted linear ERR model without any effect modifications by age at exposure, sex, or attained age. The points are dose-category-specific ERR estimates, the solid curve is a smoothed estimate derived from the points, and the dashed line indicates upper and lower one-standard-error bounds on the smoothed estimate. The right panel shows the low-dose portion of the dose-response function in more detail.***

In summary, the link between exposure to acute doses of 1 Gy or more of ionizing radiation and the development of degenerative diseases is clearly established, while the health risks of low-dose and low-dose-rate ionizing radiation remain largely unknown. These risks are more difficult to assess because multiple factors are believed to play a role in the etiology of the diseases (BEIR VII, 2006). Similarly, no human data are available on the effects of high-LET radiation on the development of degenerative heart and cardiovascular complications.

Evidence for Other Age-related Effects Caused by Radiation

Several biological processes that are commonly found to be degraded with increasing age are accelerated by radiation exposure, including changes in endocrine function, fibrosis, and premature cellular senescence. Examples of studies showing radiation effects on markers of aging include the following (NCRP Report No. 156, 2006):

- Studies of structural changes in specific organs
- General life-span longevity studies that are performed on animal models
- Analyses of biochemical and molecular markers of cellular aging, including senescence

The possibility of radiation-induced accelerated aging was noted very early on in follow-up studies of the atomic-bomb survivors (Anderson et al., 1974). Current studies show that atomic-bomb survivors exhibit a decrease in immune function that is similar to that seen during normal aging, and that the effect depends on the dose of radiation that was received (Kusunoki and Hayashi, 2007). This impairment may be associated with disease development seen in the survivors. It is also possible that the damage that was caused by oxidative stress is the basis for the link between radiation exposure and aging (Burhans and Weinberger, 2007; Toussaint et al., 2002).

Radiation Effects on Endocrine Function

The endocrine system controls hormone production, secretion, metabolism, and hormone levels in circulating blood. Age-related changes to the endocrine system occur in most older people. The hypothalamus is responsible for releasing hormones that stimulate the pituitary gland. During aging, individuals suffer impaired secretion of some hypothalamic hormones and pituitary response, resulting in a decreased capability

for the endocrine system to respond to the internal environment and external stresses of the body. Adenomas, which are hyperplasias in the parathyroid gland, are observed in patients who are treated with low-LET radiation with doses that are below 1 Gy (Tezelman et al., 1995; Tissel et al., 1985) and in the atomic-bomb survivors (Fujiwara et al., 1992).

Premature Cellular Senescence

Radiation also increases senescence in cells, which may accelerate the aging process (Campisi, 2003). Senescent cells have exited the cell cycle and are no longer capable of cell division. The principle mechanism by which senescence occurs is through shortening of telomeres, which are the DNA structure that caps the ends of chromosomes, below a critical length (~4 kilo base-pairs). The capacity to assume this phenotype may function as an anticancer mechanism in which a genetically damaged cell is shut down before it can be converted to a cancer cell (Campisi and d'Adda di Fagagna, 2007; Mallette and Ferbeyre, 2007). Telomere length has been correlated with longevity in several studies (reviewed by Shay and Wright, 2005).

Reviews of space flight issues

The NAS Space Science Board first reviewed space flight issues in 1967 (NAS/NRC, 1967) and revisited these issues in 1970 (NAS/NRC, 1970). These reviews led to the establishment of dose limits that were used at NASA until 1989. Extensive reviews of human and experimental radiobiology data for space risks were also provided to NASA in 1989, 2000, and 2006 via NCRP reports (NCRP 1989; 2000; 2006). The 1989 and 2000 NCRP Reports led to updates in the NASA dose limits. The issues of cataracts and degenerative tissue effects have been discussed in many of these reports. Reviews on other degenerative risks have been given more priority in the more recent of the reports. The more recent reviews suggest that the threshold doses may be lower than previously estimated or do not occur, especially for high-LET radiation. A major question also remains on the categorization of these risks as deterministic vs. stochastic, which has major implications for radiation protection.

The most recent external report of the evidence of space radiation effects was published in 2006 by the NCRP (NCRP Report 153, 2006). The stated purpose of this report was to identify and describe the information that is needed to make radiation protection recommendations for space missions beyond LEO. The report contains a comprehensive summary of the current body of evidence for radiation-induced health risks and makes recommendations on areas requiring future experimentation. For the non-cancer, late effects of radiation, the authors of this report recommend that experiments be conducted using protracted or extended exposure times and low dose rates of protons, heavy ions, and neutrons in energy ranges that are relevant to space radiation exposure scenarios. Specifically, the authors of the report recommend that analyses should be conducted on the effects of protracted exposures on the lens, whole-body vasculature, gastrointestinal tract, gonadal cell populations, and hematopoietic and immune systems, as well as fertility.

Cataracts in astronauts

Cucinotta et al. (2001) reported the first epidemiological evidence for an exposure-dependent increase in the risk of cataract formation in astronauts. Health records for 295 astronauts who were enrolled in the NASA Longitudinal Study of Astronaut Health, which spans more than 3 decades, were evaluated for incidence and type of cataract. Data were analyzed for astronaut age at the time at which the cataract appeared or the amount of time after the first mission when the cataract appeared (figure 7-3). Astronauts were grouped by individual occupational radiation exposure records that allowed for the separation of exposures from low-LET diagnostic X rays, atmospheric radiation that was received during aviation training, and exposure that was received during space flight. These data reveal an increased cataract incidence for astronauts who have a higher lens dose-equivalent

(average of 45 mSv) of space radiation relative to that of other astronauts with zero or low lens dose (average 8 mSv). These studies also show a significant association between radiation quality and cataract incidence. Astronauts who flew on high-inclination (>50 deg) and lunar missions, which are associated with a higher flux of high-LET heavy ions, had a higher incidence of cataract formation than those who flew on low-inclination missions, on which a large proportion of the dose is from low-LET trapped protons. Further evidence for the link between cataract formation and exposure to space radiation was presented in a 2002 study of cosmonauts and astronauts (Rastegar et al., 2002), in which a trend for increased opacification in the posterior cortical and posterior capsule regions of the lens was evident in a group of cosmonauts and astronauts as compared to that of the controls. As astronauts were screened for vision at entry into the Astronaut Corps and were observed with distinct methods, comparisons to other studies are inconclusive. In fact, it is very likely that astronauts, prior to their exposure to space radiation, have a baseline incidence of cataracts that is well below that of members of the general population.

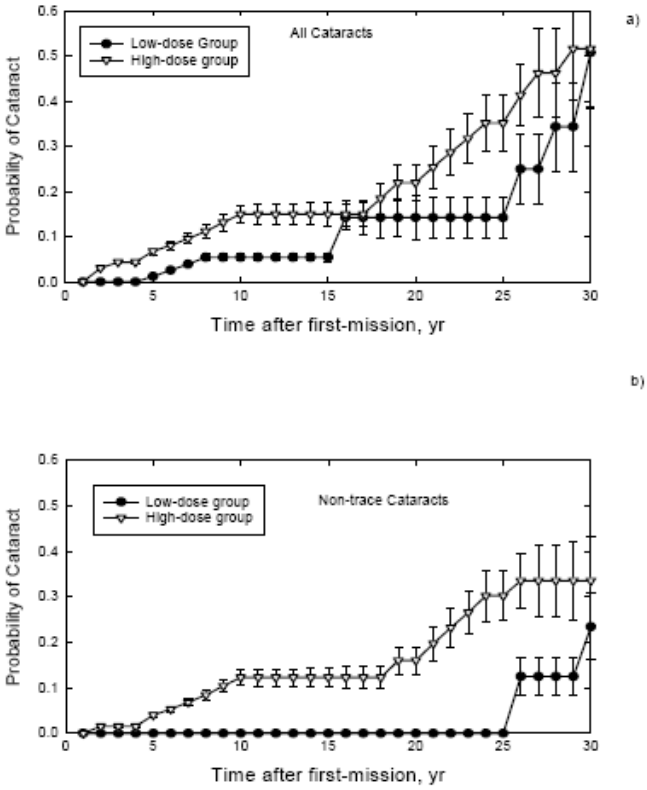


Figure 7-3. Cucinotta et al. (2001): ***Results for the probability of survival without cataracts vs. time after the first space mission for NASA astronauts for a low-dose group (closed symbols) with a lens dose below 8 mSv (average 4.7 mSv) and a high-dose group (open symbols) with a lens dose above 8 mSv (average 45 mSv). Error bars indicate standard errors of the mean. The upper panel is for all cataracts, and the lower panel is for non-trace (vision-impairing or large-area) cataracts. Only cataracts occurring after a first space mission are included.***

Radiobiology studies of the risk of degenerative tissues diseases

Cataract Studies with Protons, Neutrons, and HZE Nuclei

Although the largest body of information on radiation-induced cataractogenesis comes from studies using low-LET radiation sources, substantial data also describe the induction of cataracts in a variety of animal species by different types of particle radiation sources that are similar to those that are encountered in space, including protons and high-LET particle radiation. The United States Air Force (USAF)/NASA Proton Bio-effects Project was an effort to identify delayed or late effects of X rays, electrons, and protons of differing energies on the long-term health of a colony of Rhesus monkeys. A subpopulation of the primates that were

studied in the USAF/NASA project was monitored for about 30 years for late effects including cancer, cataracts, and shortening of life. Analyses of these primates for signs of cataractogenesis began 20 years after exposure, and significant opacifications of the eye lens were seen in these monkeys 20 to 24 years after exposure to 55-MeV protons at 1.25 Gy and higher levels. The results that were obtained from these experiments suggest that the dose-response relationship for induction of cataracts by protons is similar to that seen with low-LET radiation (Lett et al., 1991; Cox et al., 1992). These findings are supported by other studies on cataract formation in animal models using high-energy proton beams (Niemer-Tucker et al., 1999; Fedorenko, 1995). In many studies of heavy ions, cataractogenesis that was induced by individual high-LET components of the space radiation spectrum was analyzed. The conclusions that were derived from these studies are that a trend exists for the latency between the exposure and the appearance of cataract lesions to decrease, and that this occurs at lower dose thresholds for heavy ions than for low-LET X rays and protons. Table 7-4 lists representative studies for different heavy-ion species.

Table 7-4. ***References for Cataractogenesis Studies Conducted with High-LET Radiation***

High-LET Component	Selected References
Neutrons	Ainsworth, 1986; Riley et al., 1991; Worgul et al., 1996; Christenberry et al., 1956
Argon	Merriam et al., 1984; Lett et al., 1980; Worgul, 1986; Abrosimova et al., 2000; Jose and Ainsworth, 1983
Neon	Lett et al., 1980; Abrosimova et al., 2000; Jose and Ainsworth, 1983
Iron	Brenner et al., 1993; Lett et al., 1991; Medvedovsky et al., 1994; Riley et al., 1991; Tao et al., 1994; Worgul, 1986; Worgul, 1993
Protons	Niemer-Tucker et al., 1999; Fedorenko, 1985; Lett et al., 1991; Cox et al., 1992

Studies in animals showed an age-dependent sensitivity, with the younger animals exhibiting a lower dose threshold for cataract induction than the older animals (Cox et al., 1992).

Animal Studies and Heart Damage

Systematic studies on the progression of radiation-induced heart diseases were first conducted in rabbits (Fajardo and Stewart, 1970) and in rats (Yeung and Hopewell, 1985; Lauk et al., 1985) with high doses of X rays in the range of 10 to 20 Gy. Similar studies were conducted for heavy ions during the course of the JANUS program at Argonne National Laboratory, in which ultrastructural studies of the mouse heart and vasculature were performed after the animals had been irradiated with neutrons (Yang et al., 1976; 1978; Stearner et al., 1979). The results of the studies were compared with results from irradiating mice with low-LET radiation, and showed vessel morphological changes, including marked fragmentation of vascular smooth muscle layers as well as an increase in deposition of extracellular matrix in vessel walls. Clear distinctions were observed between the damage that was caused by neutrons and that caused by low-LET radiation (Yang et al., 1976; 1978; Stearner et al., 1979). RBEs for neutron effects increased with decreasing dose or fractionation of the dose, thus dividing the total dose into several doses that were spread out over time, and exceeded values of 100 when exposure protraction over 24 weekly fractions was tested. Similar results were found with low doses of Ne and Ar ions (Yang and Ainsworth, 1982). Further studies that were conducted on rats that had been irradiated in the head with low doses of heavy ions showed a clear correlation between radiation dose and bleeding in the cerebral cortex, with heavy ions inducing more hemorrhages than X rays at the same dose (Yang and Tobias, 1984). Studies of the atherogenic changes that are associated with irradiation were

conducted in dogs to compare the effects of fractionated doses of fast neutrons (15 MeV avg.) with those of low-LET photons. The RBE of neutrons was estimated at 4 to 5 from these studies (Bradley et al., 1981).

More recently, studies that were aimed at defining the mechanisms by which radiation induces heart diseases were conducted using atherosclerosis-prone animal models. Increased oxidative stress (from the formation of ROS) and promotion of inflammation have been implicated as possible mechanisms by which radiation promotes atherogenesis. For example, accelerated formation of aortic lesions occurred in a dose-dependent manner in X-irradiated mice that were on a high-fat diet (figure 7-4), while smaller lesions were observed in their irradiated transgenic littermates that over-expressed CuZn-superoxide dismutase, which is expected to decrease chronic oxidative stress and lead to a decreased susceptibility to degeneration (Tribble et al., 1999). The lowest dose in these studies was 2 Gy. In another study (Stewart et al., 2006), radiation was shown to accelerate the formation of macrophage-rich inflammatory atherosclerotic lesions in atherosclerosis-prone mice, who were lacking the gene for ApoE. These mice were given a single high dose of 14 Gy to the neck, supporting the notion that radiation promotes degenerative heart diseases though an inflammatory mechanism.

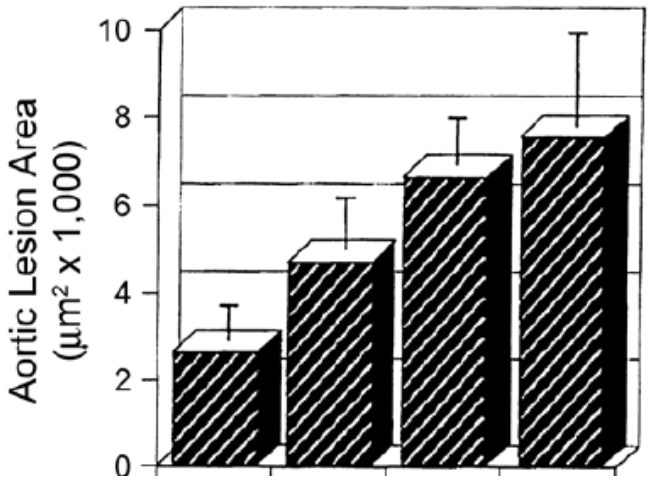


Figure 7-4. ***Dose-dependent effects of ionizing radiation on aortic lesion formation in fat-fed mice (repeated-measures analysis of variance: P = 0.02) (Tribble et al., 1999).***

In summary, substantial evidence from human epidemiology data and animal studies suggests that low-LET radiation strongly impacts the development of degenerative heart and cardiovascular diseases, which may be related to the overall acceleration of aging processes. However, data on these same effects that were caused by irradiation with protons or heavy ions are clearly lacking.

Radiobiology studies on aging

One consequence of radiation exposure and other genotoxic stressors at the cellular level is an enhancement of cellular senescence, which is a characteristic of aging. Studies that were conducted using low-LET irradiation in mouse models have shown a decline in the total number of cells and an increase in the number of cells with the senescent phenotype in bone marrow stem cells after radiotherapy and chemotherapy. These changes may contribute to the long-term deficits in bone marrow function that occur after these treatments (Wang et al., 2006).

Evidence of radiation-induced signs of aging has been uncovered in several studies that use heavy-ion irradiation of CNS targets. For example, mice that received whole-body irradiation with 1 GeV/nuc iron showed a

dose-dependent decrease in the number of newly formed cells in the hippocampus as well as altered expression of biochemical markers and alterations in the distribution of cells – changes that are consistent with the aging process (Rola et al., 2004; Casadesus et al., 2005). In fact, the newly formed cells that were affected by radiation are a type of neural stem cell. Stem cells in all tissues are of fundamental importance in the process of aging because any age-related decline in the number or functional capability of stem cells will impair the ability of the body to form and replace committed cells, with potentially deleterious cost for tissue maintenance. Genes that could modify individual susceptibility and radiation-induced aging would occur in the DNA damage response pathway, cell cycle controls, and telomere regulation, including Atm, Nbs1, Wrn, p16, and p21.

High-LET radiation also has an enhanced ability to damage the telomeres structures that are at one end of each chromosome and that are believed to be involved in the aging process (Durante et al., 2006). Some investigators report very high levels of telomere deletion in the progeny of human lymphocytes after irradiation with low doses of iron nuclei (Durante et al., 2006). Bailey (2007) is studying changes to telomeres as a function of radiation quality. Possible quantitative differences between low- and high-LET damage in causing telomere shortening or premature senescence are thus a concern for space radiation risk assessment.

Other effects

An additional effect of irradiation that was revealed by the proton bioeffects studies that were conducted in Rhesus monkeys was a significant increase in the risk of developing endometriosis, which is an abnormal growth of the uterine lining. This disease occurred in about 25% of all of the unirradiated female primates and in more than 50% of the irradiated primates. Although they are not normally life-threatening in humans, these conditions proved fatal to several of the animals before proper treatment plans were put into effect. Endometriosis was evident even when relatively low-energy protons (32 MeV; penetrating to a depth of about 1 cm) and low-exposure doses (0.2 to 1.13 Gy) were used (Yochmowitz et al., 1985; Fanton and Golden, 1991). As very few humans have been exposed to high-LET radiation, other health effects may arise that have not been documented to date for terrestrial forms of radiation at low to moderate doses (< 2 Gy).

Computer-based Simulation Information

Computer models of degenerative risks have not been developed at this time. Epidemiological data are severely lacking, precluding an approach that is similar to the ones that were used to project cancer risks. Only a few biological models are available that describe the degenerative processes that are caused by ionizing radiation, and that would be needed to form a computer model. This is probably because these processes are less studied than radiation carcinogenesis and are, in many cases, complicated by other lifestyle factors that influence the disease process. One model that was proposed by Rubin and Casarett (1968), which is called the "vascular hypothesis," states that late radiation effects are caused by damage to blood vessels. This vascular injury, which has a long latency that reflects the slow turnover time of the vasculature, leads to vessel occlusion, ischemia, and secondary loss of parenchymal cells, which are the cells that are specific to particular tissues and organs.

Risk in Context of Exploration Mission Operational Scenarios

Projections for space missions

No existing biophysical model projects degenerative risks for the entire range of particle types and energies that are found in space. The large RBEs that are found in the few studies that have been performed suggest that organ dose-equivalent based on radiation quality factors can be used to make a first approximation for risk estimates;

however, the shape of the dose-response for specific diseases and dose-rate modifiers is unknown. Dose-rate modifiers could be higher than observed for cancer risks because of the possibility of threshold effects.

The estimates for ERR per Sievert, which was provided by studies of the atomic-bomb survivors, are not sufficient alone to estimate risk for astronauts because a risk transfer approach is needed together with estimates of RBE and dose-rate modifiers. The baseline risk of CHD is several-fold larger in the U.S. than in Japan, while the risk of stroke is comparable. To determine the cancer risks, the NCRP suggests using multiplicative and additive transfer models to transfer risks between populations. Figure 7-5 (Cucinotta, unpublished) shows estimates of cancer and CHD risks if the RBE and the DDREF are assumed to be identical for cancer and CHD. In this calculation, the multiplicative transfer model is used to transfer the CHD risk from the Japanese to the U.S. population as well as to transfer the model of NCRP Report No. 132 (NCRP, 2000) for cancer risks. NASA uses the model of NCRP Report No. 132, which derives risks from the atomic-bomb survivor data using a mixture model that combines the arithmetic average of the additive and multiplicative transfer models to project cancer risks in the U.S. population. In the example calculation that is shown in figure 7-5, the CHD risk alone is about half that of the risk of cancer in all organs combined, and is less dependent on age than is the cancer risk. Death by CHD exceeds cancer deaths when an individual is 50 years or older at the time of exposure. The example that is shown in figure 7-5 uses many simplified assumptions, but clearly suggests the importance of collecting new data to estimate the factors that enter into CHD and other degenerative risk prediction models.

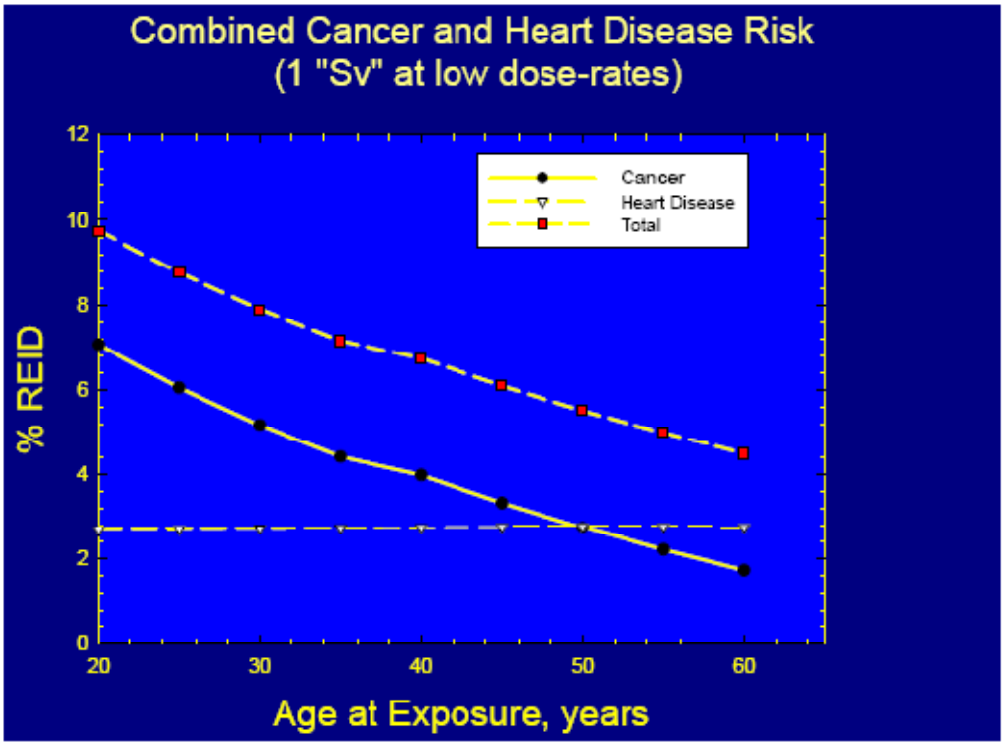


Figure 7-5. ***Comparison of projections for risk per Sievert for cancer and heart disease as a function of age at exposure. Calculations are made using the multiplicative transfer model and baseline rates for the U.S. population. Comparisons assume that RBE (quality factor) and DDREF are the same for each risk. The effects of competing risks are accounted for in the model (Cucinotta, private communication).***

Potential for biological countermeasures

Excessive production of free radicals produces oxidative damage to cellular structures, which includes proteins, DNA, and lipids, and contributes to the radiation-induced degenerative changes that are associated with aging, cardiovascular disease, and cataract formation. The identification of safe and effective agents that will protect and mitigate against these effects of radiation exposure are a high priority both for radiotherapy purposes, where the sparing of normal tissue is critical, and for the health of the general public in the event of a terrorist attack with nuclear weapons.

Two main types of countermeasures have been used to protect normal vasculature from ionizing radiation: the sulfhydryl or thiol compounds, and antioxidants. Both of these classes of compounds function by scavenging the free radicals that are produced by the interaction of ionizing radiation with water. WR2721 – which is also known as amifostine and gammaphos – is the best-described member of the sulfhydryl class and is the only drug that is approved by the Food and Drug Administration (FDA) to help prevent excess damage to normal tissues during radiotherapy. The mechanism of action of this drug is thought to be scavenging the free radicals that are produced by radiation and H-atom donation to protect against the damage that is done by free radicals. This compound has been tested as a countermeasure for both cataract formation and vascular damage (Kador, 1983; Mooteri et al., 1996; Warfield et al., 1990; Plotnikova et al., 1988). Radical scavenging vitamins such as C and E have also been shown to protect the lens and vascular system (Bantseev et al., 1997; Jacques et al., 1997; Taylor and Hobbs, 2002). In addition, growth factor treatments have been shown to decrease blood vessel stenosis (Fuks, 1994). In all of these examples, the compounds were administered prior to radiation exposure.

Synergistic effects with other flight factors

No reports have been published on the possible synergistic effects from non-radiation risk factors on the degenerative risks from space radiation. However, studies of radiation effects on bone loss due to microgravity have been suggested. No studies at doses that are below 1 Gy have been made in this area. Ambient oxygen levels may be altered in space flight. For low-LET radiation, oxygen enhancement ratios (OERs) (i.e., the ratio of doses to produce the same effects for varying oxygen levels) can exceed 2; however, for high-LET radiation, less dependence on oxygen levels is observed with OERs reducing to unity (Hall, 2000). There is only a small probability for low-LET radiation from SPEs to reach high enough doses to cause degenerative effects if proper operational procedures and radiation shielding are in place. However, chronic exposure to high-LET heavy ions is an important concern where a dose threshold will not likely occur. In this area, very little is known, and studies at nominal oxygen levels are needed to achieve a basic understanding of the mechanism and to obtain animal data for risk assessments. On completion of such studies, further studies at varying oxygen levels may be warranted.

Conclusion

The association between ionizing radiation exposure and the long-term development of degenerative tissue effects such as heart disease, cataracts, immunological changes, and premature aging is well-established for moderate to high doses of low-LET radiation. The majority of this evidence is derived from epidemiological studies on the atomic-bomb survivors in Japan, radiotherapy patients, and occupationally exposed workers, and is supported by laboratory studies using animal models (Blakely and Chang, 2007a; 2007b). The risks for these diseases from low dose-rate exposures and for HZE nuclei are much more difficult to assess due to their multifactor nature and long latency periods; therefore, these risks remain debatable for short-term lunar missions. Note, however, that the risks are more likely for long-term lunar or Mars missions. It also remains unclear whether

low-dose (<0.5 Gy) exposures influence the same biological pathways that have been shown to be involved in disease progression following moderate- to high-dose radiation exposures (Little et al., 2008). Likewise, very little information is available on the effects of space radiation on these disease processes, the role of individual susceptibility, and the possible synergistic effects from other space flight factors. It will be essential to obtain this knowledge to successfully mitigate the degenerative risk for astronauts for lunar and Mars missions.

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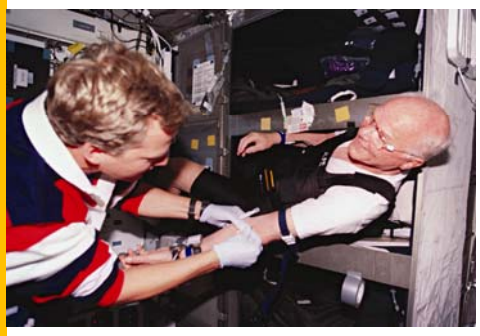
Exploration Medical Capabilities

Risk of Inability to Adequately Treat an Ill or Injured Crew Member



Chapter 8:
Risk of Inability to Adequately Treat an Ill or Injured Crew Member

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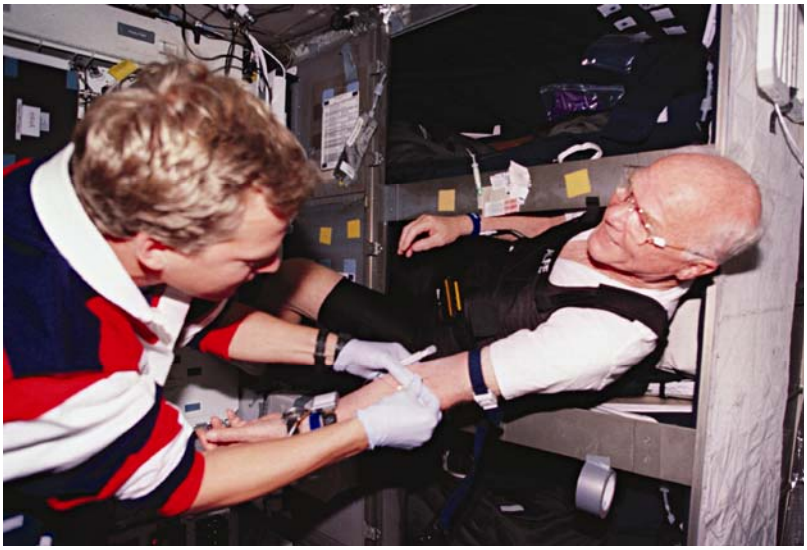
Mission architecture limits the amount of equipment and procedures that will be available to treat medical problems. Resource allocation and technology development must be performed to ensure that the limited mass, volume, power, and crew training time be efficiently utilized to provide the broadest possible treatment capability. This allocation must also consider that not all medical conditions are treatable, given the limited resources, and some cases may go untreated. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.



The promotion of crew health and safety in space requires the provision of necessary resources, despite limitations in mass, volume, power, and crew time, and must be directed toward the treatment of the conditions with high likelihood or severe consequence. The care of the crew begins with thorough pre-flight health status assessments and appropriate medical training in procedures and equipment to allow care to be crew-administered, and under certain circumstances, completely autonomous. Autonomous, crew-administered care is exemplified here, as Scott Parazynski (left) prepares to withdraw blood from the arm of John Glenn (right) while on the shuttle middeck.

Executive Summary

A review of published and non-published (e.g., NASA Longitudinal Study of Astronaut Health database) information on medical conditions that occurred during space missions (including the Russian partner experience), as well as a review of relevant information from harsh analog environments (e.g., submarine fleet health databases, Antarctic expeditions, mountaineers' expeditions) provides evidence that medical conditions of different complexity, severity, and emergency will inevitably occur during long-term Exploration missions. Depending on the medical problem, the resources that are available, and the time that is necessary for returning to Earth, different levels of medical care are required. Providing medical care for these conditions will be challenging in the resource-constrained environment of space. Plans for care to support both the health and the safety of astronauts and mission success must be made with regard to balancing the most likely conditions with those that pose the most catastrophic outcome. All medical problems have the potential to affect the mission, but significant illnesses or trauma will result in a high probability of mission failure or loss of crew. These considerations justify postulating and addressing the "risk of the inability to adequately treat an ill or injured crew member" during an Exploration mission, including not only which capabilities will be available but also how medical care will be provided and performed.

Introduction

The specific provision of medical services during space missions is authorized and required by the following documents: NPD 8900.5A, *NASA Health and Medical Policy for Human Space Exploration*; NPD 8900.1G, *Medical Operations Responsibilities in Support of Human Space Flight Programs;* NPD 8900.3F, *Astronaut Medical and Dental Observation Study and Care Program*; and NASA-STD-3001, *NASA Spaceflight Human Systems Standard – Volume 1, Crew Health*.

Medical conditions of different complexity could occur during space missions, especially during long-term space missions to the moon and Mars. An increasing number of possible medical conditions, including trauma, will have to be addressed for these missions since emergency returns become unlikely or impractical as the distance from Earth increases. Return will be nearly impossible during Mars missions and severely limited for many lunar situations. Even teleconsulting will have certain limitations due to significant delays in real-time communication on Exploration missions to Mars. Thus, health care, including emergency care and psychological support, will have to be self-administered and, under certain circumstances, completely autonomous.

Genuine difficulties in providing medical care in space include, but are not limited to: (a) resource constraints resulting from the boundaries of the mission design and architecture (volume, mass, power) and dictating that only the most critical medical equipment can be stored on board the space vehicles and delivered to the space habitats; (b) lack of trained medical professionals among the crew members; (c) limited pre-flight crew training time, necessitating the restriction of the training to only medical knowledge, techniques, and procedures that address the medical situations that are most likely to occur or that are most critical; (d) the probability that the crew members on the vehicle or in the habitation module may have to respond to emergency medical conditions without real-time support from Earth; (e) limited shelf-life of medical therapeutics and supplies; and (f) the possibility of encountering unpredicted illnesses and ailments that may be unique to the space exploration environment.

The most optimal way to achieve adequate support for crew health and to secure mission success on extended-duration missions is to establish a thorough pre-flight health status assessment, including all new technological

approaches (genomics, proteomics, etc.), and develop a systematic approach to a more comprehensive autonomous health care system in space.

Evidence

The evidence that is needed to postulate the possibility and estimate the probability of the occurrence of medical conditions during space missions can be drawn from different sources. Some sources include: (a) records of medical problems that were encountered in previous space flights by U.S. and Russian crews as well as other international partners; (b) information on the medical conditions that occurred during short- and long-term Earth expeditions (submarine, alpine, Arctic and Antarctic expeditions, expeditions to other remote ground-based locations, etc.); (c) general population studies addressing the age-related probabilities of different diseases and incidence of trauma; and (d) pre- and post-flight records of the health status and medical conditions of astronauts and cosmonauts.

Space flight evidence

In-flight illness incidence rates are partially summarized in several publications (Stewart et al., 2007; Summers et al., 2005; Davis, 1999). Evidence can also be obtained from the Longitudinal Study of Astronaut Health database that is maintained at NASA JSC. Tables 8-1 through 8-3, which are taken from a collaborative review report that was edited by John Ball and Charles Evans, are illustrative of the conditions that could occur and some estimates of the probabilities (Ball and Evans, 2001).

Table 8-1. ***In-flight Medical Events for U.S. Astronauts during the Space Shuttle Program (STS-1 through STS-89, April 1981 to January 1998)***

Medical Event or System by ICD-9[a] Category	Number	Percent of Total
Space adaptation syndrome	788	42.2
Nervous system and sense organs	318	17.0
Digestive system	163	8.7
Skin and subcutaneous tissue	151	8.1
Injuries or trauma	141	7.6
Musculoskeletal system and connective tissue	132	7.1
Respiratory system	83	4.4
Behavioral signs and symptoms	34	1.8
Infectious diseases	26	1.4
Genitourinary system	23	1.2
Circulatory system	6	0.3
Endocrine, nutritional, metabolic, and immunity disorders	2	0.1

[a]*International Classification of Diseases, 9th Ed.*

Table 8-2. ***Medical Events Among Seven NASA Astronauts on* Mir, *March 14, 1995, through June 12, 1998***

Event	Number of Events
Musculoskeletal	7
Skin	6
Nasal congestion, irritation	4
Bruise	2
Eyes	2
Gastrointestinal	2
Psychiatric	2
Hemorrhoids	1
Headaches	1
Sleep disorders	1

Note: Data from the Russian Space Agency indicate that there were 304 in-flight medical events on board the space station *Mir* from February 7, 1987 through February 28, 1998. The numbers of astronauts at risk or the incidence per 100 days was not reported.

Table 8-3. ***Medical Events and Recurrences Among Astronauts of All Nationalities on* Mir, *March 14, 1995, through June 12, 1998***

Event	Number of Events
Superficial injury	43
Arrhythmia	32
Musculoskeletal	29
Headache	17
Sleeplessness	13
Fatigue	17
Contact dermatitis	5
Surface burn	5
Conjunctivitis	4
Acute respiratory infection	3
Asthenia	3
Ocular foreign body	3
Globe contusion	2
Dental	2
Constipation	1

As most of these conditions do not represent medical emergencies, they could be treated by merely taking medications while on board, if available. About 75% of all astronauts have taken some form of medication during shuttle missions for nonemergency conditions such as motion sickness, headache, sleeplessness, and back pain. Other nonemergency conditions that the shuttle astronauts have experienced include minor trauma, burns, dermatologic and musculoskeletal conditions, respiratory illnesses, and genitourinary problems, etc.

More important is the existing evidence of potential medical emergencies during space flight, such as potentially fatal and nonfatal arrhythmias, heart attack, stroke, embolism, massive hemorrhage, emergencies that are related to renal stone formation, infection, and thrombotic complications. Among these conditions, only arrhythmias, renal colic, and infections have been documented. The documented arrhythmias were mostly mild abnormalities, such as occasional premature atrial contractions (PACs) and premature ventricular contractions (PVCs). PACs or PVCs were present in 30% of astronauts at some point during periods of strenuous activity.

Potentially serious arrhythmias (supraventricular and ventricular tachycardia) have also been reported. For example, during Apollo 15, one crew member experienced ventricular bigeminy; ventricular ectopy was reported on Skylab; and on *Mir*, a crew member experienced a 14-beat run of ventricular tachycardia (Fritsch-Yelle et al., 1998). No manifestation of coronary artery disease (CAD) was registered during any human space flight; however, considering the risk of cardiovascular events in older people and the increasing age of crew members, the possibility of such complications during long-term space missions cannot be ignored. Other medical emergencies that have been observed in space include rare, but real, cases of urological (Berry, 1974; Lebedev, 1983) and dental emergencies (Newkirk, 1990; Brown et al., 1977), as well as behavioral and psychiatric problems.

Additional evidence and consideration substantiates the risk of the inability to treat crew members on Exploration missions. For example, in a few cases in the past, episodes of renal colic and arrhythmia have required that crew members (Russian cosmonauts) be brought back to Earth, shortening their stays in space and possibly compromising the missions (Summers et al., 2005).

Radiation exposure could also cause other potential medical problems; for example, it might affect general health and cause radiation-specific pathological processes, especially given the proposed length of missions to Mars. If such emergencies were to occur, they would most likely be catastrophic and mission ending.

Moreover, when designing space medical care systems, the potential for crew exposure to toxic chemicals and gases as well as to chemical and electrical burns must be considered. There are also risks for significant trauma, both on board the spacecraft and during EVAs, due to the nature of operational activities and the closed environmental systems.

Lastly, given the length of Mars missions, there is also a certain age-related probability of the development of diverse medical conditions that are similar to those in the general population. These probabilities can be assessed based on general population health statistics as well as from information that is found in the astronaut pre- and post-flight health databases (Peterson et al., 1993; Hamm et al., 1998).

Ground-based evidence

The ground-based incidence of illness data are derived from publications and the available databases summarizing the occurrence of different medical conditions that are encountered in groups of individuals who are exposed to harsh environments that could be considered as analogs of the space environment. A sample of this information is presented in Tables 8-4 through 8-6 (Ball and Evans, 2001). As can be seen from the tables, the incidence of different medical conditions in these environments was, in general, relatively low (from 10 to ~50 events per 100,000 person-days) and mostly these were non-emergent conditions. Even these illnesses (trauma, infections, psychiatric disorders) required an evacuation that would be difficult, if not impossible, to provide in space, however, especially on future missions to the moon and Mars.

Table 8-4. ***Incidence of Health Disorders and Medical-Surgical Procedures during 136 Submarine Patrols***

Disorder	Number/ 100,000 Person-days
Injury (includes accidents)	48.8
Respiratory	24.6
Skin or soft tissue	19.0
Ill-defined symptoms	10.5
Infections	10.0
Procedure	**Percentage of All Procedures Performed**
Wound care, splinting	42.0
Suturing	18.7
Cleansing	8.2
Nail removal	6.8
Fluorescein eye examination	4.2
Incision and drainage of abscess	2.9
Tooth restoration	2.0

Table 8-5. ***Reasons for 332 Medical Evacuations from All Submarines, U.S. Atlantic Fleet, 1993 to 1996***

Reason for Evacuation	Number of Cases
Trauma	71
Psychiatric illness	41
Chest pain	34
Infection	40
Kidney stone	23
Appendicitis	21
Dental problem	31
Other	71
Total[a]	332

[a]Rate = 1.9 to 2.3 per 1,000 person-months

Table 8-6. ***ANARE Health Register Illnesses in Antarctica from 1988 to 1997***

Disorder	Number	Percent of Total
Injury and poisoning	3,910	42.0
Respiratory	910	9.7
Skin, subcutaneous	899	9.6
Nervous system or sensory organs	702	7.5
Digestive	691	7.4
Infection or parasitic	682	7.3
Musculoskeletal or connective tissue	667	7.1
Ill-defined symptoms	335	3.6
Mental	217	2.3

It is important to emphasize that crews that were living and working in harsh environments (Antarctic expeditions, submarines, and undersea habitats) also had medical emergencies, such as intracerebral hemorrhage,

stroke, myocardial infarction, appendicitis, and bone fractures. There were also cases of cancer and psychiatric illness. However, the overall rate of these serious medical or surgical emergencies was low. The most common emergencies were dental. For instance, in 100 British Polaris submarine patrols, crew members required 30 fillings and seven extractions due to intolerable pain (Glover and Taylor, 1981). Dental problems had been the cause for a transfer at sea in the U.S. Polaris submarine program (Tansey et al., 1979). Extractions and fillings have also been required in Antarctica (Lisney, 1976).

The calculated rate of significant illness or injury that is based on the meta-analysis of data from submarines, Antarctic expeditions, military aviation, and U.S. and Russian space flight experience was found to be approximately 0.06 event/person-year (Billica, 1996). Extrapolation of these data to a 2.5-year Mars mission involving six crew members provides an expected rate of a significant medical event of 0.9 people/mission (Billica, 1996). In other words, one significant medical event could be expected per Mars mission. It is understandable that risk estimations that are made by using the data from analog populations have certain limitations for Mars mission risk assessments. These estimates are likely to be conservative, as they do not account for the unique problems that are associated with the spacecraft environments, possible radiation effects, as well as exposure and physiological adaptation to low gravity (Buckey, 2006).

Of particular interest is the incidence of cardiovascular events in the harsh-environment populations. For example, the reported 5-year annual cardiac events rate by age group among USAF aviators was: 0.0054% (30–34 years), 0.018% (35–39 years), 0.038% (40–44 years), 0.14% (45–49 years), and 0.13% (50–54 years) (Osswald et al., 1996). Of all of these events, 21% were cases of sudden death and 61% were diagnosed and treated as myocardial infarction. Therefore, despite the rigorous screening that USAF aviators undergo, very often the first manifestation of CAD in this population was a significant cardiac event (Buckey, 2006). It is believed that these data are applicable to the Astronaut Corps as well, despite the fact that astronauts undergo a more-extensive medical assessment. In fact, this information emphasizes the risk of occurrence of sudden death or heart attack in space despite thorough screening (Buckey, 2006).

In the submarine program, the most common general surgical condition has been appendicitis (Tansey et al., 1979), and even a case of death due to appendicitis has been reported among the participants of the Antarctic expeditions (Ball and Evans, 2001). Other serious conditions that were also reported in the submarine program were traumatic amputations, fractures, and dislocations (Buckey, 2006). Furthermore, depression and anxiety reactions are found to be the most common two psychiatric diagnoses that are made on submarines (Tansey et al., 1979), and are also frequent among researchers who are enduring long Antarctic winters (Lugg, 2000).

Computer-based Simulation Information

Computer-based simulation of the likelihood and consequences of medical conditions is a decision tool that is used to assess medical risks. Although this methodology has not yet been used effectively to develop a probabilistic approach to support the medical management decision process, it is a promising tactic. Based on the premise that an optimal resolution is needed to synthesize the many incongruous factors and circumstances that are involved in providing medical care in space, this methodology could be used as a planning tool to address the likelihood of occurrence of different medical conditions and identify the required resources to treat these conditions. The integrated medical model (IMM), a tool of this type that quantifies the probability and consequences of medical risks, is in development.

Risk in Context of Exploration Mission Operational Scenarios

A review of the medical conditions that occurred during space missions in the past, as well as a review of relevant information from harsh analog environments, provides sufficient evidence that medical conditions of different complexity, severity, and emergency may inevitably occur during long-term Exploration mission. Understandably, the type and severity of the risks that would contribute to these conditions might fluctuate depending on the actual configuration of a mission, its longevity, and the complexity of the tasks that are to be performed on it. The major goals of the Exploration medical support system for the Constellation Program are to define the levels and specifics of risk factors for each mission to ensure that adequate health monitoring and maintenance systems are developed and implemented. The medical support system should also ensure that medical care, if needed, could be delivered with support from Earth or autonomously when communications with support personnel on Earth are excessively delayed or unavailable. The need for autonomous medical care puts additional emphasis on astronaut training and the development of computerized guides to facilitate the delivery of care. The identification of risks must be derived from a comprehensive analysis of all of the available sources of information, including analog environments. Medical care for Exploration missions will be based on the current understanding of the pathogenesis of the anticipated conditions in reduced gravity and on state-of-the-art diagnostic and treatment capabilities that are available on Earth. These diagnostic and treatment capabilities have to be modified and adjusted to the specifics of the space environments and comply with the NASA space flight health standards.

The development of appropriate risk context and the goals that are laid out within the ExMC Element necessitate identification of the "gaps" that exist between the anticipated in-flight medical conditions and the ability to mitigate or treat the conditions adequately. Documented in-flight conditions and conditions that are derived from comparable terrestrial populations will provide the basis for the Exploration medical condition list. This list will be prioritized based on the projected occurrence, possibility of being adequately diagnosed and treated on Exploration-class missions, consequences, and constrained resources (mass, volume, power, shelf-life, etc.) to diagnose and treat illnesses and injuries. This gap identification will facilitate the ability to articulate these difficult and complex problems and risk characterizations as well as to seek innovative solutions.

Conclusion

The review of the available published and non-published (JSC database) medical information that is related to astronaut health and in-flight medical conditions as well as records of medical conditions occurring in analog environments provides strong support for risk justification for both emergent and non-emergent medical events in space. At the same time, the data analysis reveals significant gaps in risk assessment, knowledge concerning potential medical conditions, and diagnostic and treatment capabilities on Exploration missions.

An Exploration medical condition list is being developed, in close collaboration with the Space Medicine Division at JSC, to focus the ExMC Element work further. This list will be further specified by Exploration mission design to assist with the planning of research and development activities so that Constellation Program development milestones and Space Life Sciences standards and requirements are met by the space vehicles. The identification and documentation of Exploration medical conditions and the associated gaps is essential for focusing and prioritizing ongoing studies in this field and for guiding the NASA HRP strategy.

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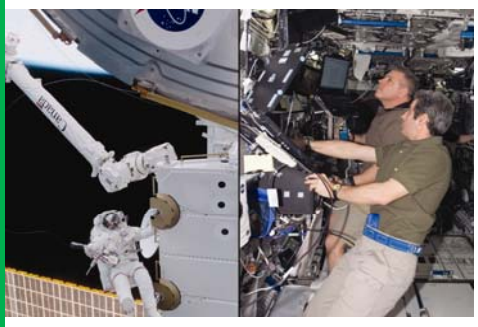
Space Human Factors and Habitability

Risk of Error Due to Inadequate Information

Risk of Reduced Safety and Efficiency Due to Inadequately Designed Vehicle, Environment, Tools, or Equipment

Risk of Error Due to Poor Task Design



Risk Factor of Inadequate Food System

Risk of Adverse Health Effects from Lunar Dust Exposure

Chapter 9:
Risk of Error Due to Inadequate Information

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Information presentation, acquisition and processing significantly affect human task performance. Effective information availability directly impacts all aspects of communication, which is a vital element to all space missions. Task errors during human spaceflight missions could have significant consequences to performance of mission objectives as well as human safety. Therefore further research regarding proper information presentation will allow for opportunities to optimize presentation of information, its timeliness, the user's level of awareness of the information, modes of information presentation, proper information comprehension, training methods, and development of procedures. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

Astronauts must monitor systems and perform critical operations daily while in space. Data monitoring in the past has required the review of numerous pages of paper data, as pictured here. Extensive ongoing NASA activity mitigates the risk of operator error by improving the display of information, the types of controls that interface between the human and the displays, and the procedures necessary to accomplish tasks.

Executive Summary

Human-centered design is essential to implement effective information management. The inadequate provision of information can increase the probability of operator error, thus impacting the safety and productivity of space flight missions. Evidence that is relevant to the risk of error due to inadequate information illustrates that effective information management and communications are critical to mission success.

Although operator errors are common in all work environments, task errors that occur during human space flight missions could have drastic consequences. Errors can be due to inadequate information, which, in turn, may be caused by (a) a lack of situational awareness, (b) forgetting, (c) an inability to access appropriate data and procedures, or (d) a failure of judgment. The causation trail that is engendered by errors leads to (a) a lack of situational awareness that can result from poorly designed interfaces, poorly designed tasks, or cognitive decrements that are caused by, for example, fatigue or exposure to toxic environments; (b) forgetting, which can result from inadequate training, poorly designed procedures, or cognitive decrements; (c) an inability to access appropriate data and procedures, which can be a result of poorly designed interfaces, poorly designed tasks, or cognitive decrements; and (d) a failure of judgment that can be the product of incorrectly perceived or interpreted cues, inappropriately estimated results of decisions, or inadequate data.

This chapter focuses on identifying the causes of risk that are associated with error due to inadequate information, and on developing information presentation standards for reducing operator errors in space flight through adequate understanding of the causes. Mitigating this risk involves addressing the display of information, the types of controls that provide an interface between the human and the displays, and the procedures that are necessary to accomplish tasks.

Introduction

Human factors and human-centered design

The study of human factors engineering embraces the design of tools, machines, systems, tasks and environments to ensure safety, efficiency, habitability, and optimized human performance (Chapanis, 1996). The study of space human factors focuses on the need for safe, efficient, and cost-effective operations, maintenance, and training in flight, on orbit, and on the ground. The purpose of space human factors is to create and maintain a safe and productive environment for humans in space. The domain of space human factors engineering consists of three sub-domains of knowledge: task design; the design of the vehicle, the environment, the tools, and the equipment; and information.

The SHFH Element contains five risks, three of which are associated with space human factors engineering. These are: (a) the risk of error due to inadequate information, (b) the risk that is associated with poor task design, and (c) the risk of reduced safety and efficiency due to an inadequately designed vehicle, environment, tools, or equipment. All of these risks have the same underlying root cause: the lack of human-centered design (figure 9-1).

Human-centered, or user-centered, design is a design approach that focuses on humans and their interaction with procedures, products, equipment, facilities, and environments. It seeks to use known information concerning human capabilities and develop designs that better match systems with human capabilities. To do this, practitioners of human-centered design capitalize on the strengths of the human in the system design while

limiting the potential impacts resulting from human limitations. Human-centered design focuses on the users throughout the planning, concept development, design, and final implementation phases of a product or a system. Good human-centered design practices reduce the elements of risk that can lead to human error in the human-machine system and improve the efficiency of operation and safety of all system components, including the human.

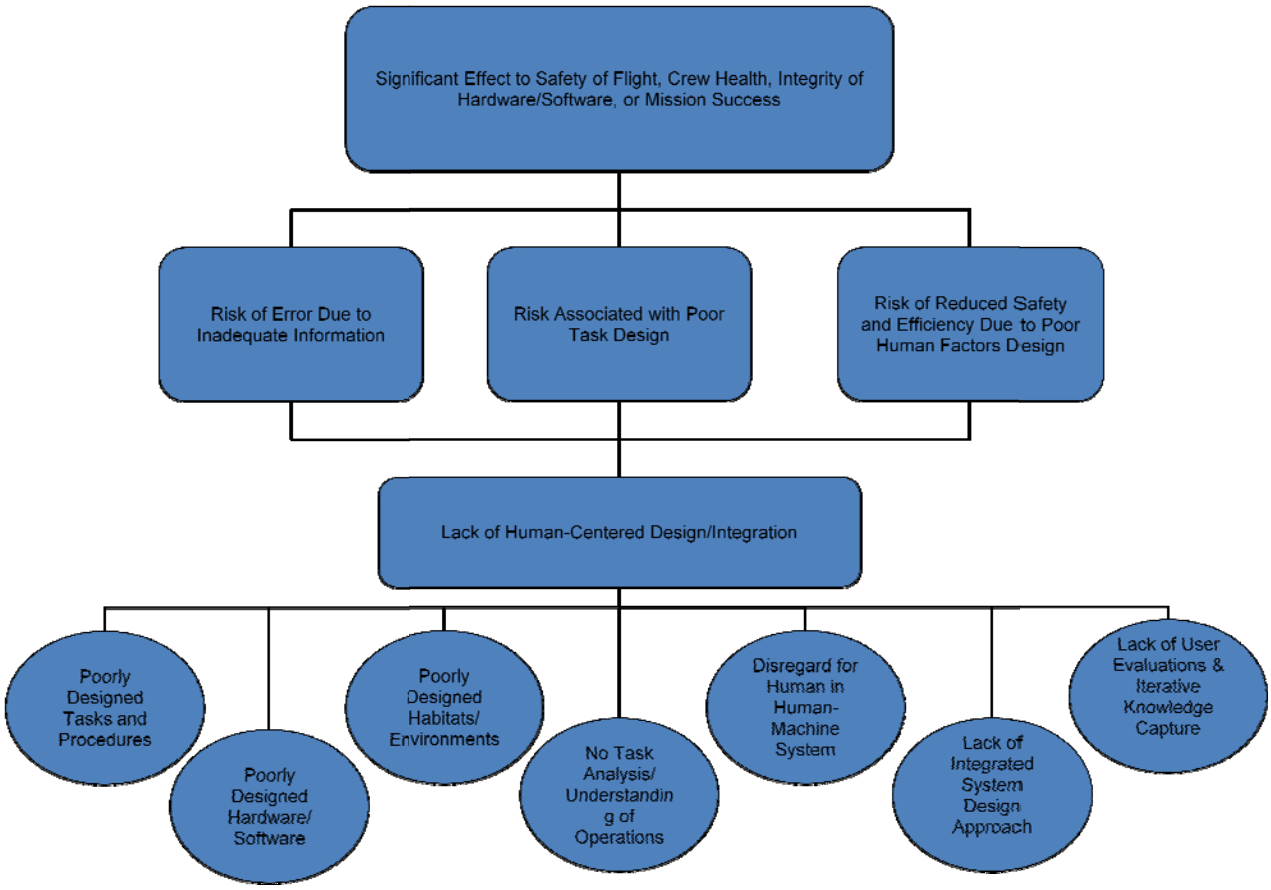

Figure 9-1. ***Fault tree for lack of human-centered design.***

Multiple contributing components can cause a lack of human-centered design. These include poorly designed tasks and procedures, poorly designed hardware and software, poorly designed habitats and environments, a lack of task analysis and understanding of operations, disregard for the human in the human-machine system, the lack of an integrated system design approach, and a lack of user evaluations and iterative knowledge capture. Without proper integration between the human and the system, the risk of reduced safety and efficiency due to poor human factors design may arise. If risks are not mitigated, the safety of the flight, the health of the crew, hardware and software integrity, and mission success may be significantly affected.

Evidence that will be presented in this and the next two SHFH chapters effectively illustrates the breadth and depth of the risks that are associated with a lack of human-centered design. These are: the risk of error due to inadequate information, the risk that is associated with poor task design, and the risk of reduced safety and efficiency due to an inadequately designed vehicle, environment, tools, or equipment. The intention of

the SHFH chapters is to provide a narrative discussion of the risk, together with the evidence that supports its existence or the potential for risk. This evidence provides the basis for analysis of the risk likelihood and consequence, and may provide the information that is needed to eventually develop standards for reducing operator errors in space flight through adequate understanding of the causes and mitigations of operator errors.

The review of these risks is important, as space flight crew performance is heavily influenced by the way in which the crews are able to obtain situational awareness and safely and effectively perform tasks. Current and future missions will require that the crews perform a wide variety of tasks under dramatically different conditions: i.e., 1g, hypergravity, microgravity, unsuited, suited, and pressurized. Mission success will require a more complete understanding of information and how it is best presented, acquired, and processed.

Evidence

The evidence that is presented in this chapter encompasses the lessons learned from 50 years of space flight experience related to the risk of error due to inadequate information. It is classified in this chapter, as it is in the other chapters, by categories and topic areas. Category I and II[16] evidence consists of quantitative and qualitative findings from research and development. Data are classified as Category I or II, depending on the specific testing protocol that is used and the data that are sought. Category III evidence consists of summaries of subjective experience data, as well as nonexperimental observations and comparative, correlation, and case or case-series studies. It should be noted that evidence that is derived from the ISS Life Sciences Crew Comments Database is essentially Category III evidence. Although summaries of ISS crew comments are presented as evidence, the Life Sciences Crew Comments Database, due to the sensitive nature of the raw crew data that it contains, is protected and not publicly available. Category IV evidence consists of expert committee reports and respected authority opinion based on clinical experiences, bench research, or "first principles."

The evidence that is presented here details human space flight issues that are related to inadequate information, specifically those that address presentation, acquisition, and processing. Inefficiencies and impacts that are related to information can restrict human performance in space flight conditions and affect safety and habitability. Therefore, these issues must be assessed and properly addressed to ensure that all potential hazards are mitigated or monitored. If the information that is necessary to complete the tasks is not presented, acquired, or processed appropriately, the likelihood of errors or the inability to successfully complete a task increases.

Information acquisition

Information acquisition is defined as the way in which a user or a system obtains information. This acquisition can occur through various means. Most of the information that is needed for space flight missions is obtained through training, both on the ground and on orbit. Information is also obtained on orbit via crew-to-crew and

[16]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

crew-to-ground communication, as well as through robotics and automation. Regardless of the mode that is used to acquire information, it is important that the process be refined to ensure that the right methods are being used, the method duration is appropriate for the type of information that is being transferred, and the amount of time between receiving and processing the information is adequate. Proper definition and execution of these elements will ensure the successful acquisition of information in the space environment, thus leading to mission success. The paragraphs below describe cases in which the acquisition of information was unsuccessful or improvements should have been made.

Improved information acquisition is needed with ISS task procedures. As documented in the ISS Life Sciences Crew Comments Database, ISS crew members have consistently commented that the procedures are too complex, lengthy, and difficult to follow. Procedures can often complicate or impede the performance of daily tasks because they may call for an inadequate number of crew members to perform a task, or the specified duration for a task may be inappropriate. Progress is being made in improving procedures and in enhancing the crew members' abilities to acquire information by including more graphic content (diagrams and images). The goal is to improve the procedures so that they can better reflect how operations are actually conducted. Other types of improvements will also be needed to adequately inform the crew.

Paper checklists are an example of inadequate information acquisition. They have been used by on-orbit crews for many years, but navigating through paper checklists has been difficult. Procedures are coded with specialized symbols, abbreviations, boundary delimiters, and spatial configurations that collectively require extensive training to decipher and understand. Individual instructions in these cue cards and checklists frequently take the form of conditional expressions (i.e., IF-THEN-ELSE statements), which crew members must evaluate by manually cross-checking systems or flight status information on cockpit instruments and displays. The outcome of this evaluation of the logical expression determines which path should be taken through the remainder of the checklist; and that path, in turn, determines which subsequent instructions must be carried out, and in what order. Wrong choices that are based on an inappropriate assessment of the state of information that was presented can endanger the crew (Hudy and Woolford, 2007) (Category III).

Data that are contained in the (ISS) Life Sciences Crew Comments Database indicate that the ISS crews rely heavily on auditory information and warnings on orbit. Auditory information has as its main advantage that the crew does not need to be looking at a display to be aware of an alarm. The acoustic levels on board the ISS have been historically high and have impacted communication and the receipt of some information. These high levels of continuous and intermittent noise require the use of earplugs or noise-canceling headsets to mitigate noise exposure. Although this protection assists with decreasing detrimental noise exposure, communications among crew members and between the crew and the ground may be degraded. On a few occasions, the elevated noise levels have prevented the crew from hearing caution-and-warning alarms and other monitoring signals. In addition, crew members may also become uncomfortable while wearing this protection (Rando et al., 2005) (Category III).

Effective information acquisition has also been decreased by other communication issues that have been encountered on the ISS, such as miscommunications, unrealistic demands, ineffective interpersonal communication techniques, and a lack of understanding of on-orbit life. Inadequate communication between the ground and the crew can cause frustration that can, in turn, negatively affect performance. Ground operators have, in the past, had difficulty understanding how much time it actually takes to complete tasks on orbit, which frustrates both the crew and the ground personnel. Many times crew members have been unaware of what the ground personnel could assist with and what tasks could be automated to facilitate crew productivity. There have also been cases

in which ground personnel should have relied on the crew to do many things and should not have overridden crew member suggestions (Rando et al., 2005) (Category III).

Information presentation and processing

Information is presented most effectively when the users' interests, needs, and knowledge are considered. Effective presentation of information can be accomplished by ensuring that (a) operations concepts are fully developed, (b) task analysis is conducted at a low enough level of detail, and (c) task analysis is accurate and its completeness is verified. The designer must also ensure that the user has complete awareness by considering both perceptual thresholds and good information display design. Lastly, information must be presented using the correct mode. If information is not presented clearly, the user may process the message incorrectly, and may misinterpret, overlook, or ignore the original intent of the information.

Information processing can be accomplished either through individual or multi-agent distribution. In designing for individual information processing, the thought process of the receiver should be considered, as well as how the individual may execute the information. This consideration is critical for successful task execution. Although for multi-agent or distributed processing the elements for individual processing also apply, the processing is more complex because additional users and/or automation are involved. When information is not processed as intended, the outcome of a task can be jeopardized and mission success can be put at risk. The following examples are cases in which the presentation or processing of information was degraded or unsuccessful, or could have been improved to be more effective.

As simulated environments and ground-based full-scale models or mockups cannot be completely representative of flight conditions, representing a true zero-g environment on the ground has presented many challenges for training and information presentation. Thus, simulations may not provide adequate information during preflight training. As documented in the ISS Lessons Learned Database, a true representation of the stowage of equipment and materials aboard the ISS is very difficult to achieve on the ground and can create issues for the crew. Stowage mockups in 1g are limited because gravity restricts operations and translation in the training facilities. Given the constraints of a 1g-based translation path, it is neither possible nor safe to place things where they would potentially be stowed on board the ISS. The weightless environment on orbit benefits the crew in that it allows items to be stowed on any axis with proper restraint. In addition, the crew members can translate through the available volume and position their bodies to move around obstructions or protrusions in the translation paths.

In summary, given the gravitational differences between Earth and orbit and the disconnect between ground training and actual life on orbit, crew members often experience steep learning curves once they are on board the ISS because the simulators and mockups, which are not completely representative of zero-g conditions, do not provide adequate information. The result is that on arrival on board the ISS, crew members often experience difficulty managing stowage and operating nominally, and errors result (see figures 9-2 and 9-3) (Category III).

Figure 9-2. ***JSC2007-E-46438 (September 2007) — Astronaut Peggy A. Whitson, Expedition 16 commander, and cosmonaut Yuri I. Malenchenko, flight engineer representing the Russian Federal Space Agency, participate in a training session at the Gagarin Cosmonaut Training Center, Star City, Russia (NASA Human Spaceflight Gallery, 2008).***

Figure 9-3. ***ISS016-E-022130 — Cosmonaut Yuri I. Malenchenko, Expedition 16 flight engineer representing the Russian Federal Space Agency, uses a communication system while working in the Zvezda service module of the ISS (NASA Human Spaceflight Gallery, 2008).***

Computer displays and software technology that are on the ground are constantly changing and improving. Computer and software technologies on board the ISS have historically lagged behind these available ground-based technologies. Displays and software platforms often differ from application to application, depending on the task that is being supported. Many interfaces on the ISS are not the same as those that are commonly used on Earth. This inconsistency between ground and space has been a source of operational frustration for crewmembers. Therefore, it is important to provide crews with systems that are similar to those used on the ground to improve in-flight information presentation and avoid impacts on human and system efficiency and performance in space.

As documented in the ISS Life Sciences Crew Comments Database, usability issues have occurred that are associated with the use of displays that lack a common overall infrastructure and layout that would promote ease of use and understanding of intended operations. Valuable ISS crew time has been lost in trying to understand the use of disparate displays, which has led to incorrect data entry, navigational errors, or inaccurate interpretation of data in the displays. When display interfaces are dissimilar and the information is not presented consistently, crew members may require additional training and time to master the use of the displays. Crew members may also revert to an uncomplimentary skill base from another display design. This natural human tendency may override training and lead to errors that can compromise crew safety, especially in the event of an emergency (Category III).

ISS crews are inundated daily with information concerning procedures. Some ISS electronic procedures and formats have been especially difficult to use. Frequently, crew members have spent excessive amounts of time

navigating among various menus because the procedures were difficult and lengthy or contained unnecessary information. In many cases, the content of a procedure contributed to inadvertent skipping of steps in the procedure and poor task execution.

A number of complaints have been received from ISS crew members concerning the implementation and overabundance of cautions and warnings (C&Ws) in procedures. The primary reason for using C&W advisory blocks in procedures is to protect the crew members and the hardware from potentially unsafe conditions or incidents. The overuse of C&Ws in procedures has contributed to the desensitization of the crew to C&W (as shown by accidental procedure step-skipping and inattention to important C&Ws because they are embedded in trivial warnings).

Issues that are associated with procedures have occurred during ISS missions and are directly related to the provision of too much information, lack of diagrams and schematics to illustrate necessary information, and confusion and missed steps caused by multiple links in procedures. These issues have frustrated crew members and directly affected the efficient performance of tasks because the information that was needed for a given task was not presented in a usable format (Rando et al., 2005) (Category III).

As documented in the ISS Life Sciences Crew Comments Database, other issues occurred because electronic updates to procedures often have to be printed out to update procedure books with new information, costing the crew time to print and change out the affected pages. Moreover, printing compounds the issues with information processing as issues often arise with printers on orbit, leading to frustration among crew members. These crew members have commented that although the ISS printing procedure worked during ground training in the simulator, it did not work on orbit because the on-orbit printer was not the same printer as the one that was used during training. Clearly, therefore, the information and hardware that are provided for training must be as similar as possible to what will be provided on orbit to avoid learning curves once crew members arrive at the ISS (see figure 9-4).

Figure 9-4. ISS015-E-17702 — *Cosmonaut Fyodor N. Yurchikhin, Expedition 15 commander representing the Russian Federal Space Agency, holds a camera while looking over procedures checklists in the Zvezda service module of the ISS (NASA Human Spaceflight Gallery, 2008).*

On Apollo 10, at the end of the second pass over lunar landing site 2, the two crew members were preparing to separate the two stages of the lunar lander and return to the command module in orbit around the moon when the mode of the guidance and navigation system was inadvertently changed by one of the crew members. A couple

of seconds later, the other crew member reached up, without looking, and changed the mode of the guidance system, which canceled the change that had been made by the first crew member. As a result, the lunar module, *Snoopy*, began firing thrusters in all axes, pushing the gyroscopes into gimbal lock and making the navigation system useless until it was reset. The crew member then toggled the navigation system switch again and, although he now put it into the mode it should have been in to start with, it made things worse. At this point the crew overrode the computer and took manual control.

The incident lasted about 15 seconds, during which *Snoopy* made eight complete rolls. It was estimated that if the crew members had not regained control within another 2 seconds, it would have been too late to avoid impact with the moon. Without clear information processing and communication between crew members concerning their dedicated duties, there is real risk to safety from accidental operations (Shayler, 2000) (Category III).

Computer-based Simulation Information

Understanding human integration with systems and identifying the risks that may be inherent in a concept or a design is often achieved via computer-based simulation. Computer-based simulation tools have multiple uses including detection of potential risks to the human. Computer-based simulation and virtual environments create a metaphor for the real world with which the user interacts. With the aid of equipment such as head-mounted displays, data gloves, three-dimensional audio, and haptic or tactile feedback, the individual can interact with a virtual world as that world simulates reality. These virtual environments can be used to create simulations for training or, perhaps, interacting with prototypes that do not yet exist in the real world.

Inefficient or inadequate presentation of information presents a risk to crew effectiveness and safety, especially during off-nominal operations. In 1999, NASA JSC initiated the process of upgrading the cockpits of the space shuttle orbiters. The primary impetus for this upgrade was the perceived risk of reduced safety and efficiency of shuttle operations due to the lack of a human-centered design approach to information conveyance by the 1970s-era display formats.

The product of the cockpit avionics upgrade (CAU) effort was a new suite of explicitly task-oriented display formats that (a) consolidated and integrated task-related information; (b) more clearly supported fault detection, isolation, and recovery operations; (c) used color-coding to guide and manage the attention of operators; and (d) streamlined display navigation with new display control devices.

As part of the CAU project, engineers conducted a thorough human-in-the-loop evaluation of the CAU display formats in the Shuttle Mission Simulator that directly measured operational efficiency and error rate in a series of full-mission simulations of off-nominal ascent and entry scenarios. The scenarios were completed with both the existing (i.e., 1970s-era format) display suite and cockpit interface devices and the upgraded displays and interfaces. The results provided an empirical database quantifying the performance benefits and enhanced operational efficiency that accompanied the human-centered redesigns. When questioned concerning conditions during their just-completed scenarios, crew members who had trained in the CAU cockpit answered almost 75% of the questions correctly as compared to the typically less than 40% who had trained in the existing cockpit. The workload was rated 38% lower with the CAU cockpit. The incidence of a particularly safety-critical form of operator error (the percentage of system malfunctions and flight anomalies that went unrecognized) stood at 30% in the existing cockpit; however, in the CAU cockpit, the rate of error was only 10%, which is a 67% reduction.

Finally, while little difference was apparent between the existing and CAU cockpits when crew members diagnosed the easiest malfunctions, there was a distinct latency advance for the CAU cockpit for the more difficult

malfunctions. In the very slowest (most difficult) cases, the average CAU advantage was 40 seconds. This demonstrates how improved display formats can reduce the risk of operation error due to inadequate information (McCandless et al., 2005; Hayashi et al., 2005) (Category II). Figure 9-5 demonstrates how Man-machine Integration Design and Analysis System (MIDAS) simulations reproduced the findings of the CAU display suite evaluation.

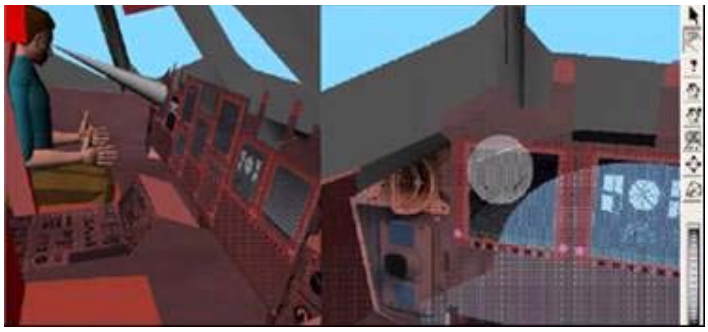

Figure 9-5. ***MIDAS simulations were conducted to reproduce the findings of the CAU display suite evaluation. Task timelines and workload outputs were examined as part of these simulations (NASA Human Spaceflight Gallery, 2008).***

Risk in Context of Exploration Mission Operations Scenarios

Future Exploration missions will increase in length. Lunar missions will provide a substantial set of independent lessons learned, experiences, and more definitive knowledge gaps that will apply to Mars exploration. Crews will face the challenges of physical deconditioning, prolonged isolation and confinement, significant communication latencies, environmental stressors, and increased responsibility and autonomy. Effective design solutions for vehicles, habitats, and missions need to allow the management and control of all aspects of Exploration mission operational scenarios.

Human-centered design must be implemented in all aspects of the design process to mitigate or prevent space human factors engineering risks from occurring. Designing for reduced gravity will be critical. Lunar and martian environmental conditions – air quality, lunar or martian dust, radiation exposure, and lighting – must be addressed. Stowage provisions need to ensure that appropriate spares and stowage volumes are available and accessible in a timely manner. Intuitive human-computer interaction will be necessary owing to increasingly complex task demands and the need for autonomy. A reduction in required maintenance and interface with complex systems should be implemented. Commonality in design and implementation should cross all hardware and tool designs. Procedures and training should accommodate the increased autonomy to provide appropriate information and avoid excessive workload.

Conclusion

The risk of error due to inadequate information stems from a broader cause of human error: the lack of human-centered design. To reduce or eliminate this risk requires that designers focus on the user throughout the design process. Good human-centered design practices strive to improve the efficiency of operation and safety of all system components, including the human, and should reduce the life cycle cost of the project. The risk that is

associated with error due to inadequate information focuses on identifying the causes of that risk – e.g., the lack of situational awareness that might be due to poorly designed interfaces or tasks – and the subsequent development of information presentation standards for reducing operator errors in space flight through the development of an adequate understanding of the causes and mitigations of the errors.

The human-machine system emphasizes the importance of the human element as the central focus of the human-centered design process. This includes consideration for human capabilities, limitations, and interaction with automation and hardware. Knowledge gaps or holes that are related to the lack of an integrated system design approach for information acquisition, presentation, and processing must be addressed to ensure quality standards, requirements, tools, and techniques are developed that will allow positive crew-system integration and interaction, and, ultimately, mission success.

The evidence that is discussed in the SHFH chapters identifies risks. To alleviate these risks, "knowledge gaps" or "holes" and future research directions have been identified. Some of these knowledge gap considerations are related to the constant need for efficient information acquisition, presentation, and processing, and an improved understanding of the crew and mission requirements and constraints for task design and training.

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Chapter 10: Risk of Reduced Safety and Efficiency Due to Inadequately Designed Vehicle, Environment, Tools, or Equipment

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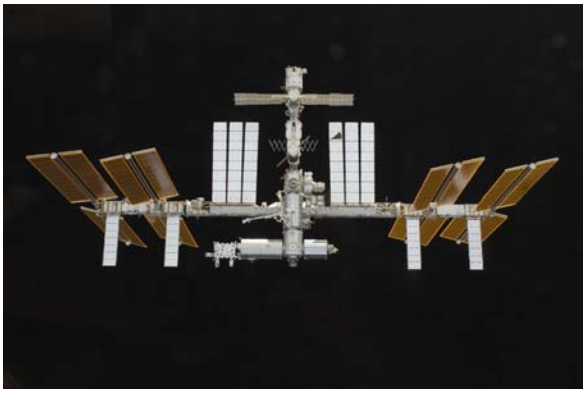
The habitability of the architecture, habitable environment, tools, and equipment is critical for the existence of humans in space. Any inadequacies in the design of the environment or architecture can restrict or prevent the user from surviving in such extreme conditions and may impact safety and performance. Factors that affect the habitability must be assessed and properly addressed to ensure all potential hazards are mitigated or monitored. If the workspace, equipment and tools are not designed to be usable by the full range of crew members, and are not properly laid out, the likelihood of errors or crew inability to complete a task in a timely manner increases. Inconsistent design among subsystems and vehicles leads to negative transfer of training and increased likelihood of errors. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.



The ISS (photographed by the departing STS-127 astronauts as they begin their return to Earth) is a highly visible example of a successful cooperative endeavor. Integrating human factors principles into environmental and architectural designs for hardware, software, vehicles, and habitats is required to ensure the usability of space systems and the safety of space travelers.

Executive Summary

The primary goal of the SHFH Element for human space exploration is to preserve the safety of the crew, promote human performance, and increase efficiency while on orbit. This goal is achieved by integrating human factors principles into the environmental and architectural design for hardware, software, vehicles, and habitats. In particular, optimal on-orbit environmental conditions and architectural design are critical for the health and well-being of space flight crew members as well as the habitability of vehicles and habitats. Optimized usability in the design of workspaces, equipment, and tools for the remote space flight environment is also important. Evidence that is captured in this chapter emphasizes the importance of human factors design considerations, and also illustrates how operator safety and efficiency can be jeopardized when these considerations are not addressed throughout the system life-cycle process for vehicles, environments, tools, and equipment. For a more detailed summary of overall concepts that are related to space flight human factors and human-centered design, refer to Chapter 9 of this document.

Introduction

The purpose of the space human factors discipline is to create and maintain a safe and productive environment for humans in space, which requires an understanding of human performance and limitations. Inadequate implementation of human factors design in work environments will result in reduced human performance, an increased likelihood of human errors, and decreased mission safety and effective mission execution. These potential, negative outcomes emphasize the need for focused, human-centered design that will assist in the development of hardware, software, and tools that are better designed to fit the human and reduce overall human safety risks to the program. With missions using new technologies at an ever-increasing rate, it is imperative that these advances enhance crew performance without increasing crew workload, stress, or risk. It is important to identify concerns that require a space human factors assessment and highlight the value of space human factors and safety on orbit.

This chapter focuses on evidence that is related to the risk of reduced safety and efficiency due to inadequately designed vehicles, environments, tools, and equipment. This evidence emphasizes the importance of human factors design considerations, and illustrates how operator safety and efficiency can be jeopardized when these considerations are not addressed throughout the life cycle of vehicles, environments, tools, and equipment.

Evidence

Evidence that is presented in this chapter encompasses lessons learned from 50 years of space flight experience that is related to the risk of reduced safety and efficiency due to inadequately designed vehicles, environments, tools, or equipment. As with the rest of this book, evidence is classified by categories. Category I and Category II evidence consists of quantitative and qualitative findings from research and development. Data are classified as Category I or Category II, depending on the specific testing protocol that was used and the data that were sought. Category III evidence consists of summaries of subjective experience data, as well as non-experimental observations and comparative, correlation, case, and case-series studies. It should be noted that some evidence, which is essentially Category III evidence, is derived from the ISS Life Sciences Crew Comments Database. Although summaries of ISS crew comments are presented as evidence here, the Life Sciences Crew Comments Database is protected and, therefore, is not publicly available due to the sensitive nature of the raw crew data that it contains.

Category IV[17] evidence consists of expert committee reports and respected authorities' opinions that are based on clinical experiences, bench research, and "first principles."

Evidence that is described in this chapter details human space flight safety and human performance efficiency issues that are related to environmental and architectural design as well as to the usability and design of workspaces, equipment, and tools. When these aspects of design are inadequate, overall habitability is affected; these issues must therefore be assessed and properly addressed to ensure that all potential hazards are mitigated or monitored. If the workspace, equipment, and tools are not designed to be usable by the full range of crew members and are not properly laid out, the likelihood of errors or of the inability of the crew to complete a task in a timely manner increases. Inconsistent design of subsystems and vehicles leads to negative transfer of training and an increased likelihood of errors.

Environmental and architectural design

Optimal on-orbit environmental conditions and architectural design are critical for the health and well-being of space flight crew members and the habitability of vehicles and habitats. Any inadequacies in the design of the architecture or the environment that is built can affect the safety and performance of the human. The environmental and architectural factors affecting habitability must be assessed and properly addressed to ensure that all potential hazards are mitigated or, at a minimum, monitored. Noise and lighting issues are specific environmental issues that are experienced on orbit that affect habitability. Issues that are related to environment depend on the manner and extent of exposure to environmental elements. Architecture issues that impact habitability are related to the design, configuration, and topology of the interior volume of space vehicles and modules and to the co-location of systems and tasks. They include issues that are related to human translation (movement from one location to another) and orientation information as well as problems that have occurred when vehicles, habitats, or other hardware designs did not accommodate the user.

For example, noise is a pervasive aspect of all living and working environments that can, at times, present hazards. The ISS acoustic environment, in particular, is complex, and includes many types of noise-generating hardware because the ISS provides not only home for the space flight crew, but also their workshop and laboratory (Rando et al., 2005). The cumulative effects of the ISS acoustic environment manifest themselves in two forms: continuous and intermittent noise (Baggerman et al., 2004). Continuous noise is generated by the operation of pumps, fans, compressors, avionics, and other noise-producing hardware or systems. Intermittent noise is caused by hardware that operates cyclically, e.g., exercise equipment or the carbon dioxide removal system. Onboard acoustics measurements in various ISS modules often exceed the ISS flight rules for noise exposure and can be at 67 dB or higher over a cumulative 24-hour period (Goodman, 2000; Clark and Allen, 2008). Issues and constraints that are related to the acoustics environment increase the risk of impacts on crew safety as the crew may not be able to hear the C&Ws. Although C&W tones are typically audible, noise within the ISS from daily operations and activities has sometimes impeded the crew's ability to hear the C&W tones.

[17]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

This inability to hear can also affect efficient mission performance by interfering with communication between crew members as well as between the crew and the ground. As documented in the ISS Life Sciences Crew Comments Database, noise has interfered with communication between crew members in different modules as well as between crew members in the same module. Noise has cost crew members time as they translate between modules to communicate directly. Wearing hearing protection because of high noise levels also impacts communication (figure 10-1). In addition, some crew members have reported that excessive noise on station has negatively contributed to their perception of ISS habitability. For instance, on-board noise has wakened some sleeping crew members. These examples show the need for optimal environmental conditions, such as acoustic levels that are below unacceptable noise thresholds, and the appropriate provision of auditory information (Category III).

Figure 10-1. ***ISS018-E-027439 — Cosmonaut Yury Lonchakov, Expedition 18 flight engineer, wears a hearing-protection device as he uses an oscilloscope to measure voltage in the Pirs docking compartment of the ISS (NASA Human Spaceflight Gallery, 2008).***

The provision of adequate lighting conditions is also essential for any living and working environment, including on board ISS. Although the station has increased substantially in size, it still remains a confined environment in which crew members live and work. It limits them to only the lights that are provided in modules and the additional lighting that is provided by portable and handheld lights. The evidence that is described below emphasizes the importance of providing appropriate lighting conditions.

Several issues have arisen with lighting on board the ISS (Baggerman et al., 2004). Lighting in some of the ISS modules was not originally installed in a manner that would provide the maximum amount of light output that had been designed into the lighting fixture. In addition, lights have failed throughout the life of the ISS, and limits on shuttle and Soyuz launch mass and volume have prevented the delivery of replacement light fixtures. Lighting in the ISS Node 1 module has been further affected by excessive stowage that has blocked operational lights, thus reducing the reflectivity of the surrounding surfaces. Because of the low lighting levels, some crew members have had to move certain tasks out of Node 1 to perform them, which both increases the time that is necessary to perform tasks and decreases efficiency. Working behind panels or racks without dedicated lighting has been difficult for some of the crew members. This situation forces them to accommodate and make up for the poor design by using other types of portable lighting while they are searching for items or working behind

panels. In summary, these impedances and inadequacies related to the ISS lighting have contributed to risks to efficiency on board the station (Category III).

Inefficiencies in space flight vehicle and habitat architectural design as well as the co-location of systems and tasks can affect crew safety, efficiency, and habitability. The co-location of certain functional habitability areas has been problematic throughout long-duration space flight due to vehicle size and topology constraints (figure 10-2). Lessons-learned summaries from the data that were collected in the ISS Life Sciences Crew Comments Database provide evidence that, on board the ISS, the adjacency of sleeping quarters with waste and hygiene facilities has not proven optimal due to the noise that is made by the equipment, which disrupts crew sleep. The co-location of the dining facilities near the exercise equipment and waste collection facilities compromises meal scheduling by influencing when food preparation and dining can be done. Although it is still possible to conduct dining activities while other crew members are exercising or using the Waste Collection System, it is not optimal. In addition, locating the dining facilities near the laboratory work jeopardizes both the habitability of the station and the integrity of its science activities. The integrity of science can be compromised by the introduction of foreign debris (e.g., food products), which can alter the results of an experiment by contaminating an environment that should be controlled.

Figure 10-2a. ***ISS008-E-21921 — Astronaut C. Michael Foale, Expedition 8 commander and NASA ISS science officer, equipped with a bungee harness, performs squat exercises on the Treadmill Vibration Isolation System in the Zvezda service module (NASA Human Spaceflight Gallery, 2008).***

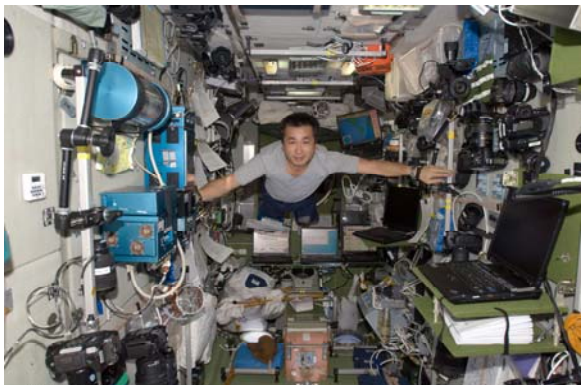


Figure 10-2b. ISS019-E-010232 — ***Japan Aerospace Exploration Agency astronaut Koichi Wakata, Expedition 19/20 flight engineer, floats in the Zvezda service module of the ISS (NASA Human Spaceflight Gallery, 2008).***

The movement of crew and hardware through the confined spaces of the ISS has been an ongoing topic of concern. As documented in the ISS Life Sciences Crew Comments Database, frequently used ISS translation passages have been blocked by large items, such as stowage or exercise equipment, which has contributed to congestion (figure 10-3). The location of the dining table in a high-traffic area such as the Zvezda service module (pictured in figure 10-2(a) and (b), above), with other colocated habitability hardware, has made translation difficult for crews. These co-location issues are caused by the lack of available habitable volume and resources that is endemic when living in space. This design concept has been suboptimal, however, and will not benefit future space habitat designs, as it presents numerous operational hazards to crews. Indeed, these vehicle design and topology constraints can affect daily tasks, habitability, and overall mission objectives so much that they impede crew safety; clearly, therefore, they must be improved (Category III).

Issues can also arise when safety precautions for the space environment do not take into account pre-flight ground activities. An example of what can occur when on-orbit and pre-flight activities are not well melded took place during the Apollo Program on January 27, 1967, when the Apollo 1 crew initiated what should have been a routine countdown drill. Disaster struck when a flash fire erupted in the command module at the NASA Kennedy Space Center, Pad 34 (figure 10-4). All three of the crew members lost their lives because they were unable to open the hatch and escape the command module to safety (Kranz, 2000). Numerous factors contributed to this incident, including an inadequate hatch design. The hatch, which had been designed to open inward, was impossible for a human to open at the pressure levels that were extant within the vehicle. Procedures or processes had not been put in place to deal with this type of emergency event because little consideration had been given to the risks and hazards that were associated with any of the pre-flight activities, only with those pertaining to space flight. This oversight contributed to the unsafe situation in the capsule and, ultimately, led to the crew members' deaths (Category III).

Figure 10-3. ISS011-E-06401 — ***Astronaut John L. Phillips, Expedition 11 NASA ISS science officer and flight engineer, is photographed among stowage bags in an airlock on the ISS. This photograph illustrates the physical transition/movement difficulties that are encountered on board station (NASA Human Spaceflight Gallery, 2008).***

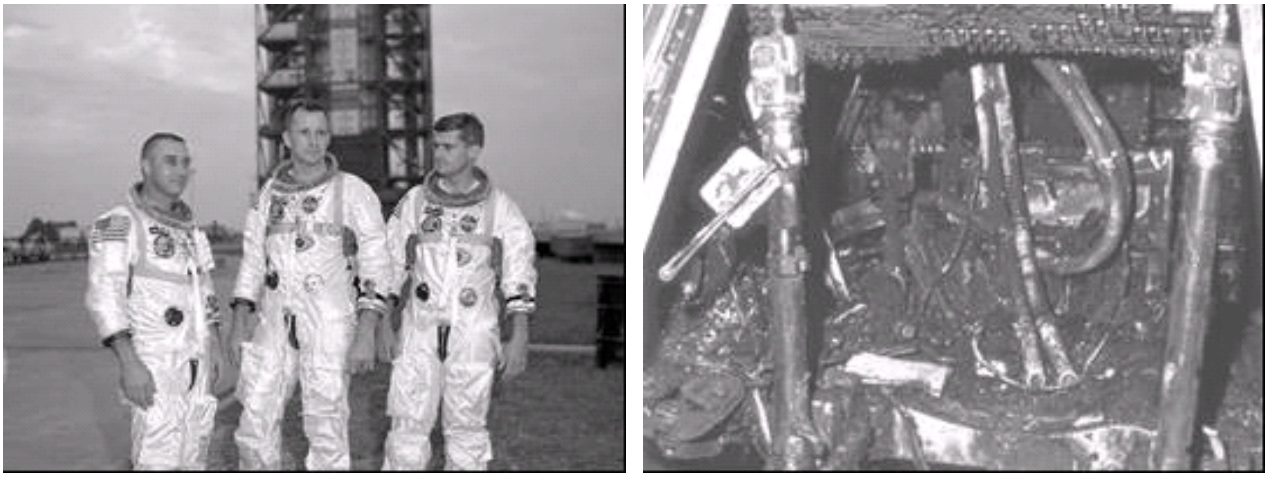


Figure 10-4. ***Apollo 1 crew prior to the tragic fire (left; from left, Virgil I. Grissom, Edward H. White II, and Roger B. Chaffee) and the vehicle after the fire (right) (United States Centennial of Flight Commission, 2003).***

The data that have been amassed on space flight crew postural changes are limited. Currently, space flight researchers are attempting to assess postural changes in zero g and related effects on crew health and safety for future Constellation Program missions. These postural changes directly affect the architectural design constraints and considerations for these future missions in which crew members will experience an increase in height of about 3% during the first day or two of weightlessness. These crew members will retain this increase throughout the mission until they are exposed again to 1g, at which time the process is reversed (*Anthropometric source book*, 1978). Current research indicates that weightless posture differs from any normal 1g posture on Earth, and that the body rebels with fatigue and discomfort against any attempts to force it into 1g postures or appliances that are consistent with 1g postures. The occurrence of crew member height changes was recognized when height data were collected on Skylab 4 and during the Apollo-Soyuz Test Project (ASTP) and were then compared to pre- and post-flight data. The design and usability of any human-machine interface can be affected by changes in the height and length of the trunk (Brown 1975; 1977). Examples of design problems include the design of pressure suits, clothing, workstations, and cockpit seating. New research is planned for upcoming shuttle missions to determine the potential for increased impacts on future vehicle crews from postural limitations on seated height and changes in it, and from the architectural design constraints of the vehicle. These assessments are aimed at increasing safety and efficiency for future missions (Category II).

Usability and design of workspaces, equipment, and tools

The importance of optimized usability and the design of workspaces, equipment, and tools increases in the remote space flight environment. As stated by the authors of the SHFH Risk description, if the workspace, equipment, and tools are not designed to be usable by the full range of crew members and are not properly laid out, the likelihood increases of errors or the inability of the crew to complete a task in a timely manner. Inconsistent design among subsystems and vehicles can also lead to the negative transfer of training, which risks the safety of the crew, and an increased likelihood of errors.

A high level of human-machine interdependence exists in space systems. To promote safe and efficient human factors designs, it is important to consider in the design process not only the biological effects of microgravity, but also the capabilities and limitations of both people and machines. For example, when tools are designed for use during an EVA, the strength that is required to use the equipment should be guided by that of the weakest and smallest individuals (i.e., the 1st-percentile female), as all crew members will have an equal likelihood of needing to use the equipment in an emergency (Category III).

The poor design of workspaces, equipment, and tools on orbit, which will result in poor usability, can lead to performance degradation and reduced situational awareness. As documented in the ISS Life Sciences Crew Comments Database, some ISS hardware items and tools do not have common or consistent interfaces. In addition some hardware items require unique tools, and the metric and English systems are used inconsistently because station hardware and tools are designed by U.S. and International Partners.

Spacesuits are an essential tool for crew members who are living and working in extreme environments such as the moon or Mars as well as for space shuttle and ISS EVAs. Achieving suit comfort has been a challenge for designers. In a study that was conducted in January 2008, data were collected on three subjective measures of comfort in the advanced crew escape suit (ACES), the Mark III suit, and the rear entry ILC Dover suit (REI) (Harvey et al., 2007). With regard to overall discomfort, subjects documented that no matter which spacesuit they were in, they experienced some level of discomfort, and this level of discomfort increased during pressurized testing. Specific anatomical regions where discomfort was noted were the shoulders, back, neck, knees, and lower arms. Discomfort while suited was attributed to the pressure demand regulator in the ACES and to bearing and resting

weight in the two planetary suits (i.e., the Mark III suit and the REI). These concerns will figure more prominently for long-duration planetary habitation because of the large number of anticipated EVAs that will be required. Suit discomfort can reduce the safety and efficiency of all aspects of crew performance (Category II).

Stowage is a critical component of the usability and design of space flight vehicle and habitat workspaces (Clark and Allen, 2008). On-orbit stowage includes not only the location of, but also the organization of, stowed items. Operations are impeded if stowed items cannot be easily located or identified (figures 10-5 through 10-7). With increased and accumulating stowage on board the ISS, there has been a need to stow items in front of panels and in translation paths, resulting in the crew members' reduced ability to access items quickly. In addition, cable routing blocks access to panels and stowage locations.

Figure 10-5. ***S118-E-07630 — Astronaut Alvin Drew, STS-118 mission specialist, moves a stowage container through the Destiny laboratory of the ISS while Space Shuttle*** **Endeavour** ***remains docked with the station (NASA Human Spaceflight Gallery, 2008).***

Figure 10-6. ISS010-E-25228 — ***This view shows supplies and equipment stowed in the functional cargo block (FGB) or Zarya photographed by a crew member on the ISS. (NASA Human Spaceflight Gallery, 2008).***

Figure 10-7. ISS016-E-028889 — ***Cosmonaut Yuri I. Malenchenko, Expedition 16 flight engineer representing the Russian Federal Space Agency, works in the Unity node of the ISS while Space Shuttle*** **Atlantis** ***(STS-122) is docked with the station. (NASA Human Spaceflight Gallery, 2008).***

ISS accessibility problems are caused both by obstructions and by the design and integration of hardware (Clark and Allen, 2008). The interior components of the U.S. segment of the ISS are grouped into a series of "racks" that individually rotate, or tip over, to provide crew access to the rack utility connections and the module wall. However, crew feedback has indicated that rotating the racks is not an effective way to access utilities and connectors in the microgravity environment on station. The clearance that is required for human accessibility has been repeatedly cited as an issue in rack rotation capability. The design of the panels and drawers with these racks has compromised crew accessibility because many of them "stick" on orbit because the design does not operate as intended in zero g, or too many items are placed in the stowage locations and are not organized to afford easy operation.

Finally, overall topology of workspaces has negatively affected crew accessibility. As an example, the U.S. cycle ergometer blocks access to the U.S. Laboratory window. As physical and visual access to on-board windows is very important to crew members for their mental health and overall judgment of habitability, restricted access and blocked translation paths contribute negatively to the overall safety and efficiency of the crew, especially in the event of an emergency (Category III).

The ISS on-board stowage accumulation has also been exacerbated by the buildup of packing materials that arrive with each shipment (by either space shuttle or a resupply vehicle, such as the Russian Progress module) (Baggerman et al., 2004). The limitations that are associated with the ability to dispose of packing materials on station result in excessive amounts of space being used to stow waste. The amount of stowage on board the ISS has increased to the point that all of the designated stowage areas are full and items are now being stowed in areas that were intended for habitability and work-related functions. Items are now stowed in passageways as well as in front of other stowage areas. In some instances, the stowage violates the allowable limits requirements that were originally set for the habitable volume areas. The result of this is that when crew members are searching for items, they must move many other stowed items out of the way to gain access to the place in which a desired item is located. During some ISS Expeditions, stowage has been located in the translation aisle, thereby blocking the emergency fire ports. This specific issue serves as an example of the risk that excessive stowage can impose on crew safety (Category III).

Balancing the launching of ISS supplies (manifest) with the ability to dispose of waste and to return items to Earth (down mass) is necessary to maintain habitable conditions on the ISS (Baggerman et al., 2004). The stowage situation became a habitability issue because of an imbalance between the space shuttle launch and return mass limits due to the grounding of the shuttle fleet after the *Columbia* accident and the reluctance of ISS Program personnel to dispose of unused hardware and supplies. As the amount of on-board stowage has, at times, exceeded the allowable ISS requirements for acceptable levels of stowage in the habitable volume, stowage levels are constantly tracked and evaluated. Over time, the on-board inventory of supplies (e.g., clothing and hygiene supplies) has increased, and the manifesting of these supplies still continues. Each ISS Expedition crew member brings a selection of personal items with him or her to station, and at the end of that crew member's stay the unused items remain. This increase in inventory contributes to crew safety risks, as ample stowage space is not available to accommodate placement of items outside of the habitable volume and translation paths. As the inventory management function has improved and the manifesting process has been streamlined, this situation has improved somewhat; stowage nevertheless continues to be a problem due to the lack and inconsistent nature of disposal capability due to space shuttle flights and inconsistent practices for tracking hardware and supplies (Category III).

Computer-based Simulation Information

Understanding human integration with systems and identifying risks that may be inherent in a concept or a design is often achieved via computer-based simulation. Computer-based simulation tools have multiple uses, including detection of potential risks to humans that are associated with reduced safety and efficiency due to inadequately designed space vehicles, environments, tools, or equipment. Computer-based simulation and virtual environments create a representation of the real world, and the user interacts with this representation with the aid of head-mounted displays, data gloves, and three-dimensional audio, haptic, or tactile feedback. Such environments can be used for training or, perhaps, interacting with prototypes that do not yet exist in the real world.

In the 1990s, NASA and the Federal Aviation Administration (FAA) engaged in several joint research efforts with the goal of providing safer, faster, and more fuel-efficient routing operation in flight management through use of automation in air traffic control (Pisanich and Corker, 1995). It was thought that integrating automation technologies into the air traffic control system could optimize routing, sequencing, and scheduling in the terminal areas and, ultimately, improve efficiency while relaxing constraints during flight to accommodate user-preferred routing and schedules. Man-machine Integration Design and Analysis System (MIDAS) was adapted to model a predictive flight crew performance (figure 10-8) that focused on predicting the performance of a two-pilot flight crew responding to information that was generated by an automated air traffic control system, the Center Terminal Radar Approach Control (TRACON) Automation System (CTAS).

During the course of research, experimenters conducted two computer simulations. The first of these employed a model of top of descent (TOD). This model was developed with the goal of determining an optimal range of time in which the CTAS descent clearance would be issued so that the aircrew would be likely to accept the clearance and enact it using flight deck automation rather than by manually commanding the descent. This model confirmed that as the TOD point draws closer, the aircrew will select the less-automated alternative mode of control. In this study, as the aircraft approached within 5 to 8 miles of the CTAS-required TOD point, the number of successes in any clearance compliance was reduced significantly. It was found that multiple simulated trials could be conducted without compromising human safety when determining the optimal range of time in which to issue CTAS descent clearance. Moreover, multiple scenarios could be tested that did not require the use of an aircraft, and the aircrew's trust in the automation could also be determined. Results of the study assisted

designers in integrating automation technologies into the system to improve crew efficiency by optimizing routing, sequencing, and scheduling. This provides evidence that inadequately designed equipment could lead to a risk of reduced safety and efficiency (Category II).

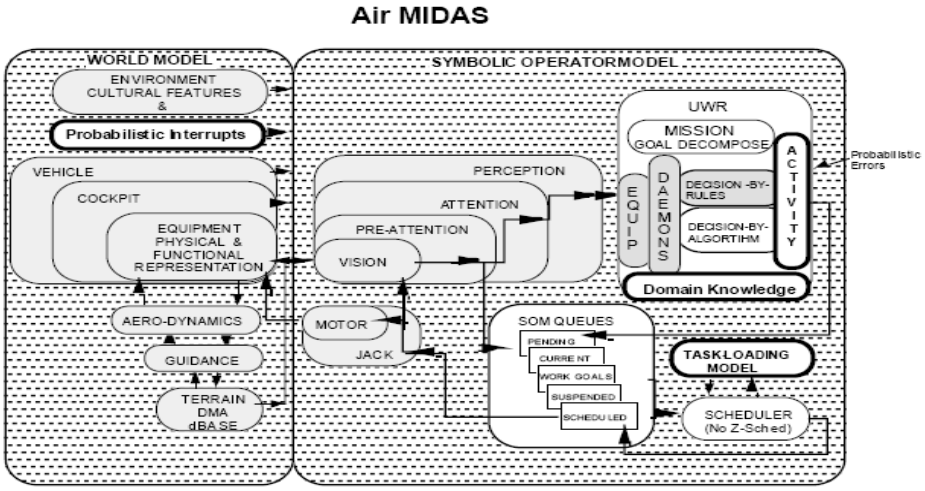


Figure 10-8. ***Full MIDAS closed-loop model (Pisanich and Corker, 1995).***

Risk in Context of Exploration Mission Operational Scenarios

Future Exploration mission durations will substantially lengthen. During this extended timeframe, crews will face the challenges of physical deconditioning, prolonged isolation and confinement, significant communication latencies, environmental stressors, and increased responsibility and autonomy. Effective human-centered design techniques for vehicles, habitats, and missions allow Exploration mission operational scenarios to be managed and controlled. For further information, see Chapter 9 of this report.

Human-centered design must be implemented in all aspects of the design process to mitigate or prevent space human factors engineering risks from occurring and specifically to ensure the safety and efficiency of the crew. Designing for reduced gravity will be critical. Lunar and martian environmental conditions – air quality, dust, radiation exposure, and lighting – must be addressed. The interior configuration of the spacecraft must support expected crew tasks. Hardware commonality and standardization will support interchangeability and reduce the amount of time that is needed for training. Spacecraft designers need to ensure that appropriate spares and stowage volumes are available and can be accessed in a timely manner. A reduction in required maintenance and interface with complex systems should also be implemented.

Conclusion

The risk of reduced safety and efficiency due to inadequately designed vehicle, environment, tools, or equipment stems from a broader cause of human error – the lack of human-centered design, which requires a focus on the user throughout the design process. Good human-centered design practices will result in improved efficiency of operation and safety of all system components, including the human, and should reduce the life-cycle cost of the project. The evidence that is discussed in this chapter identifies concerns that are associated with the risk. To alleviate these concerns, knowledge gaps, or "holes," and future research directions have been identified. Some

of these knowledge gaps are related to poorly designed hardware, software, environments, and habitats as well as the lack of appropriate design considerations, guidelines, and countermeasures for systems on future vehicles.

The human-machine system emphasizes the importance of the human as the central focus of the human-centered design process. This focus includes consideration for human capabilities, limitations, and interaction with automation and hardware. Knowledge gaps, or "holes," that are related to the lack of an integrated system design approach for environmental and architectural design and usability and the design of workspaces, equipment, and tools must be addressed to ensure that quality standards, requirements, tools, and techniques are developed to allow positive crew-system integration and interaction to occur and, ultimately, mission success.

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Acknowledgments

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Chapter 11:
Risk of Error Due to Poor Task Design

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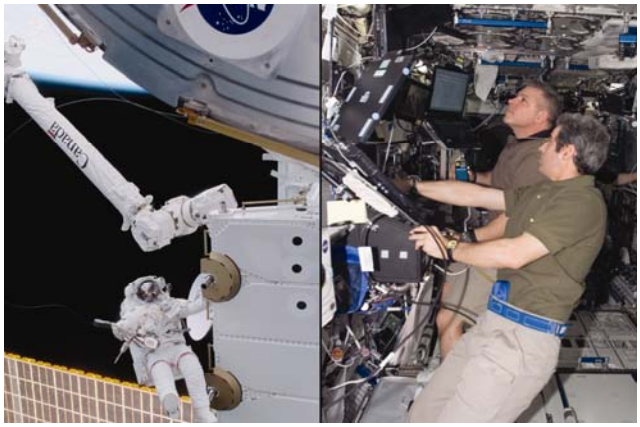
If roles and responsibilities for accomplishing tasks are not clearly defined, there will be a risk of serious errors of omission or commission. This risk may relate to interaction between multiple crew members, to interactions between crew and robotics/automation, and between crew and ground control. Understanding the characteristics of the elements involved, how each communicates, and establishing guidelines to adhere to during task design and procedure development are all essential to mission success. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.



EVAs are accomplished by human-robotic teams, where EVA crew members work outside of the vehicle with the robot arm and additional crew members work inside the vehicle at the robotics workstation. Using human-robotic teams for tasks reduces human workload and increases task efficiency.

Executive Summary

Many human performance errors that have been experienced in long-duration space flight have been directly related to poor system and task design. Poor task design results from a lack of integration and consideration of the human throughout the operational process. The human-system interface and tasks that require human performance must be designed to elicit appropriate inputs from the operator. If the roles and responsibilities for accomplishing tasks are not clearly defined, there will be a risk of serious errors of omission or commission. This risk may relate to interactions among multiple crew members, to interactions between crew and robotics/automation, and between crew and ground control personnel. Evidence for the risk that is associated with poor task design is related to both human and automated tasks. The authors of this chapter emphasize that the success of long-duration missions with highly complex systems relies heavily on effective task design. For a more detailed summary of the overall concepts related to space flight human factors and human-centered design, refer to Chapter 9 of this document.

Introduction

The risk of errors due to poor task design relates to the definition and development of mission tasks, and to the interactions among multiple crew members, between the crew and robotics/automation, and between the crew and ground control personnel. Accomplishing mission-related tasks involves multiple crew members, robotic or automated systems, and ground control personnel. To achieve successful task performance, each person and system must have clearly defined roles and responsibilities. If the roles and responsibilities for a task are not correctly assigned, serious errors of omission or commission can occur.

To design mission tasks for optimal performance, task designers often must integrate human and automated tasks or integrate the actions of more than one crew member or the actions of crew members and ground support personnel. The interactions among crew members, between crew members and ground support personnel, and between crew members and robotics and automated systems depend on the humans' understanding of their assigned roles and responsibilities. It is crucial for designers also to have an understanding of the appropriate allocation of roles and responsibilities to the various participants in a task. Appropriate allocation of roles and responsibilities is facilitated by the task designers' ability to understand the characteristics and limitations of all of the humans and automated systems that are involved in the task, and how each of them communicates. The use of such knowledge to allocate roles and responsibilities should be included in the guidelines to which the designers will adhere during task design and procedure development.

Evidence

The evidence that is described in this chapter encompasses the lessons learned from 50 years of space flight experience as these lessons learned relate to the risk of error due to poor task design. Evidence is classified by specific categories and topic areas. Specifically, Category I and Category II evidence consist of quantitative and qualitative findings from research and development. Data are classified as Category I or Category II, depending on the specific testing protocol that was used and the data that were sought. Category III evidence consists of summaries of subjective experience data as well as non-experimental observations or comparative, correlation, and case or case-series studies. It should be noted that some evidence in this chapter is derived from the ISS Life Sciences Crew Comments Database, which is made up essentially of Category III evidence. Although summaries of the ISS crew comments are presented as evidence, the ISS Life Sciences Crew Comments Database

is protected and not publicly available due to the sensitive nature of the raw crew data that it contains. Category IV[18] evidence consists of expert committee reports or respected authorities' opinions based on clinical experiences, bench research, or "first principles."

If the number of task errors increases, task performance decreases. Task performance, which may or may not involve a person, is the outcome of a task. It can be quantified by the results and the duration of the task (Sanders and McCormick, 1993).

The evidence that is presented here focuses on the concept that the root cause of task performance error is the poor design of human and automated tasks. Without proper consideration for task design, the task performance of both humans and automated systems will degrade, and the mission will be unsuccessful.

Human task design and performance

Poor task design can result in human errors and, possibly, degraded overall performance. These errors can be related to the type and purpose of tasks, the level of completion, and who or what is performing the task. Some tasks are best suited for humans and should not be automated. Humans are generally better at recognizing unexpected events, reasoning, and developing solutions (Sanders and McCormick, 1993). To achieve optimal human task performance for space missions, adequate workload and situational awareness levels of humans must be maintained. Humans who are given too many responsibilities to perform may become overloaded, and their performance may degrade. Conversely, if all tasks are automated, humans can become complacent and lose situational awareness. When tasks are automated, it is important to keep a crew member "in the loop" to ensure that the automation is performing as anticipated. Maintaining even low-level crew involvement provides crew members with a complete understanding of both manual and automated tasks and allows them to efficiently and appropriately conduct their tasks, which include monitoring automated tasks for issues or failures. A few examples of poor performance due to poor human task design follow.

In June 1997, the Russian spacecraft Progress 234 collided with the Russian *Mir* space station, causing the pressure hull to rupture and nearly causing the *Mir* to be abandoned (figure 11-1). A number of contributing factors were cited in the post-accident analysis of the incident, including the condition of the vehicle and the decision to shut the Kurs radar system down during Progress 234 docking because of concern that the radar system had caused radio interference during a previous flight. This action deprived the crew of the necessary range data that would have prevented the collision. It was later determined that the crash had three immediate causes: an initial closing rate that was higher than planned, a late realization that the closing rate was too high, and incorrect final avoidance maneuvering.

[18]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

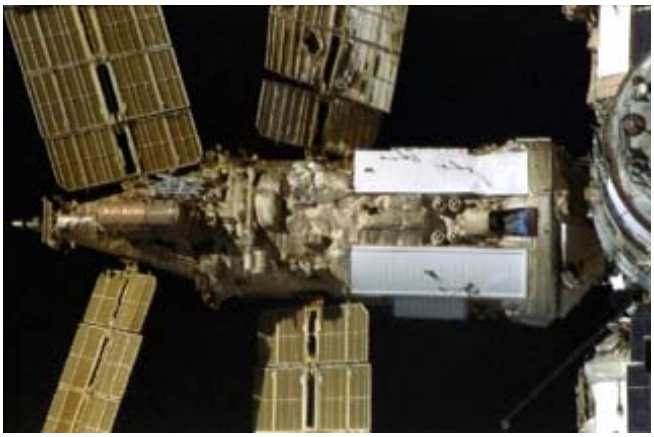


Figure 11-1. ***Spektr module showing the damaged radiator and solar array on*** **Mir (NASA photograph).**

Several types of human factors task design issues may have contributed to this incident; among these are: psychophysical (manual docking system display issues), sensory-motor (issues with the tele-operation of the Progress and difficulty determining the relative velocity from visual information), and cognitive (lack of information about the position of the crew and the range and range rate, thereby decreasing spatial awareness) (Ellis, 2000). The crew also experienced stress because of an overly demanding workload and repeated system failures, which continuously commanded their attention and contributed to reduced vigilance (Ellis, 2000). In addition, the last formal training that the crew members received took place 4 months before the docking event, and they may not have had sufficient or timely practice in task design to handle the conditions. After the Progress collision with Mir, the emergency situation required closing the hatch of a module that was leaking air. This task took extra time because the cables that were running through the open hatch did not have easily operable disconnects and, therefore, the crew had to cut them. All of the aforementioned factors contributed to the degraded overall task performance of the crew (Category III).

Crew performance of tasks on the ISS, such as EVAs, maintenance, and medical tasks, relies heavily on the provision of adequate procedures (figure 11-2) (Rando et al., 2005). Poor design of procedures for station tasks has impeded crew task performance by preventing the completion of scheduled activities within the allotted time. Well-designed procedures play a critical role in ensuring optimal, on-schedule crew task performance. Inadequately structured procedures will ultimately lead to a reduction in human task performance.

Figure 11-2. ISS009-E-19837 — ***Astronaut E. Michael Fincke, Expedition 9 NASA ISS science officer and flight engineer, looks over a procedures checklist while working with an extravehicular mobility unit (EMU) spacesuit in the Quest airlock of the ISS.***

ISS crew members have often reported that the procedures with which they deal are complex, lengthy, and contain too many C&Ws (Baggerman, 2004). In general, procedures are felt to be too detailed, especially for simple operations. Pictures and diagrams, which are considered helpful for many procedures, are not always integrated appropriately. In addition, some of the procedures reference multiple steps in other procedures. Locating the necessary steps costs the crew additional time and has resulted in missed or skipped steps (Category III). The overall usability of procedures has been an ongoing issue for ISS crew members and mission designers, which emphasizes the need for common standards and simplification where possible in procedure development.

Performance degradation that is due to poor ISS task design was illustrated during a ground-based study to test the usability of a procedure (as written on a "cue card," figure 11-3) for the respiratory support pack (RSP), which is a piece of ISS medical equipment, to support redesign of the cue card (Hudy et al., 2005). The RSP was designed for use during medical contingencies involving respiratory distress; therefore, the complicated RSP cue card procedure would be used in time-critical situations in which a crew member's life could depend on the outcome. During the study, data were collected as subjects executed the procedure checklists, and results demonstrated that some procedures and training could be both a source of errors and, ultimately, a risk to crew health. The procedures and the sequence of using the equipment did not enable a crew member to establish a patient's airway in the time necessary to prevent irreversible brain damage. The CMO typically receives very limited training in using the medical equipment, and the cue cards thus hold vital information on how to execute the procedures. This example illustrates the importance of appropriate procedures and training to ensure that tasks can be performed successfully, especially in case of an emergency. The cue card was subsequently redesigned to support a simpler task (figure 11-4) (Category III).

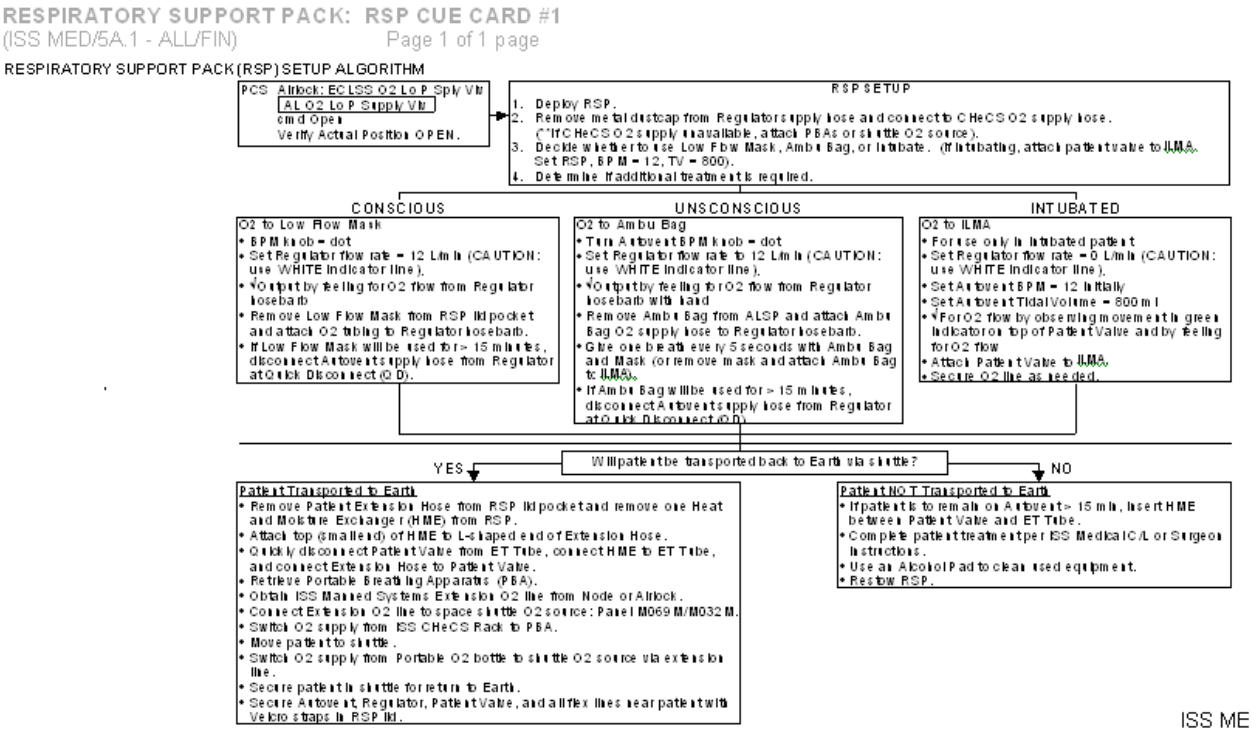


Figure 11-3. ***Respiratory support pack information card before evaluation*****.**

Human-computer interaction brings together humans and technology to accomplish a certain task. Future human exploration vehicles, including lunar and Mars habitats, will be highly dependent on computerized, automated systems, necessitating the development of accurate methods for crew members to use to interact with computers. Human-computer interaction involves the processes, dialogs, and actions that a user employs to interact with a computer in any given environment.

Human-computer interfaces allow the user to input an instruction to the computer. In turn, the computer should provide a response or feedback to the user's input. Through input devices and output devices such as displays, the user is able to see, hear, touch, and recognize the interaction. Many different kinds of input devices can facilitate human-computer interaction. These include keyboards, mice, joysticks, and other devices. Historically, output devices have consisted of various types of displays, ranging from computer monitors to the head-mounted displays that are worn by users to interact with virtual environments, for example.

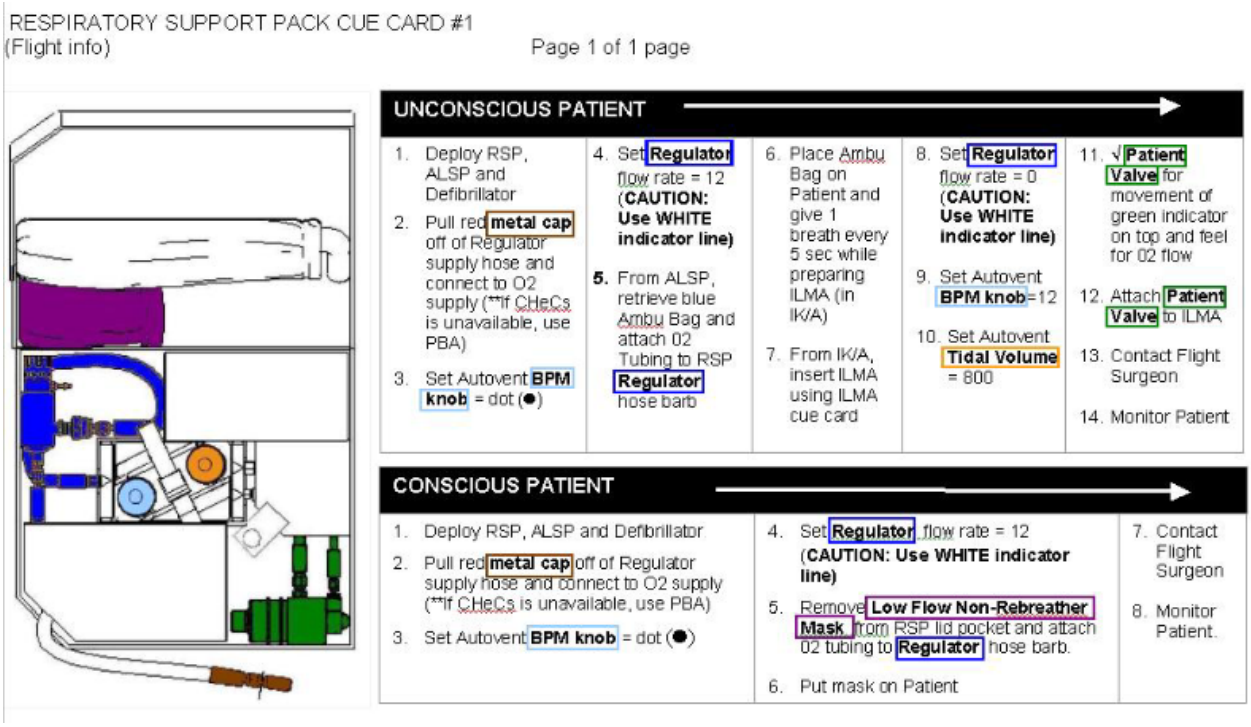


Figure 11-4. ***Respiratory support pack information card after evaluation.***

Human-computer interfaces should match the physiological characteristics and expertise of the user, be appropriate for the task that is to be performed, and be suitable for the intended work environment. It is thus critical to determine the characteristics of the user, what tasks are to be performed, and the characteristics of the work environment. Designers can then determine which human-computer interfaces are suitable and appropriate to the task at hand.

If the performance of controls that operate optimally in a 1g setting become degraded in a microgravity or partial-gravity environment, task performance can be affected. Interfaces need to be designed that will operate and respond in all gravity environments in which they might be used. The selection of appropriate interfaces that

allow direct manipulation by the user provides the best solution to operating computer systems in a microgravity environment. Designers must still consider and accommodate the specific tasks that are to be performed. Different control devices are suited for different tasks.

The design of a cursor control device illustrates some of the issues that are associated with human-computer interface task design. Designers of cursor control devices have to consider a number of environmental factors, including g-forces, vibration, and gloved operations, as well as task specificity. The participants in eight flight studies (both parabolic and space flight) performed structured cursor control tests that involved pointing, clicking, and dragging of on-screen objects of various sizes (Holden et al., 1992). The cursor control devices that were used in these flight studies included mouse devices and trackballs. The general findings from these studies were that the mouse did not function in microgravity, and the trackballs (both attached and unattached) had too much or little to no "play." A follow-up study was conducted, in which data that involved performance timing and error were collected on several commercial and proprietary cursor control devices, in both gloved and ungloved conditions (Sandor and Holden, 2007). The selected devices included a roll bar device, four different trackball devices, a track pad mouse, two optical air mouse devices, and a joystick. For both the gloved and the ungloved conditions, the results indicated that, overall, the trackball devices performed better (with regard to accuracy and timing) than the other devices, and that different devices were preferred for different tasks. This example illustrates how important the design of the human-computer interface is in dictating which support items will be needed to achieve optimal operational efficiency (Category II).

Maintenance of equipment and vehicles is often a difficult and labor-intensive task (Baggerman, 2004). The difficulty is compounded when maintenance is performed on orbit (figure 11-5). A typical maintenance task will require that the maintainer use various tools and hardware. Many tools and hardware items are required to successfully complete the maintenance tasks on complex systems. This situation can be problematic in the reduced-gravity environment of current and future space vehicles and habitats. Unstowed tools can easily become misplaced or damaged or interfere with the task, unnecessarily increasing the time that is needed in which to repair the system and ultimately degrading the performance of the task.

Figure 11-5. (top) ISS019-E-009823 — *Japan Aerospace Exploration Agency astronaut Koichi Wakata, Expedition 19/20 flight engineer, performs in-flight maintenance on the Treadmill Vibration Isolation System in the Zvezda service module of the ISS*;(right) ISS018-E-019725 — *Astronaut E. Michael Fincke, Expedition 18 commander, works on hardware in the Destiny laboratory of the ISS*.

Human-centered design of whole systems for maintainability can also improve the performance of individual tasks, as well as system reliability, and can prevent system failures. Maintainability of systems on a long-duration orbiting vehicle such as the ISS is critical (Baggerman, 2004). Many hardware items require frequent maintenance and multiple tools with which to effect maintenance. The ISS toolkit has improved greatly since the early ISS Expeditions, but the quantity of tools that are required for a designated task is excessive for a microgravity environment. This situation significantly impacts crew time, particularly when the need for frequent maintenance is coupled with the problems that are encountered when accessing hardware for repair. Poor maintainability has also resulted from the initial perspective of system designers that the systems would not need to be maintained because they were reliable. In reality, however, system failures and reliability issues have been experienced, ultimately requiring additional maintenance time and unanticipated task redesign (Category III).

Automation task design and performance

The core human factors issues for task design are determining the necessary tasks and how these tasks are expected to be performed. Task analysis and human factors guidelines should ensure that tasks do not exceed human capabilities. As increasing numbers of automated systems are designed to assist the human, a synergistic relationship must be developed between the human and the automation to allow them to work together to accomplish tasks.

Machines and automation are often used to monitor systems, collect information, and repeat actions (Sanders and McCormick, 1993). Machines, however, are not always reliable. When designers are allocating increasing numbers of tasks to automation, they must maintain awareness that the machines are not always reliable. When an automation failure occurs, it is imperative for the humans who rely on that automated system to be prepared to take over its functions and tasks. This contingency must be reflected in task design requirements for both the human and the automated systems. In addition, when automation fails, especially in the early stages of use, operator trust can decrease and the humans who were meant to rely on the automated system may prefer to perform the automated tasks themselves. Conversely, an operator may come to rely too heavily on the automation and, thus, fail to monitor the performance of the system. When assigning roles to humans and automation within systems, it is important to allocate appropriately and facilitate human situational awareness when tasks are automated. This is especially true when those responsibilities were once performed by humans.

As documented in the ISS Life Sciences Crew Comments Database, which is not publicly available, ISS crews currently rely on ground support teams for most of the planning and scheduling of daily tasks. Software tools such as the Onboard Short Term Plan Viewer provide crew members with detailed schedules for daily activities. Although the crew can provide input into these schedules, ground support is often relied on to adapt and change the schedules as needed (Category III). The higher level of autonomy that is required for lunar and Mars missions will increase the need for automated planning capabilities and tools. These tools would provide the requisite automated support to determine alternative plans and solutions for managing daily tasks. Although crew input and ground support, as available, would still be helpful, automated support for these planning tasks will allow crew members to manage daily tasks on their own, thus ensuring that these tasks are performed appropriately when ground support is unavailable.

One example of a current, poorly designed ISS task is the management of stowage. The ISS Inventory Management System (IMS) was designed to act as a crew-driven series of tasks using a barcode reader and a database. As noted in the ISS Life Sciences Crew Comments Database, the tracking methodology for items that are stowed on ISS has historically been unique for each Expedition. As it is not well designed, the IMS has not been used consistently to track items that are to be stowed, and not all items have been scanned or tracked. When items were moved, they were subsequently not replaced in their designated area, and the IMS is not always

updated to reflect the new location. Stowage locations of items have not always been based on their functional use, causing crew members to search at opposite ends of the ISS for equipment that is needed to perform a single task. This has resulted in the crew spending time searching for items that they needed for daily tasks, and has contributed to a poor task structure in terms of how things are stowed and collected.

In summary, issues with the ISS IMS have stemmed from both problems with the use of the IMS and the design of the system and its related tasks. ISS IMS-related stowage management tasks have been rife with errors, and this has decreased crew efficiency. Stowage management could benefit from increased automation (Category III).

Additional examples of ISS tasks that are deemed poorly designed and that are cited in the ISS Life Sciences Crew Comments Database are the daily tasks of sampling microbial growth and water, as well as providing medical, exercise, and acoustics measurement or photographic data to the ground. These can be time-consuming tasks for crew members. Collecting samples and providing data to the ground are often perceived by the crew as occurring too frequently. Sampling and measurements could be automated to require minimal crew effort or input; this would allow crew members to conduct more critical tasks while still avoiding performance errors and ensuring efficient communication of data for ground support (Category III).

Computer-based Simulation Information

Understanding human integration with systems and the identifying risks that may be inherent in a concept or a design is often achieved via computer-based simulation. During the evaluation of possible locations for the second treadmill to be placed on board the ISS to support a crew of six, the Boeing Human Modeling System (BHMS) software identified risks to the ability to install a treadmill in each of the possible locations chosen (figure 11-6) (Rice, 2007). One location would have the treadmill co-located with the crew quarters in the ISS Node 2 module; accessibility was identified as a problem there, however, because of the configuration of the crew quarters bump-outs, which extended into the translation paths for astronauts and the access area for the planned second treadmill. The BHMS modeling software was thus successfully used to identify accessibility

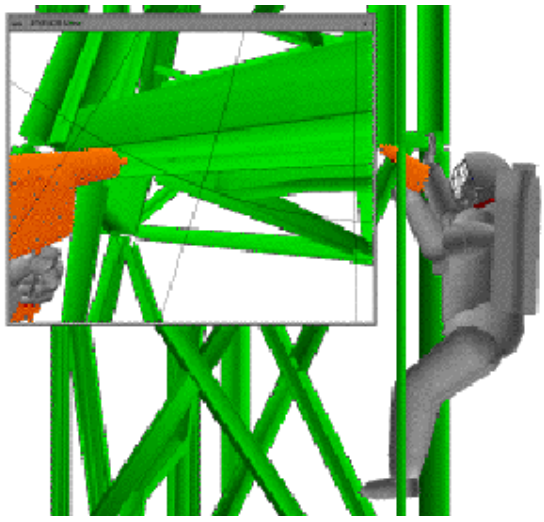


Figure 11-6. ***BHMS sample photo. (Photograph from http://www.boeing.com/assocproducts/hms/case4.htm.)***

issues and a noncompliance with ISS requirements for accessibility. After the evaluation was complete, it was established that the location would not allow the crew to conduct the installation task successfully, and new tool options would need to be pursued to reduce the risk that was associated with the poor task design (Category III).

Risk in Context of Exploration Mission Operational Scenarios

Current space flight crews rely on on-board automated systems to perform tasks, and future crews, who will be facing increased flight duration and increased autonomy, will rely even more on these systems to provide information that is appropriate, accurate, and recent. This increased reliance on automation will result in the need for additional training to ensure that the crew members can perform the automated tasks in the event of automation failure. Automated tasks must be carefully designed to prevent the crew from becoming unaware of, or complacent about, potential hazards. This situation could ultimately result in system errors, degraded crew performance, and compromised crew and vehicle safety.

A specific requirement for increased autonomy for lunar and Mars missions is automated planning capabilities and tools. These tools would provide the necessary automated support to determine alternative plans and solutions for managing daily tasks. For further information, see Chapter 9 of this document.

Conclusion

The risk of error due to poor task design stems from a broader cause of human error; namely, the lack of human-centered design. This type of design requires a focus on the user throughout the design process. Good human-centered design practices will result in improved efficiency of operation and safety of all system components, including the human element, and should reduce the lifecycle cost of the project. The evidence that is discussed in this chapter demonstrates why this risk is a concern.

Knowledge gaps that are related to this risk have, and will continue to be, defined, and future research directions should lead to filling these gaps and, eventually, to alleviating the concerns that have been identified. Some of these knowledge gaps are related to a lack of task analysis and understanding of operations, which is necessary to ensure awareness of crew and ground personnel functions, and how autonomy and automation will be integrated and applied. Knowledge gaps that are associated with a lack of user evaluations and iterative knowledge capture have also been identified. These gaps emphasize the need for the development of methods to evaluate human and system performance, especially with the expected increased requirement for automation and autonomy in future long-duration space flights.

The human-centered design process emphasizes the importance of the human as the central focus of the human-machine system. This focus includes consideration of human capabilities, limitations, and interaction with automation and hardware. Knowledge gaps, or holes, that are related to the lack of an integrated system design approach for human and automated task design must be addressed to ensure that quality standards, requirements, tools, and techniques are developed that will allow positive crew-system integration and interaction, and, ultimately, mission success.

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Chapter 12:
Risk Factor of Inadequate Food System

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If the food system does not adequately provide for food safety, nutrition and taste, then crew health and performance and the overall mission may be adversely affected. Furthermore, if the food system uses more than its allocated mission resources, then total required mission resources may exceed capabilities, the mission deemed unfeasible, or allocation of resources to other systems may be unduly constrained. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

Ongoing advances in space food nutrition, palatability, and storage will continue to provide astronauts with meals that promote their health and safety, while minimizing the use of vehicle and crew resources. Here, astronaut Leland Melvin displays several food items while orbiting the Earth on board the space shuttle.

Executive Summary

An adequate food system is required to enable safe, reliable, and productive human space exploration. This food system will be required to deliver safe, nutritious, and acceptable provisions to the crew while efficiently balancing appropriate vehicle resources such as mass, volume, waste, and food preparation time for Exploration missions. A dual system consisting of a packaged food system (with a shelf-life of 3 to 5 years) and a bioregenerative food system on the planetary surface is being considered for the Mars missions. Understanding the potential risks to the food system for long-duration missions is an important step on this path.

The safety of food is of highest importance as the incidence of food-borne illness could compromise the success of a mission. While current pre-flight procedures have ensured food safety so far, the ongoing development of the mission architecture for lunar and Mars explorations necessitates a reexamination of these existing procedures as well as the development of new processes.

Since the food system is the sole source of nutrition to the crew, a significant loss in nutrition, either through the loss of nutrients in the food or inadequate food intake, may also significantly compromise the performance of the crew. The nutritional content of food may be inadequate due to losses during processing or environmental factors (e.g., temperature and radiation) encountered over the shelf-life of the food. Providing adequate levels of acceptability, variety, and usability is important to prevent inadequate caloric intake.

The ineffective use of vehicle resources such as mass, waste, and crew time can affect mission success. The mass of the packaged food system is based on the mass of the food and the packaging surrounding the food, which could produce a significant amount of waste. A bioregenerative food system that could provide the crew with fresh foods will use more crew time, so the benefit to the performance of the crew must be shown to offset this additional burden.

The paramount importance of the food system in a long-duration human Exploration mission should not be underestimated. Vehicle resources must be balanced with safety, nutrition, and acceptability to provide an adequate food system. The food system will provide not only the nutrients that will be needed for the survival of the astronauts, but also will enhance the psychological well-being of the crew by serving as a familiar element in an unfamiliar and hostile environment.

This document presents the evidence that supports the risk factor of an inadequate food system as well as the knowledge gaps that still remain and that need to be filled.

Introduction

The primary goal of the Advanced Food Technology (AFT) Project is to develop the requirements and technologies that will enable NASA personnel to provide an adequate food system that is characterized by the provision of safe, nutritious, and acceptable food while also efficiently balancing appropriate vehicle resources such as mass, volume, waste, and crew time in the Exploration missions. AFT, which is a project within the SHFH Element, is expected to directly relate to the HRP objective of developing capabilities and technologies in support of human space exploration, focusing on mitigating the highest risks to crew health and performance. Further details on the HRP can be found at http://humanresearch.jsc.nasa.gov/about.asp.

The authors of space program food system literature have documented the evolution of the space food system. Several types of food and beverage packaging have been used in NASA space programs. With the exception of Skylab, there has not been a refrigerator or freezer on board a spaccraft that was dedicated to food storage. Therefore, the food must be shelf-stable. This requires inactivation of the microorganisms in the food during ground processing before flight. While processing the packaged foods to commercial sterility provides a safe food system, this level of processing can reduce the quality of the food, including nutritional content and acceptability.

The different forms in which food has been provided include the following:

1. *Thermostabilized* – This process, which is also known as the retort process, heats food to a temperature that renders it free of pathogens, spoilage microorganisms, and enzyme activity. Food items are placed in cans or pouches and are heat-processed with steam- or water-overpressure to remove excess air/oxygen for specified times and temperatures to render the food commercially sterile.
2. *Irradiated* – Although irradiation is not typically used to process foods to commercial sterility, NASA has special dispensation from the FDA to prepare nine irradiated meat items to commercial sterility (21CFR179, 2008). Irradiation involves the use of gamma rays, x rays, or electrons, and uses energy levels that assure the negative induction of radioactivity in the irradiated product. It controls naturally occurring processes such as ripening or senescence of raw fruits and vegetables, and is effective for inactivation of spoilage and pathogenic microorganisms.
3. *Rehydratable* – A number of technologies are available that allow for the drying of foods. Examples of these technologies are drying with heat, osmotic drying, and freeze drying. These processes reduce the water activity of foods, which results in the inability of microorganisms to thrive.
4. *Natural form* – Natural-form foods are commercially available and shelf-stable. The moisture of the foods may range from low moisture (e.g., almonds and peanuts) to intermediate moisture (e.g., brownies and dried fruit). These foods rely on reduced water activity to prevent microbial activity.
5. *Extended shelf-life bread products* – Items such as scones, waffles, and dinner rolls can be formulated and packaged to give them a shelf-life of up to 18 months.
6. *Fresh food* – Fresh fruit, vegetables, tortillas, and other foods that have a short shelf-life are provided on a limited basis, more for psychological support than as part of meeting dietary requirements.
7. *Beverages* – The beverages that are currently being used on the ISS and shuttle are either freeze-dried beverage mixes (e.g., coffee or tea) or flavored drinks (e.g., lemonade or orange drink). The drink mixes are prepared and vacuum-sealed inside a beverage pouch. In the case of coffee or tea, sugar or powdered cream can be added. Empty beverage pouches are also provided for drinking water.

One of the goals of the Constellation Program (CxP) lunar long missions is to use the lunar surface as a test bed for future Mars missions. Although it is possible for CxP mission planners to continue using current food technologies, a change in missions will necessitate a change in the food system. The CxP missions will require longer shelf-life packaged foods with improved nutrition and acceptability. These missions will also require more attention to resource utilization such as mass, volume, power, crew time, and water use. The Mars missions, in particular, will require that technologies be developed so that the crew is more self-sufficient and less dependent on resupply missions. In addition, once the crew is out of LEO, space radiation is higher, and space-irradiated food may lose nutritional content and acceptability. The research that AFT conducts will allow for the food system to change when necessary.

To further address the limitations in vehicle resources to accommodate prepackaged foods, mission designers also envision that once the crew is on the lunar or Mars surface, crops will be grown. Fresh fruits and vegetables, such as spinach, lettuce, tomatoes, carrots, bell peppers, onions, potatoes, and strawberries, could be grown hydroponically in environmentally controlled chambers. In addition, baseline crops, such as soybeans, wheat, rice, peanuts, and dried beans, could be grown on the surface or launched in bulk from Earth. These crops would be processed into edible ingredients. These edible ingredients, the freshly grown fruits and vegetables, and packaged food items would be used to prepare meals in the galley. Dependence on the processing and preparation of bioregenerative and bulk commodity foods presents unique risks for these missions.

A mission to Mars will use prepackaged foods, which are similar to those that are used on ISS, for transit and may include positioning food on Mars prior to crew arrival. Prepositioned food may be 3 to 5 years old at the time of consumption. Currently, prepackaged foods have a stated shelf-life of 18 months but will need a 5-year shelf-life for the Mars missions. Shelf-life criteria are safety, nutrition, and acceptability. Any of these criteria can be the limiting factor in determining the shelf-life of food.

Safety

Food safety is the protection of food from physical, chemical, and microbiological contamination. The food system must be designed to ensure that the initial provisions are safe from contamination and are packaged to remain safe from contamination for up to 5 years of storage in multi-environments. Good manufacturing practices, which include employee qualifications and training, sanitation, recordkeeping, process validation, and facilities and equipment maintenance and verification, are followed to prevent food contamination during processing and packaging (21CFR110, 2008).

Microbiological contamination of food can negatively affect crew health and possibly compromise crew survival. Most food items are monitored by the NASA JSC Microbiology Laboratory (as specified in JSC 16888 (publicly unavailable)) to ensure that preparation and packaging procedures result in products that conform to established microbial standards for flight foods. Table 12-1 lists the items that are tested and the associated limits.

NASA adheres to the hazard analysis and critical control point (HACCP) system, which is a systematic and preventive approach to food safety that was developed by NASA, the United States Army Laboratory, and the Pillsbury Company in the 1960s. Both the Centers for Disease Control (CDC) and the United States Department of Agriculture (USDA) cite the implementation of the HACCP system of inspection as a principal reason why the incidence of food-borne illness appears to be declining (PBS Frontline, 2002). The use of HACCP, including the strict use of good manufacturing practices, standard operating procedures, and testing of processed foods, is associated with the prevention of food-borne illness events during space missions.

Nutrition

Adequate nutrition has two components: necessary nutrients and energy in the form of calories. Without adequate nutrition, there is a risk of not being able to live a healthy, productive life. It is possible to consume enough calories without a well-balanced selection of individual nutrients. This can result in diseases that are noticeably different from those resulting from an overall insufficiency of nutrients and energy. For example, a vitamin C deficiency may result in scurvy while a deficiency in niacin may result in pellagra. It is important that crew members who are on a long-duration mission are provided with the required level of nutrition throughout their mission. Table 12-2 summarizes the required nutritional requirements as stated in the CxP 70024, *Human-Systems Integration Requirements* document, section 3.5.1.3.1 (publicly unavailable).

Table 12-1. ***Microbiological Testing for Flight Food Production***

Area/Item	Microorganism Tolerances	
Food Production Area	**Samples Collected***	**Limits**
Surfaces	Three surfaces sampled per day	3 CFU/cm^2 (Total aerobic count)
Packaging Film	Before use	
Food Processing Equipment	Two pieces sampled per day	
Air	One sample of 320 liters	113 CFU/320 liters (Total aerobic count)
Food Product	**Factor**	**Limits**
Non-thermostabilized**	Total aerobic count	20,000 CFU/g for any single sample (or if any two samples from a lot exceed 10,000 CFU/g)
	Coliform	100 CFU/g for any single sample (or if any two samples from a lot exceed 10 CFU/g)
	Coagulase positive staphylococci	100 CFU/g for any single sample (or if any two samples from a lot exceed 10 CFU/g)
	Salmonella	0 CFU/g for any single sample
	Yeasts and molds	1,000 CFU/g for any single sample (or if any two samples from a lot exceed 100 CFU/g, or if any two samples from a lot exceed 10 CFU/g *Aspergillis flavus*)
Commercially Sterile Products (thermostabilized and irradiated)	No sample submitted for microbiological analysis	100% inspection for package integrity

*Samples collected only on days that the food facility is in operation.
**Food samples that are considered "finished" products that require no additional repackaging are only tested for total aerobic counts.

Table 12-2. ***Nutrition Composition Breakdown***

Nutrients	Daily Dietary Intake
Protein	0.8 g/kg And ≤ 35% of the total daily energy intake And two-thirds of the amount in the form of animal protein, and one-third in the form of vegetable protein
Carbohydrate	50%–55% of the total daily energy intake
Fat	25%–35% of the total daily energy intake
Ω-6 Fatty Acids	14 g
Ω-3 Fatty Acids	1.1–1.6 g
Saturated fat	< 7% of total calories
Trans fatty acids	< 1% of total calories
Cholesterol	< 300 mg/day
Fiber	10–14 grams/4187 kJ
Fluid	1–1.5 mL/4187 kJ And ≥ 2000 mL
Vitamin A	700–900 μg

Table 12-2. Nutrition Composition Breakdown (Concluded)

Nutrients	Daily Dietary Intake
Vitamin D	25 µg
Vitamin K	Women: 90 µg Men: 120 µg
Vitamin E	15 mg
Vitamin C	90 mg
Vitamin B12	2.4 µg
Vitamin B6	1.7 mg
Thiamin	Women: 1.1 µmol Men: 1.2 µmol
Riboflavin	1.3 mg
Folate	400 µg
Niacin	16 mg NE
Biotin	30 µg
Pantothenic Acid	30 mg
Calcium	1,200–2,000 mg
Phosphorus	700 mg And ≤ 1.5 × calcium intake
Magnesium	Women: 320 mg Men: 420 mg And ≤ 350 mg from supplements only
Sodium	1,500–2,300 mg
Potassium	4.7 g
Iron	8–10 mg
Copper	0.5–9 mg
Manganese	Women: 1.8 mg Men: 2.3 mg
Fluoride	Women: 3 mg Men: 4 mg
Zinc	11 mg
Selenium	55–400 µg
Iodine	150 µg
Chromium	35 µg

The ability of the food system to meet the nutritional requirements of a crew can only be determined when the nutritional profile of the entire space food system is known at the time at which the food is consumed. However, there has only been limited measurement of the nutritional content of the flight food items. Macronutrients and some minerals are determined chemically at the NASA JSC Water and Food Analytical Laboratory (WAFAL). Other nutrients, such as vitamins, are currently calculated with a computerized nutrient database that was developed by the USDA and the food industry. However, the level of processing that is done by NASA can reduce the quality of the food, including its nutritional content and acceptability. In addition, it is unknown whether processed foods will maintain nutritional adequacy for 3 to 5 years.

Nutrient losses may also occur due to environmental conditions, such as the higher radiation levels that will be encountered during planetary missions. The addition of antioxidants to the food may help prevent the formation

of free radicals that contribute to food spoilage (Wilson et al., 2007; Gandolph et al., 2007). In the case of a bio-regenerative food system, in the absence of sufficient protection, radiation may affect the ability of plants to germinate and grow, and it may also affect their resulting functionality (Wilson et al., 2007).

During the short-duration lunar missions, it is assumed that EVAs will be scheduled to occur not less than every other day for 8-hour periods during surface missions (NASA, 2005). As stated in the CxP 70024, *Human-Systems Integration Requirements* document, these EVAs will require no less than an additional 200 kilocalories per EVA hour above the nominal metabolic intake, with a similar nutrient composition to the rest of the diet. Requirements for long-duration lunar or Mars missions have not been determined but would likely be similar to those for the short-duration lunar missions.

Acceptability

Food acceptability can be defined and determined in several ways. The first way is in terms of appearance, flavor, texture, aroma, and serving temperature. Currently, flight foods are evaluated using sensory analysis, for acceptability on the ground, by a panel of 30 or more consumers. The products are rated based on appearance, flavor, texture, and aroma using a 9-point Hedonic Scale.[19] Food products must receive an overall score of 6 or higher to be included in the space food system. Similarly, prior to flight, a crew member will evaluate the foods on the 9-point Hedonic Scale. If the score that is assigned to a food item is less than 6.0, that food item will not be on the crew member's personal preference menu.

Product acceptability can also be affected by factors such as product formulation, product age, how the product is stored, and where the product is consumed. Menu variety and usability of the food system also contributes to food acceptability. A large variety of food items is recommended to provide the crew choices and to avoid menu fatigue. If the food is difficult to prepare or eat, the overall acceptability of the food is reduced (Smith et al., 1975).

Finally, food acceptability can also be affected by social context and the timing of meals. Food and mealtimes can play a primary role in psychological-social benefit, such as reducing the stress and boredom of prolonged space missions or promoting unity by dining together.

Resource utilization

During the development of a space flight food system, several resources must be considered including: mass, volume, power, crew time, and waste disposal capacity. Misuse of these resources may affect mission success. The balancing of resources with food quality is dependent on the specific mission. For example, the 2-week initial missions to the moon will consider mission resource utilization more important due to the small usable volume in the vehicle. Since the missions will be shorter, nutrition and acceptability may not be as critical.

Food packaging is a major contributor to mass, volume, and waste allocations for NASA missions. Packaging is integral to maintaining the safety, nutritional adequacy, and acceptability of food, as it protects the food from foreign material, microorganisms, oxygen, light, moisture, and other modes of degradation. The higher the barrier properties of the packaging, the more that packaging can protect the enclosed food from oxygen and water ingress from the outside environment. Oxygen ingress can result in oxidation of the food and loss of quality or nutrition. Water ingress can result in quality changes such as difficulty in rehydrating the freeze-dried foods.

[19]The Hedonic Scale is used by tasting panels to indicate the extent of the like or dislike of panel members for a particular food item.

The current packaging that is used for the freeze-dried foods and natural-form foods for the ISS does not have adequate oxygen and moisture barrier properties to allow for an 18-month shelf-life. Therefore, these foods are overwrapped with a second foil-containing package that has higher barrier properties. The packaging materials that are used for the thermostabilized, irradiated, and beverage items that are consumed on station contain a foil layer to maintain product quality beyond the required 18-month shelf-life. Although the foil layer provides excellent protection, it is not compatible with all of the technologies that produce commercially sterile foods. For example, two emerging technologies – high-pressure processing and microwave sterilization – cannot use the foil package. This will require NASA to continue using the foil packaging and forego those emerging technologies or to acquire packaging that is compatible with both of those technologies.

Tables 12-3 and 12-4 list the oxygen and water vapor permeability of the current NASA food packaging materials.

Table 12-3. ***Oxygen Permeability of Packaging Materials (CC/100IN2/DAY)***

	73.4ºF@100% Relative Humidity
Overwrap	0.0065
Thermostabilized and Irradiated Pouch	< 0.0003
Rehydratable Lid and Natural Form	5.405
Rehydratable Bottom (heat formed)	0.053

Table 12-4. ***Water Vapor Permeability of Packaging Materials (G/100IN2/DAY)***

	100ºF@100% Relative Humidity
Overwrap	< 0.0003
Thermostabilized and Irradiated Pouch	0.0004
Rehydratable Lid and Natural Form	0.352
Rehydratable Bottom (heat formed)	0.1784

The food system generates both wet and dry waste. Dry waste may include items such as dry food packaging. As it is cost prohibitive to plan on launching the trash from the lunar or Mars surface, another alternative is required for trash disposal. Although the foil layer that is within a food package protects that food from oxygen and water migration, it may provide complications if the decision is made to incinerate the trash on the lunar or martian surface. Wet waste may include cleaning materials and wet food packaging. Because of the spoilage of food substances that are left on cleaning materials and in packaging, food system wet waste materials must be properly disposed of to limit microbial contamination to the crew.

If a bioregenerative food system is used during the lunar or Mars surface missions, some mass and volume savings will be seen from the use of less packaged foods. However, the processing and preparation equipment will contribute to the mass and volume of the habitat. In addition, the use of this equipment will require more water, power, and crew time than would be required by simply heating or hydrating packaged foods. The benefits of bioregenerative food systems will require a vigorous defense if the resources that they require are to be allocated on such resource-constrained missions.

Evidence

Safety

Good manufacturing practices, including microbiological testing of food products pre-flight, have likely prevented food-borne illness in the past. Freeze-drying prevents food-borne illness by eliminating the water that is necessary for microorganisms to grow. Safe freeze-dried foods depend, at the beginning of the process, on high-quality ingredients and clean surfaces with minimal microorganism contamination. However, there still can be viable microorganisms in the food. These foods are therefore tested for viable microorganisms pre-flight. There have been instances in which freeze-dried foods did not pass microbiological testing due to contamination from mold, yeast, or bacterial pathogens. Mark Ott from the NASA JSC Microbiology Laboratory reported at the 2006 Spring Meeting of the American Society for Microbiology, Texas Regional Branch, Wimberley, Texas, that 14 items over several years – including chicken salad and shrimp – failed to meet the microbiological testing for flight food production specifications (see Table 12-1) and, hence, were not approved for shuttle and ISS flights. Although this is a small number based on the number of samples that were tested in the JSC Microbiology Laboratory, even one food lot can result in several crew members becoming sick during a mission (Category I)[20].

Thermally processed foods are processed to a high enough temperature for a long enough time to provide commercial sterilization. As with the freeze-dried foods, safe foods are still dependent on good HACCP practices. After processing, the thermostabilized pouches are tested for pouch integrity and swelling to determine whether adequate heat was applied to the food to produce commercial sterility (Category IV).

Nutrition

Crew members during Apollo missions often experienced reduced appetite, possibly due to a combination of effects such as fluid shifts, pressure changes, nausea, and workload. Rambaut et al. (1975) state that the importance of nutrition in the adaptation of astronauts to weightlessness has been recognized since Project Gemini. Smith et al. (1975) note that throughout the Mercury, Gemini, and Apollo missions, weight losses among the flight crews were noticed with few exceptions, including two crew members on Apollo 14. Food intake during these missions was consistently below the quantities that were necessary to maintain body weight. Although the energy intake from the NAS, NRC Recommended Daily Dietary Allowance (RDA) is 2,870 kcal/day, the mean energy intake during these missions was only 1,880 ± 415 kcal/day. Rambaut et al. (1975) also state that Apollo nutrition guidelines provided only marginal amounts of nicotinate, pantothenate, thiamine, and folic acid. The occurrence of arrhythmias in Apollo 15 astronauts was attributed to a potassium deficiency due to inadequate nutrition in the space food system (Smith et al., 1975). The potassium deficiency in this short-term mission was mitigated in later missions through potassium supplementation. Instances of scurvy, rickets, and other nutritional deficiency conditions occurred in the earlier explorer expeditions due to poor nutrition. Therefore, an unexpected deficiency of one or more nutrients in a long-duration space mission may significantly affect mission success (Category III).

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[20]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

Longer-term effects of space travel on nutrition have been documented through physiological changes during the 6-month-long ISS Expeditions, in which urine, blood, plasma, and serum nutrient contents and body mass were measured post-flight and statistically compared to pre-flight baselines. Of particular concern were the decreased levels of several vitamins and minerals in the urine, blood, plasma, and serum. For example, vitamin D levels, antioxidant capacity, γ-tocopherol levels, and folate levels were all significantly lower after flight, creating concern for weight loss and associated malnutrition during ISS Expeditions 1 through 8 (Smith et al., 2005). The results detail a reduced caloric intake (around 80% of recommended intake during space flight) leading to an average of a 5% weight decrease and potentially explaining some, or all, of the measured nutrient decrease. It has also been suggested that dietary intake may have been low due to time constraints for meal preparation and consumption (Smith et al., 2005). The Skylab crews, who were required to eat enough to meet their caloric needs, preserved body mass (Thornton and Ord, 1975) (Category III). More information on inadequate nutrition through inadequate caloric intake can be found in Chapter 12 on the HRP Website at: http://humanresearch.jsc.nasa.gov/elements/smo/hrp_evidence_book.asp.

Inadequate intake is not the only reason for inadequate nutrition. If the food loses nutrients through processing or storage, a crew member will not have adequate nutritional intake. Available data on the vitamin content of certain processed foods at various temperatures over 2 years of storage demonstrate the potential for significant vitamin loss (Kamman et al., 1981; Kim et al., 2000; Kramer, 1974; Lund, 1975; Pachapurkar and Bell, 2005). Cameron et al. (1955) compiled data on the loss of ascorbic acid, riboflavin, and thiamine over 2 years in several canned fruits and vegetables, showing vitamin losses as great as 58% in some canned products that were held at 80°F, while the same products that were held at 50°F only showed maximum losses of 38% (Category I). Therefore, nutritional loss at 3 to 5 years, which has not been studied, could likely result in inadequate nutrition in the food system (Category I).

Nutrient changes during processing and over the shelf-life of processed foods include isomerization of vitamins or vitamin precursors, changes in the bioavailability of amino acids and vitamins as the food structure is broken down, and nutrient degradation, including oxidation of several vitamins and amino acids (Gregory, 1996; Chen et al., 1995; Rock et al., 1998; Dewanto et al., 2002; Graziani et al., 2003; Seybold et al., 2004). The bioavailability of vitamins may be more important than overall quantity in a food, as other components in the diet and the form of the vitamin may influence absorption and function. Therefore, the bioavailability of vitamins in individual foods may vary, making it important to have an understanding of the available nutrients as well as the overall quantity (Gregory, 1996) (Category I).

Some emerging technologies will be approved by the FDA for commercial sterility in the next few years. The two technologies with the most promise are high-pressure processing (HPP) and microwave sterilization. HPP is a method of food processing in which the food is subjected to elevated pressures (up to 87,000 psi or approximately 6,000 atmospheres), with or without the addition of heat, to achieve microbial inactivation or alter the food attributes to achieve consumer-desired qualities. Pressure inactivates most vegetative bacteria at pressures that are above 60,000 psi. HPP retains food quality, maintains natural freshness, and extends the microbiological shelf-life (Balasubramaniam, 2007). Microwave sterilization is a high-temperature, short-time process in which packaged food is cooked at 265°F for 10 minutes (U.S. Army Soldiers System Center (Natick), 2004). Current thermostabilized NASA food products are cooked to about 250°F, but for a much longer time. Preliminary studies suggest that the quality of the foods is much higher using these promising technologies. Lund (1988) determined that food quality (i.e., color, texture, etc.) may provide a general indication of the nutritional loss of the food.

While lower temperatures during storage could help alleviate the storage issues, ISS and space shuttle missions do not have the mass or power capabilities to provide cold storage (Perchonok and Bourland, 2002) (Category I). Currently, the commercial food industry does not require foods to have shelf-lives longer than 2 years (Category III).

Acceptability

The acceptability of the food system has been linked to caloric intake and associated nutritional benefits. If food is not acceptable to a crew, the crew will not eat an adequate amount of it and will be compromised nutritionally. Large improvements and advances in space food systems were achieved during the Apollo food program. Nevertheless, the majority of the Apollo astronauts did not consume sufficient nutrients. Loss of body weight, fluids, and electrolytes were the rule, with few exceptions (Smith et al., 1975).

A thorough review of the Apollo experience was provided by Scheuring et al. in the NASA document TM-2007-214755, *The Apollo Medical Operations Project: recommendations to improve crew health and performance for future Exploration missions and lunar surface operations* (not publicly available). The objective of the study was to provide evidence to modify medical requirements for future Exploration missions by identifying Apollo 7 through 17 mission medical issues. This historical database was generated based on the responses of 14 of 22 surviving Apollo astronauts to 285 questions. Among the 11 categories that were addressed, Food/Nutrition had 76 responses and eight recommendations. Scheuring et al., in addition to Rambaut et al. (1975), report that reduced food consumption may be partially attributed to a combination of physiological effects such as fluid shifts, pressure changes, nausea, issues with preparing food and with the water system, and workload, but acceptability of and familiarity with the food are also critical to consumption. Scheuring et al. also report that changes in the sensory perception of the food have been noted between ground-based taste test participants and Apollo and shuttle mission crew members, making it important to understand the effect of pressure and fluid shifts on sensory perception. Apollo crew members have also stated that having hot water with which to prepare hot drinks (e.g., having coffee in the morning) was important, providing them with a psychological boost (Category III).

Consistently during ISS crew debriefings (the documents are not available externally due to confidentiality issues), the crews have stated that their food preferences change from pre-flight to flight. Similar to the Apollo and space shuttle experiences, the ISS crews have also noted that their tastes for certain foods changed in microgravity, and that they may crave different foods on orbit as compared to on Earth (Category III).

ISS crews have also noted in crew debriefings that they would prefer more food variety for the length of the missions, and that they tire of certain foods over 6 months. When the menu cycle repeated after only 8 days (as opposed to the current 16-day menu cycle for ISS missions), the crews noted that there was not enough variety in the menu (document not available externally due to confidentiality). As the diets of the crew members during a mission are limited to just the available items, the long-term acceptability may decrease for some of the menu items. Vickers (1999) reports that studies that were conducted by the U.S. armed forces in the 1950s showed that most foods decreased in acceptability when they were repeatedly consumed. The degree of loss of acceptability depended on the specific food (Category III).

The next-generation NASA space vehicle, Orion, is considerably smaller than the shuttle and the ISS. For this reason, the food system for the Orion vehicle is being challenged with the possibility of no food warmer or hot water. A study that was conducted in 2006 at the NASA JSC Space Food Systems Laboratory measured the acceptability of food, which is normally consumed hot, when it is hydrated with ambient water or not heated. Using a 9-point Hedonic Scale (in which food scores of 6.0 or better suggest acceptability), the study showed that the

food lost about 20% of its acceptability when it was consumed at room temperature and about 17% of the food items were determined to be unacceptable. Hence, there is a risk of decreased in-flight nutrition for astronauts on an Orion vehicle due to lower acceptability and fewer foods available for the mission.

Perchonok and Antonini (not publicly available) reported at the 2008 Human Research Program Investigators Workshop on the results of an accelerated shelf-life study of seven thermostabilized items and three bulk ingredients. These items were stored at 40°F (control), 72°F (storage temperature of actual flight food), and 95°F (accelerated temperature). Sensory evaluations were conducted every 4 months for the first 2 years and every 6 months for the third year. The conclusions of the study were that the shelf-lives of the thermostabilized items range from 0 months for egg products to 87 months for a representative meat product. The thermostabilization process does not result in acceptable products for all formulations. For example, thermostabilized egg products tend to be rubbery and darken in color (Juliano et al., 2007). Meat products have been thermostabilized (canned) for many years and tend to maintain their quality even after processing (Category II).

Furthermore, if food preparation takes too much crew time, the consumption of that food may also decrease (Smith et al., 1975). Providing adequate sensory attributes and ease of use (preparation difficulty and time) with respect to crew scheduling will be necessary to prevent inadequate caloric intake and associated nutritional and psychological issues (Category III).

It can be concluded that if a food system has adequate levels of acceptability, variety, and usability, crew members will consume more food during their mission.

Resource utilization

The ineffective use of vehicle resources such as mass, waste, and crew time can affect mission success. Mass of the packaged food system is based on the mass of the food and the packaging that is surrounding the food. The mass of the food is dependent on the type of food and the quantity that is required to meet the caloric requirements of a crew. Smith et al. (1975) noted that the mass of the Apollo 7 food system for the crew was 1.8 lbs. of food per person per day. By the time of the Apollo 14 mission, the mass of the food for the crew averaged 2.48 lbs. per person per day. The Apollo 8 crew, in 1968, preferred the newly added thermostabilized foods, which were referred to as “wetpack foods.” According to Smith et al. (1975), the improved crew acceptance of the thermostabilized product justified the weight increase. Even with the added “wetpack foods,” the Apollo food system still contained a significant number of freeze-dried foods since water from the fuel cells was available for food rehydration (Category III).

Perchonok, at the 2002 annual meeting of the International Conference of Environmental Systems (not publicly available), reported that the ISS and shuttle crew members receive about 4 lbs. of food plus packaging per person per day. A higher percentage of the food on the shuttle and the ISS is thermostabilized compared to the Apollo flights due to the higher acceptability of thermostabilized food. Since ISS uses solar panels for a power source and not fuel cells that produce water as a by-product, there is no mass advantage to using freeze-dried foods. Furthermore, the average number of calories for ISS crew members is based on the actual caloric needs of a crew member based on that crew member’s body weight and height, which results in an average caloric requirement of 3,000 kcal as opposed to the 2,500 kcal that were provided to Apollo crew members. Based on mass challenges, CxP designers are considering the possibility of reducing the food system mass while still providing the crew with adequate calories (Category III).

The results of a preliminary study that was conducted at NASA JSC by French and Perchonok suggest that the total mass of a food system may be reduced in a long-duration surface mission if that food system moves more towards a bioregenerative and bulk commodity food system. (The food system that would be used in transit between Earth and Mars would remain a packaged food system to be compatible with the microgravity environment.) French and Perchonok, at the 2006 Habitation Conference, reported on a preliminary study – the Bulk Ingredient Menu project. The designers of this project assumed that fresh fruit and vegetables would be grown in the crew habitat on a planetary surface; however, the mass of the environmental growth chambers was not included in the project mass calculations. It was projected that some food processing would be conducted using bulk ingredients (e.g., turning soybeans into tofu and milling wheat into wheat flour for bread production). The study assumed a 600-day stay on a planetary surface with six crew members. French and Perchonok report that the mass of a food system using food preparation would be about 4,200 kg. For the same length of a surface stay mission (600 days) with a crew of six, the mass of an ISS-style food system would be about 6,600 kg (Category I).

Food packaging produces a significant amount of waste. In the course of confidential crew debriefings, the NASA *Mir* crew members stated that the overwrapped foods created a trash management problem as there were two food packages per food item for the rehydratable and natural-form foods. Although the foods are not overwrapped on shuttle missions, the trash that is produced by the food system can still be significant. Lee (2000) reports that 60% of the mass that was measured from waste on STS-99 was generated from the food system (including food, drinks, and packaging) while STS-101 demonstrated an even greater percentage (i.e., 86% of the mass). An analysis of the food waste on STS-51D showed a total trash mass of 50.7 lbs. that included 26.9 lbs. of uneaten food and 23.8 lbs. of food packaging. Eighty-five percent of the trash by volume on STS-29 and STS-30 was food packaging, and 7% of the trash volume was food (Wydeven and Golub, 1991) (Category II).

In a 2001 trade study (not publicly available), Levri et al. evaluate five potential menus for use during a Mars mission. From the study it was determined that for prepackaged foods, generally 3% of the food would be left in the package if an attempt were made to eat everything. As packaging is about 9.5% of the mass of the total food system, it would therefore be expected that, at a minimum, 12.5% of the rehydrated food system on a Mars mission would become waste (Category I).

To avoid the issues that are associated with trash accumulation on a lunar or Mars surface mission, the trash will need to be disposed of. One option is to incinerate it; however, the foil layer within the food package will not incinerate completely and will leave some ash from the foil (Perchonok, 2007) (Category IV).

Several studies, which attempt to balance mass, volume, crew time, and power requirements with nutrition and acceptability, have been conducted to determine the effect of a bioregenerative food system on a lunar or Mars mission. In the Levri et al. (2001) trade study, five menus were evaluated (Table 12-5) that use equivalent system mass (ESM). ESM converts mass, volume, power, cooling, and sometimes crew time requirements into one mass value. The volume, power, cooling, and crew time requirements are converted to mass using equivalency factors. These equivalency factors are based on mission length and location.

The Shuttle Training Menu was similar to the menu for the shuttle and ISS food system. The various menus supplemented the Shuttle Training Menu with frozen foods, bulk-packaged snack foods, and/or salad and/or potatoes. The salad and potatoes would be grown on the Mars surface. Levri et al. (2001) determined that if only ESM was considered in choosing a menu, either case 2, case 4, or case 5 would be chosen (Table 12-6). However, the authors also concluded that non-quantifiable issues (with respect to ESM), such as food palatability and the psychological benefits of plant-crew interaction, must come into play in making a decision (Category I).

Table 12-5. ***Food System Options*** **(Levri et al., 2001)**

Case	Food System	Packaging Approach	Crop Growth
1	ISS Assembly Complete (some frozen food)	Individual Servings	Salad
2	Shuttle Training Menu	Individual and Multiple Servings	Salad
3	Shuttle Training Menu	Individual Servings	Salad and White Potato
4	Shuttle Training Menu	Individual Servings	Salad
5	Shuttle Training Menu w/reduced water content	Individual Servings	Salad

Table 12-6. ***Non-crew -time ESM, Crew-time ESM, and Total ESM*** **(Levri et al., 2001)**

ESM	1 (frozen)	2 (multiple serving)	3 (potato)	4 (indiv)	5 (reduced water content)
ESM_{NCT}*	27,587	23,246	27,198	23,324	23,351
ESM_{CT}**	4,398	3,635	4,848	3,650	3,654
ESM_{TOTAL}	31,984	26,881	32,047	26,974	27,005

*Non-crew time
**Crew time

During a Lunar Mars Life Support Test Project simulation in a closed chamber, a four-person crew tested a 10-day vegetarian diet that was based on crops that were expected to be grown during long-duration missions. These crops were processed into ready-to-use ingredients outside of the chamber, leaving general cooking activities and cleanup to the crew. The general preparation and cleaning activities required 4.6 crew hours total per day. The amount of waste, which was accrued mostly from leftovers, ranged between 20% and 80%. This experience demonstrated a need for automated processes, a diverse menu, and improvements in recipe scaling based on crew size (Kloeris, 1998) (Category I).

French and Perchonok, at the 2006 Habitation Conference (not publicly available), reported that the preliminary Bulk Ingredient Menu project determined that food preparation would require, for a crew of six, about 3 hours per day. However, in addition to the 3 hours actively spent preparing food, about 6 hours per day of passive time was required for food preparation. Passive time was defined as the preparation time that did not require a crew member to constantly watch over the process, such as the time that is involved in baking. Note that only 30 minutes are set aside for crew preparation on ISS missions (Category I).

Computer-based Simulation Information

Shelf-life can be defined as the time at which a product no longer maintains its specified quality. Changes in food, whether nutritionally or in quality, occur through chemical reactions and can be modeled to determine the theoretical shelf-life. Actual shelf-life testing is required not only to confirm the rate of reactions, but also to de-

termine which chemical reaction in the food will determine the ultimate endpoint of the shelf-life. For example, the endpoint may be the Maillard Browning reaction[21] or the loss of a vitamin.

All chemical reactions in food adhere to the simple general rate equation of

$$-\frac{d[A]}{dT} = k[A]^n$$

where A is the quality attribute that is being measured, T is the time, k is the rate constant, and n is the reaction order (Labuza and Schmidl, 1985). Most quality reactions in food are zero or first order. Zero-order reactions exhibit a constant change in quality over time. Typical zero-order reactions ($n = 0$) are enzymatic browning, non-enzymatic browning, and lipid oxidation. Typical first-order reactions ($n = 1$) are protein and most vitamin deterioration as well as microbial growth. Although there are not many second-order reactions ($n = 2$) in food, it has been reported that, in limited oxygen, the degradation of vitamin C is second order (Labuza, 1982).

Q_{10}, which is a measure of how the rate changes for every 10°C (50°F) change in temperature, is defined as

$$Q_{10} = \frac{\text{Shelf life at temperature T°C}}{\text{Shelf life at temperature (T°C + 10)}}$$

If the color change reaction happens in half the time at 10°C higher temperature, then $Q_{10} = 2$ (Perchonok, 2002).

Since food is not a model system, it is not simple to estimate Q_{10}; but typical Q_{10} values are shown in Table 12-7. Table 12-7 shows that there is no definitive Q_{10} for a given type of food such that each food must be tested to determine its own Q_{10}. Note that a given type of food may have several Q_{10}s. The lipid oxidation may have one Q_{10} value and the Maillard browning may be a different Q_{10} (Perchonok, 2002).

Table 12-7. Q10 Values for Various Food Preservation Methods

Food Preservation Method	Q10
Thermally Processed	1–4
Dehydrated	2–10
Frozen	3–40

With the Q_{10} values calculated, product shelf-life can be projected using the formula

$$t_s = t_0 e^{-aT}$$

[21]The Maillard-Browning reaction is a chemical reaction, usually requiring heat, which takes place between an amino acid and a reducing sugar.

where:

t_s = desired shelf-life
t_0 = shelf at a reference temperature
a = slope of the line equal to ln*Q*10/10
T = temperature difference between temperature at which the shelf-life, t_s, is desired and the reference temperature

Shelf-life information may be collected at a faster rate using accelerated shelf-life testing and the Q_{10} value. Accelerated shelf-life testing requires a control temperature in which no changes are expected to occur through the shelf-life. The product may also be stored at the current storage temperature and an accelerated temperature, in which the reaction rates and resulting shelf-life at the accelerated temperature are used to determine the shelf-life at the current temperature using the Q_{10} value (Evans et al., 1981). However, the accelerated temperature may cause changes that would not normally occur in foods at regular storage temperature, such as melting, protein denaturation, and increased water activity (Labuza and Schmidl, 1985). These changes must be considered when analyzing shelf-life data.

The complexities of food structure and variety of components make food a dynamic system, which increases the difficulty in quantifying changes with kinetic models. The loss of vitamins to leaching (even when the vitamins are consumed in the leach liquid), the loss of nutrients during thermal processing, and the potential for increases in nutrient bioavailability as the food matrix is broken down during processing create an ambiguous picture of the actual nutritional content of processed foods. While the literature attempts to quantify the changes in nutritional content, the answers are not always obvious. However, the literature data provide an estimate for kinetic changes in the space food system and insight into the potential countermeasures, such as alternative processing methods and formulation interactions.

While kinetic data are available for the loss of nutrition during processing and storage, the rate constants that are provided are specific to the food and conditions in each test (Evans et al., 1981; Feliciotti and Esselen, 1957; Mulley et al., 1975; Kirk et al., 1977; Lanthrop and Leung, 1980; Rao et al., 1981; Kamman et al., 1981) (Category I). Therefore, the use of the models that are in the literature will only provide a rough estimate of the remaining nutrition if kinetic models were prepared using these data. Accurate nutrition loss data on the thermostabilized pouches that are specific to the space food system need to be acquired over a 3- to 5-year shelf-life to avoid the use of a food system that has inadequate nutrition for a Mars mission. Food quality (i.e., color, texture, etc.) may provide a general indication of the nutritional loss of the food, as quality factors have a similar temperature dependence to that of many nutrients (Lund, 1988).

Risk in Context of Exploration Mission Operational Scenarios

Safety

As long as the use of HACCP (including the strict use of good manufacturing practices, standard operating procedures, and testing of processed foods) continues for packaged flight food approval, food-borne illness events should be prevented during missions. There is always a small risk of food-borne illness during flight. Once NASA builds the lunar habitat to use as a test bed for Mars missions and travels to Mars, the source of food for the crew may not be limited to only packaged food, so the risk of food-borne illness will increase.

During surface preparation of fresh food, safety is no longer ensured as it is through ground operations. Consideration must therefore be given to food safety from microbial, chemical, and physical sources during

food processing and preparation on the surface to prevent adverse effects on crew health and performance. If fresh fruits and vegetables are consumed without a heat step (cooking), there is a potential for food contamination and, hence, food-borne illness. There may be a need to wash or sanitize the fresh fruits and vegetables. The risk still needs to be quantified for a closed environment, especially in light of the fact that from 1991 to 2002, there were several produce-related *Escherichia coli* O157:H7 outbreaks reported for field-grown produce (Aruscavage et al., 2006).

If the prepackaged food or bulk ingredients are prepositioned on the Mars surface, there is a risk that the food will have been compromised prior to the arrival of the crews. Packaging can be torn or the food may be adversely affected by the martian environment.

Fresh food and bulk ingredients processing and subsequent preparation of meals from edible ingredients and packaged foods during the long-duration lunar and Mars missions will provide the crew with more variety and fresh foods. However, during these processes, it is necessary to reach a certain temperature/time combination to ensure safety and functionality. It is being proposed by mission designers that the lunar habitat will maintain an 8-psi atmospheric pressure. Heat and mass transfer are affected by partial gravity and reduced atmospheric pressure. At an 8-psi pressure, the boiling temperature for water is 181°F. Consideration must therefore be given to changes in the environment and the required processing equipment and procedures to ensure safe food processing on the lunar surface.

It is critical to quantify and reduce the risk of food preparation and processing safety before sending out human crews on a long-duration lunar mission. This risk could delay a long-duration lunar mission even if all other elements of the mission are ready. Mission loss or major impact to post-mission crew health would likely occur if this risk is not quantified and reduced.

Nutrition

Although it is common for crew members to lose weight during ISS missions, the crew members have still been able to perform their duties. The degree of weight loss for the 6-month lunar missions is assumed to be similar to that for the ISS missions. However, for the Mars missions, the food will need to have a shelf-life of about 5 years (as opposed to 18 months for ISS missions) to accommodate the 1,000-day Mars mission. The packaging will also have to maintain its physical and chemical barrier properties for 5 years. Any pre-positioning of the food or delay in the consumption of the food will potentially decrease the nutritional content of the food even more. With no resupply options, it is critical to quantify and potentially reduce the risk of inadequate nutritional content of the food prior to a Mars mission. Once the crew members begin their mission, they will have no opportunity to mitigate a loss of nutrition with resupplied foods or supplements.

The lunar short-duration missions may require that each crew member perform 8-hour EVAs every other day. If the crew members cannot access adequate nutrition during the EVAs, the risk of loss of performance can increase.

Unique to space travel are nutrient losses due to space radiation. Although the extent of loss is unknown, one flight study is currently examining the nutritional loss of five food items that were stored on board the ISS for about 2 years. Ground controls are also being analyzed to help determine the effect of radiation. There is also a potential risk of nutritional loss of the chamber-grown fresh fruits and vegetables and the bulk ingredients that may be launched for use in food processing and preparation during surface missions.

The use of bulk ingredients and fresh fruits and vegetables on the lunar and martian surfaces can provide the crew with a variety of fresh foods and associated nutrients. These fresh foods should provide at least some of the vitamins that may be lost over time in the processed foods, thereby enhancing the nutritional intake of the crew members and their associated health and well-being while reducing the risk. While the processing of bulk ingredients and preparation of edible ingredients and fresh vegetables into meals can provide some of the lost nutrients, any failure in the growth, processing, and preparation of the foods could increase the risk of loss of nutrition. The overall risk of this type of food system has not been quantified yet.

Acceptability

Although the acceptability of the food, including its variety and usability, is important in the 6-month ISS and lunar missions, it will be critical in the 1,000-day Mars missions. For the Mars missions, as the acceptability of the food system must be ensured for 5 years, enough variety and ease of use must be provided to ensure that the crew consumes adequate quantities throughout the period. With the addition of food processing and preparation during surface missions, there is an increased risk that the additional crew time that will be involved will counter-act the increased acceptability of the overall food system. This risk could delay a Mars mission even if all other elements of the mission are ready. Mission loss or major impact to post-mission crew health would likely occur if this risk is not quantified and reduced.

The addition of freshly grown fruits and vegetables may increase the acceptability of the lunar and Mars mission food systems. These fresh foods would increase the acceptability of the food system by introducing bright colors, crunchy textures, and fresh aromas, thus encouraging more caloric intake and boosting crew morale by creating a more familiar food system in a hostile and unfamiliar environment.

Resource utilization

The Orion food system is being challenged to reduce the mass due to the smaller Orion vehicle. The high volumes of packaging material that will be required to keep food safe, nutritious, and acceptable as well as the power and weight requirements for heating the water and food will need to be minimized to meet the mass requirements. The challenge will be to bring the mass from its current level of 4 lbs. per crew member per day to 2.5 lbs. per crew member per day; that is, to the mass of the Apollo food system. It is not obvious that this goal is attainable; moreover, as noted previously, the Apollo crews were not provided with adequate calories. The variety of foods provided is also at risk because the galley equipment (e.g., hot water and the food warmer) may be removed from the Orion manifest. Without food mass reduction, other systems may not be able to launch their required equipment.

There is a further risk that radiation or simply age may affect the functionality of the bulk ingredients that are launched for food processing during a Mars mission. For example, the soybean proteins may chemically change, resulting in a reduced yield in the production of tofu.

As resupply will not be an option for Mars missions, it is especially critical that the food system be robust in its use of resources for 3 to 5 years. This includes the packaged food system and the bioregenerative food system. There is a danger that the packaged food system may be too high in mass. There is also a risk that acceptable food may not grow on Mars or the moon, given the reduced gravity, available water, radiation, and other aspects of the growing environment. Moreover, the equipment may not work or the water quantities may be inadequate for food hydration, processing, or preparation. Finally, there is the risk that the bioregenerative food system could require too much crew time, or that there will be too much food and packaging waste during a Mars mission.

It is worth repeating that any of these constraints on the system could delay a Mars mission, even if all other elements of the mission are ready. The risks increase with the increased length of the Mars mission; longer-term effects of radiation, especially during transit; and the lack of resupply.

Conclusion

It is a possible that on a lunar or Mars mission crew health and performance will be compromised without an adequate food system. In developing future NASA food systems, a balance must be maintained between the use of resources (e.g., power, mass, and crew time) and the safety, nutrition, and acceptability of the food system to provide an adequate food system. Each of the four components – safety, nutrition, acceptability, and resource utilization –may take on different priorities based on mission duration and distance from the Earth. The incorporation of fresh foods and/or food processing and food preparation during long-duration missions may increase the risk in safety and resource utilization, but it may decrease the risk of inadequate nutrition and acceptability.

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Chapter 13:
Risk of Adverse Health Effects from Lunar Dust Exposure

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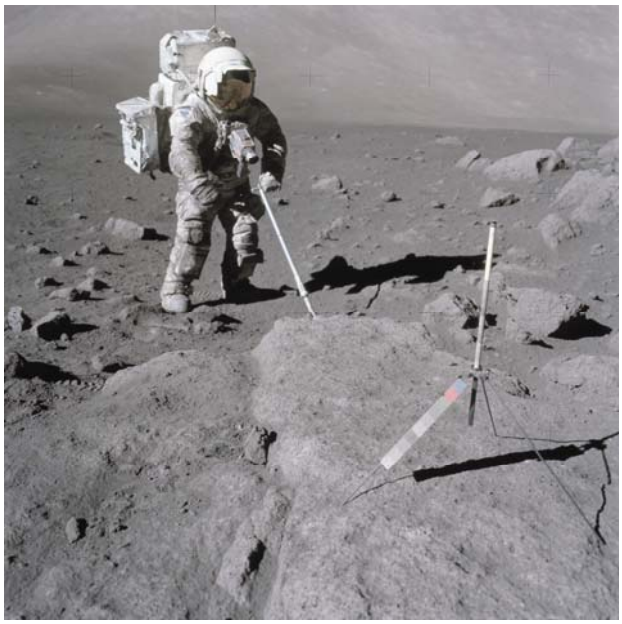
The toxicological effects of lunar dusts have not been studied in sufficient depth to develop an exposure standard for operations on the lunar surface. Lunar dusts have a high content in the respirable size range, they have a high surface area that is chemically reactive, and elemental iron "nano-particles" are imbedded in the dust grains. These unusual properties may cause the respirable dusts to be at least moderately toxic to the respiratory system, and larger grains to be abrasive to the skin & eye. NASA needs to set an airborne exposure standard based on scientific evidence so that vehicle designs can effectively control exposure. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.



During an Apollo 17 EVA, lunar dust is obviously seen to cling to astronaut Harrison Schmitt while he uses an adjustable sampling scoop to retrieve lunar samples. Efforts to understand the properties of lunar dust and to prevent its introduction into vehicles and habitats will minimize the risk of inhalation, dermal, and ocular injuries on future lunar missions.

Executive Summary

The respirable fraction of lunar dusts may be toxic to humans. NASA has therefore determined that an exposure standard is necessary to limit the amount of respirable airborne lunar dusts to which astronauts will be exposed. The nominal toxicity that is expected from ordinary mineral dust may be increased for lunar dust due to the large and chemically reactive surfaces of the dust grains. Human exposures to mineral dusts during industrial operations and from volcanic eruptions give researchers some sense of the relative toxicity of lunar dust, although the Earth-based analogs have serious limitations. Animal and cellular studies provide further evidence that mineral dusts can be somewhat toxic. Earth-based research of mineral dust has shown that freshly fractured surfaces are chemically reactive and can elicit an increased toxic response. Since lunar dust is formed in space vacuum from highly energetic processes, we expect the grain surfaces to be reactive indefinitely on the lunar surface. We predict that this chemical reactivity will change once the dust is brought into a habitable environment.

Dust from lunar soil that was carried into spacecraft during the Apollo missions proved to be a nuisance. The lack of gravity, or the existence of gravity at a small fraction of the gravitational force of the Earth, increases the time during which dust remains airborne, thereby increasing the probability that these dust particles will be inhaled. Lunar dust particles that are generated by impaction in a deep vacuum have complex shapes and highly reactive surfaces that are coated with a thin layer of vapor-deposited mineral phase. Airborne mineral dust in a variety of forms has been shown to present a serious health hazard to ground-based workers. The health hazards that are associated with volcanic ash, which is a commonly used analog of lunar dust, have not been reported to be especially serious; however, this type of ash quickly loses its reactive surfaces and is often aggregated into particles that are not readily respirable into the deep lung. Crew members who will be at a lunar outpost can be directly exposed to lunar dust in several ways. After crew members perform spacewalks or EVAs, they will introduce into the habitat a large quantity of dust that will have collected on spacesuits and boots. Cleaning of the suits between EVAs and changing of the Environmental Control Life Support System filters are other operations that could result in direct exposure to lunar dusts. In addition, if the final spacesuit design is based on the current spacesuit design, EVAs may cause dermal injuries, and the introduction of lunar dusts into the suits' interior, which may enhance skin abrasions. When the crew leaves the lunar surface and returns to microgravity, the dust that is introduced into the crew return vehicle will "float," thus increasing the opportunity for ocular and respiratory injury.

Introduction

In 2004, President George W. Bush unveiled a plan directing NASA to return humans to the moon by the year 2015, and to use the lunar outpost as a stepping-stone for future human trips to Mars and beyond. To meet this objective, NASA will build an outpost on the lunar surface near the south pole for long-duration human habitation and research. Because of the various activities that will require the astronauts to go in and out of this habitat on numerous spacewalks (EVAs), the living quarters at the lunar outpost are expected to be contaminated by lunar dust.

The president's *Vision for Space Exploration* and charge to return to the moon have resulted in questions about health hazards from exposure to lunar dust. Lunar dust resides in near-vacuum conditions, so the grain surfaces are covered in "unsatisfied" chemical bonds, thus making them very reactive (Taylor and James, 2006). When the reactive dust is inhaled, it can be expected to react with lung surfactant and pulmonary cells. The fine, respirable lunar dust could thus be toxic if the astronauts are exposed to it during mission operations at a lunar base. Although a few early attempts were made to understand the toxicity of the lunar dust that was obtained by the

Apollo astronauts or the Luna probes, no scientifically defensible toxicological studies have been performed on authentic lunar dust.

Awareness of the toxicity of terrestrial dusts has increased greatly since the original Apollo flights, which occurred circa 1970, in which the crew members were exposed to lunar dust for a relatively brief time. The first National Ambient Air Quality Standard (NAAQS) was issued by the Environmental Protection Agency (EPA) in 1971 and was indexed to total suspended particles (TSP) on a mass per unit volume basis. In 1987, this NAAQS was refined to include only particles that were of less than 10 μm in aerodynamic diameter (PM_{10}) because this was the size that was most likely to reach the bronchial tree and deeper into the lung. Finally, in 1997, the EPA Administrator issued standards for particles that were less than 2.5 μm in aerodynamic diameter ($PM_{2.5}$) based primarily on epidemiological associations of increased mortality, exacerbation of asthma, and increased hospital admissions for cardiopulmonary symptoms. None of these standards specified the composition of the particles. In fact, the last standard was a bit contentious because mechanisms of toxic action were not understood (NRC, 1998).

In a review article, Schlesinger et al. (2006) list the properties of particulate matter that might elicit adverse effects. The properties that seem pertinent to lunar dust include: size distribution, mass concentration, particle surface area, number concentration, acidity, particle surface chemistry, particle reactivity, metal content, water solubility, and geometric form. In attempting to consider each of these properties, one property emerges as the most difficult to study; particle surface chemistry may be difficult to understand because the environment on the lunar surface is unlike any on Earth, and is likely to alter the surface of dust grains in a way that will render them highly reactive. Recreating the processes that could affect grain surface reactivity on the moon is not easy to do in an Earth-bound laboratory. Although this problem will be discussed in detail later, we note here that freshly fractured quartz is distinctly more toxic to the rat respiratory system than aged quartz (Vallyathan et al., 1995). Our point is not that quartz and lunar dust may have similar toxic properties, but that breaking of surface bonds on mineral substrates has been shown to increase the toxicity of the well-studied mineral quartz.

The site at which various sizes of particles are deposited is critical to an understanding of any aspect of their toxic action. The fractional regional deposition of particles shows that between 10 and 1 μm, the portion of particles that is deposited in the upper airways falls off from 80% to 20%, whereas the pulmonary deposition increases from near zero to about 20%. Pulmonary deposition, after falling off near 1 μm, peaks again near 40% for particles of 0.03 μm, whereas upper airway deposition remains low until a new peak deposition is found at less than 0.01 μm. The portion and pattern of deposition can be modified under conditions of reduced gravity; however, human data during flights of the gravity research aircraft show that particles in the 0.5 to 1 μm range are deposited less in the respiratory system at lunar gravity than at Earth gravity. This finding is consistent with the reduced sedimentation of the particles when the gravity is less. However, a larger portion of the particles is deposited peripherally in reduced gravity (Darquenne and Prisk, 2008).

The first encounter in which a particle deposits in the distal airways occurs with the bronchoalveolar lining fluid (BALF). The thickness of this fluid in the lung varies as the alveolar sacs expand and contract, but lies in the range of 0.1 to 0.9 μm (Bastacky et al., 1995). In the case of biological particles such as bacteria, this fluid opsonizes the particles to facilitate ingestion by macrophages. A similar process has been demonstrated for non-biological carbonaceous particles (Kendall et al., 2004). This process removes some components of the BALF that participate in opsonization, and it is postulated that this might enhance the toxicity of particles with a surface chemistry that is capable of selectively removing opsonizing components. The agglomeration of the grains is also affected by the interactions between the BALF and the grains. Preliminary data on authentic lunar dust

has shown that in aqueous suspension, lunar particles agglomerate rapidly. Artificial surfactant has been found to greatly reduce this particulate agglomeration.

Particles that are deposited in the pulmonary region are eliminated according to their surface area and chemical composition. If a particle is relatively soluble, its dissolution products end up in the bloodstream. Relatively insoluble particles are ingested by macrophages and removed by mucociliary clearance or the lymphatic system, or they persist in the interstitial areas of the lung. Ultrafine particles (<0.1 μm) that deposit in the upper airways have been shown, under some conditions, to translocate to the brain (Oberdörster et al., 2004), whereas similar particles reaching the pulmonary regions can translocate to adjacent organs such as the liver (Oberdörster et al., 2002).

The effects of particles on the respiratory system include *de novo* causation of clinical disease as well as exacerbation of existing disease. If particulate inhalation is to directly cause disease, the exposure levels typically must be at levels that are encountered in industrial settings. For example, silicosis is a well-known disease of persons working for years in conditions in which dust containing quartz is inhaled. Epidemiological studies show that ambient dust levels such as those that are encountered in some cities can exacerbate respiratory conditions such as asthma and chronic obstructive pulmonary disease. At certain times, sand dust that originates in Asia or Arizona, for example, has been associated with exacerbation of allergenic respiratory inflammation (Ichinose et al., 2008).

Of particular concern in addition to the respiratory system is the ability of small particles to affect the cardiovascular system. Epidemiological studies suggest that exposure to ambient particulate matter increases the incidence of angina, arrhythmia, and myocardial infarctions. The increased acute mortality that is associated with particle "events" is attributed to cardiovascular disease (NRC, 2004). Clinical studies involving concentrated ambient air particulate have shown increased blood fibrinogen and reduced heart-rate variability (Devlin et al., 2003); exposure to ultrafine particles causes "blunted" repolarization response following exercise (Frampton et al., 2002). The role of C-reactive protein in mediating the effect of ambient particle exposures on the causation of CAD has been reviewed (Sandu et al., 2005). Batalha (2002) has drawn attention to the ability of particles to elicit vasoconstriction of small pulmonary arteries. Although the mechanistic details have not been fully elucidated, the evidence favors a strong link between exposure to particulates and to both acute and chronic heart disease (NRC, 2004). There is some evidence from the Apollo missions that, in susceptible individuals, lunar dust exposure may lead to cardiovascular effects that are similar to those produced through exposure to air pollution (Rowe, 2000).

The fact that no accepted health standards or policies exist concerning exposure limits to lunar dust is a critical challenge to the design of vehicle systems in the CxP. The multi-center Lunar Airborne Dust Toxicology Assessment Group (LADTAG) was formed and responded to a request from the Office of the Chief Health and Medical Officer to "… develop recommendations for defining risk criteria for human lunar dust exposure and a plan for the subsequent development of a lunar dust permissible exposure limit." The LADTAG is comprised of technical experts in lunar geology, inhalation toxicology, biomedicine, cellular chemistry, and biology from within the agency as well as of leading U.S. experts in these fields. Based on the opinions that were expressed by the LADTAG experts, NASA scientists will develop and execute a plan to build a database on which a defensible exposure standard can be set (Khan-Mayberry, 2008).

LADTAG experts recommend that the toxicity of lunar dust on the lungs (pulmonary toxicity), eyes (ocular toxicity), and skin (dermal toxicity) be investigated, and that this investigation is to be conducted by the Lunar Dust Toxicity Research Project (LDTRP) using various assays including in vivo and in vitro methods. In an initial

LADTAG workshop that was held in 2005, experts noted that they were unable to reconcile individual expert opinions to set an inhalation standard. The array of opinions from these experts spanned a 300-fold range (i.e., 0.01 to 3 mg/m^3). The members of the LADTAG concluded that research is necessary to narrow this wide uncertainty range, the lower end of which cannot be met by known methods of environmental control, and that there is an urgency to determine the standard so that environmental systems for the lunar vehicle can be appropriately designed. Therefore, in keeping with the LADTAG experts' recommendations, members of the LDTRP have reviewed first-hand accounts of Apollo astronauts who were exposed to lunar dust during their missions as well as of terrestrial-based human exposures to dust generated in the mining industry and to volcanic ash. In accordance with the LADTAG recommendations to increase our evidence base, the LDTRP is conducting studies of Apollo spacesuits, filters, vacuum bags, and rock-collection boxes. These studies will enable us to focus our understanding of the grain-size distribution that is present in the lunar surface samples and in the habitat, but the dust surfaces are expected to be fully passivated.

Evidence

Ground-based evidence

Ground-based evidence includes data that are derived from people who are exposed occupationally to mineral dusts in industrial settings, from people who live in close proximity to active volcanoes and have been exposed to volcanic ash, and from animals and cells that are in controlled experimental studies. Mechanistic insights also guide our thinking concerning the potential toxicity of lunar dusts.

Evidence from Human Exposures During Industrial Operations

Workers in the mining industry are often exposed to dust from freshly fractured mineral deposits. When these workers use inadequate, or lack, respiratory protection completely, the consequences are devastating. A prime example of this is the Hawks Nest mining activity in West Virginia beginning in 1927. During the boring of a tunnel, deposits of silica were identified and mined; however, the workers did not use respiratory protection during the operations. Estimates of the proportion of workers who died, often within a few years, are typically about 30% of the 2,000 exposed workers (Cherniack, 1986). This rapidly lethal form of silicosis has been called "acute silicosis," which is characterized by alveolar proteinosis and interstitial inflammation (Driscol and Guthrie, 1997). The respiratory effects are not exactly like those one would expect from simple silicosis, a disease that usually requires decades to develop after prolonged exposure to lower concentrations of silica dust. The latter disease is characterized by silicotic nodules that are clearly distinct from surrounding tissue and often surrounded by an inflammatory response (Driscol and Guthrie, 1997).

Evidence from Humans and Laboratory Animals Exposed to Volcanic Ash

Volcanic ash originates from processes resulting in explosive eruptions into the atmosphere or pyroclastic flows oozing from the surface and discharging ash as they cool, or some combination thereof. Under any plausible condition, the ash will have had hours to days to react with the oxygen and water vapor of the atmosphere to passivate all surfaces before being inhaled by humans. The mineral composition of ash is determined by the composition of the magma. The particle size, mineral composition, and form of the minerals vary considerably from volcano to volcano as well as from one eruption to another eruption of the same volcano.

Shortly after Mount St. Helens erupted in 1980, a number of experts began to investigate the effects of volcanic ash on those who had been exposed to the dust (Bernstein et al., 1986). The crystalline silica content of this dust ranged from 3% to 7%. The primary acute effects were reflected in increased emergency room visits for asthma, bronchitis, and eye discomfort (Baxter et al., 1981). The ash was noted to exacerbate chronic

respiratory conditions. The increase in hospital admissions lasted approximately 3 weeks (Nania and Bruya, 1982), and immune parameters were affected even 1 year later (Olenchock et al., 1983). The British West Indian Montserrat volcano began erupting in 1995, causing an ash fall from pyroclastic flows that contained 10% to 24% crystalline silica (Baxter et al., 1999). Recorded incidences of childhood wheezing increased as a result of relatively intense exposures to the ash (Forbes et al., 2003). To our knowledge, sustained long-term health effects have not been reported in association with exposures to volcanic ash, although there is speculation that the high cristobalite content of the Montserrat ash could lead to silicosis many years later.

Animal studies that focused on the biological effects of chronic inhalation exposure to Mount St. Helens volcanic ash or quartz, under controlled laboratory conditions, indicate significant dose-response to both materials (Wehner et al., 1986). The quartz that came from the volcano was found to be markedly toxic and fibrogenic; by contrast, the volcanic ash was much less toxic (Martin et al., 1984; 1986). Similar results were noted in other animal studies (Wiester et al., 1985; Raub et al., 1985; Beck et al., 1981), suggesting that quartz is a much more potent pulmonary toxicant than volcanic ash (Martin et al., 1986; Raub et al., 1985; Beck et al., 1981). However, the presence of volcanic ash in the inhaled air did increase the "histamine sensitivity" of the epithelial irritant receptors (Wiester et al., 1985) as well as inhibit the ability of alveolar macrophages to protect against infection (Vallyathan et al., 1995).

The toxicity of volcanic ashes has been evaluated in rats that were dosed once by intratracheal instillation (Lam et al., 2002). Ashes that were obtained from the San Francisco volcano field in Arizona (lunar dust simulant) and from a Hawaiian volcano (martian dust simulant) were compared to the toxicity of titanium dioxide and quartz. Lungs of mice that have been harvested 90 days after receiving a dose of 1 mg of lunar simulant showed chronic inflammation, septal thickening, and some fibrosis. No changes were seen at the low dose of 0.1 mg/mouse (Lam et al., 2002). The martian dust simulant elicited a response that was similar to that of the lunar simulant, except that there was an inflammatory and fibrotic response even at a dose of 0.1 mg/mouse. The response of the mouse lungs to 0.1-mg quartz was comparable to the response to the martian dust simulant. In another study, the effect of these same simulants was assessed on human alveolar macrophages (Latch et al., 2008). The lunar dust simulant was comparable in cell viability reduction and apoptosis induction to the TiO_2 (titanium dioxide) negative control. Both were less toxic than the quartz positive control. Both simulants showed a dose-dependent increase in cytotoxicity.

Evidence that Surface Activation and Trace Impurities Increase Toxicity

Inhalation of freshly ground quartz, when compared to inhalation of aged quartz, results in a significant increase in animal lung injury (Lam et al., 2002; Shoemaker et al., 1995). Freshly ground quartz has increased reactive silicon-based oxygen radicals, and animals that are exposed to freshly ground quartz have been found to have decreased concentrations of antioxidant enzymes (Vallyathan et al., 1995; Dalal et al., 1990). Activated quartz particles decay with age in ambient air (Dalal et al., 1990). Quartz dusts containing surface iron as an impurity have been shown to deplete cellular glutathione, contributing to the oxidative damage that is caused by particle and cell-derived ROS (Fenoglio et al., 2003). Castranova et al. (1997) suggest that freshly ground quartz dust that is contaminated with trace levels of iron may be more pathogenic than quartz dust alone.

Crystalline silica exposure studies indicate that the generation of oxidants and nitric oxide, which play an important role in the initiation of silicosis (Castranova et al., 2002), has been shown to cause pulmonary inflammation in rats (Porter et al., 2002). Other studies indicate that the mode of action of crystalline silica cytotoxicity and pathogenicity lies in the ability of the mineral to induce lipid peroxidation (Vallyathan, 1994). Respiratory exposure to freshly ground silica causes greater generation of ROS from macrophages

than exposure to aged silica, which is one piece of evidence that proves that freshly fractured silica is more toxic than aged silica (Porter et al., 2002; Vallyathan et al., 1988).

Further evidence linking increased toxicity to surface activation must await data that show that lunar dust that is activated by methods other than grinding adversely affects cells. We have been able to demonstrate that dust that is activated by processes that are analogous to those that are understood to be present at the lunar surface (i.e., ultraviolet [UV] irradiation in a vacuum) are able to produce more ROS in aqueous solution than dust that is not activated by these processes (Wallace, unpublished data). In addition, mineral coupons that are activated by proton and alpha-particle bombardment that is analogous to the solar wind show increased ROS (Kuhlman, unpublished data). We expect to assess the impact of these activation techniques on cellular systems in early 2009.

Evidence from Mechanistic Understandings

As we know from lunar geologists (Category I[22] evidence) that iron is present in lunar dust, especially in the fraction of its smallest particles (nano-Fe), we can postulate that a reaction involving iron could be important for activated lunar dust when it comes in contact with the mucous lining of the respiratory system. A good model of the issues and problems that are associated with testing surface-activated dust can be found in the studies of freshly fractured silica, which is highly toxic to the respiratory system via oxidative damage, and perhaps also in the testing of volcanic ash. The problem of the enhancement of toxicity in quartz by freshly fractured surfaces has been extensively investigated in animal and cellular systems (Castranova, 2004; Porter et al., 2002; Ding et al., 1999; Vallyathan et al., 1991). Fracturing silica cleaves the Si-O bonds, leaving Si and SiO radicals, which, in turn, produce OH radicals in an aqueous environment. Aged crystalline silica still produces radicals, but at a much lower level, perhaps by the Fenton reaction that occurs between iron and H_2O_2 that is generated by macrophage phagocytosis of the particles (Castranova, 2004).

Passivation of Reactive Surfaces as Dust Surfaces Age

Since surface activation, which is produced primarily by grinding, is known to increase the toxicity of various mineral dusts, it is critical to ask how quickly surface activation disappears once the dust encounters an oxygen- and water-vapor-rich environment. Vallyathan et al. (1988) demonstrated a bimodal decay by measuring the rate of disappearance of hydroxyl radical formation in an aqueous medium from silicon-based radicals on the surface of ground silica, when that ground silica was kept in air until the time of assay. The half-life of the fast decay was approximately 30 hours, whereas even after 4 weeks approximately 20% of the original activity that was induced by grinding was present on the surface of the quartz. This is similar to the ability of the 24-hour half-life in air of freshly fractured quartz to produce OH radicals (Castranova, 2004). Although quartz is not lunar dust and grinding is merely a surrogate for activation of dust at the lunar surface, the longevity of the surface reactivity requires careful attention to better understand how surface-activated lunar dust becomes passivated in a habitable environment.

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[22]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

Space flight evidence

Samples of lunar dust that have been returned to Earth have enabled NASA to learn the mineralogical properties of the dust at several lunar landing sites. First and foremost, one must keep in mind that the properties of the lunar dust may vary considerably depending on location; hence, lunar dusts may show a range of toxicity. Initially, NASA assessed the expected nature of dust at the proposed South Pole landing site on the rim of Shackleton crater.

All space flight evidence pertaining to the effect of lunar dust on astronauts is anecdotal (Category III). The post-flight debriefing reports of the Apollo astronauts serve as a base of evidence (Portree and Trevino, 1997). Although the astronauts attempted to remove the lunar dust before they reentered the command module (CM) by brushing the spacesuits or vacuuming, a significant amount of dust was returned to the spacecraft, which caused various problems. For instance, astronaut Harrison Schmitt complained of "hay fever" effects caused by the dust (Portree and Trevino, 1997), and the abrasive nature of the material was found to cause problems with various joints and seals of the spacecraft and spacesuits (Wagner, 2006). In these reports, the Apollo crews provided several accounts of problems with lunar dust exposure as follows:

- During Apollo 11, crew members reported: "Particles covered everything and a stain remained even after our best attempts to brush it off"; a "[d]istinct pungent odor like gunpowder [was] noted when helmet [was] removed"; and "[t]exture like graphite" (Portree and Trevino, 1997).

- During Apollo 12, regarding dust in the lunar module (LM), the crew members noted several issues: "Both LM and CM contaminated with lunar dust"; "[LM] was filthy dirty and had so much dust that when I took my helmet off, I was almost blinded. Junk immediately got into my eyes"; and "[t]he whole thing was just a cloud of fine dust floating around in there." After the LM docked to the CM, dust infiltrated the CM. Crew members gave the following account of this period of contamination: "On the way back in the CM the system could not handle the dust, so it was continuously spread inside the spacecraft by the system"; "[w]e chose to remain in the suit loop as much as possible because of the dust and debris floating around"; and "[t]o keep our eyes from burning and our noses from inhaling these small particles, we left our helmet sitting on top of our heads" (Portree and Trevino, 1997).

- By contrast, the Apollo 14 crew members stated: "Dust was not a problem for us in the cabin"; and "[t]he dust control procedures were effective" (Portree and Trevino, 1997).

- The Apollo 15 crew members stated: "Cabin smelled like gunpowder when we first came into LM from EVA"; "[p]article matter floated around in spacecraft"; "[l]unar dust is 'soluble' in water"; and "[t]he vacuum cleaner did a good job of clearing the dust from the LM" (Portree and Trevino, 1997).

- Apollo 16 crew members provided the following accounts: "The LM was extremely clean until the first EVA and then it was extremely dirty"; "I question whether the vacuum cleaner ever worked properly"; and "I thought it was quite a hazard over there floating through the LM with all the dust and debris. A number of times I got my eyes full of dust and particles. I felt like my right eye was scratched slightly once" (Portree and Trevino, 1997).

- The Apollo 17 crew members recalled: "You knew [that] you were in a very heavily infiltrated atmosphere in the LM because of the lunar dust"; "[t]he dust clearing was remarkable considering the amount of dust we had"; "[a]lthough there was a lot of irritation to my sinuses and nostrils soon after taking the helmet off, by 2 hours that had decreased considerably"; "I did all the transfer with my helmet

> off and I am sorry I did because the dust really bothered my eyes and throat. I was tasting it and eating it"; and "[w]hen I climbed in the tunnel I could tell there was a lot of dust in the LM and you could smell it" (Portree and Trevino, 1997).

We also have the observations of a crew surgeon (Category IV), Dr. Bill Carpentier (Scheuring et al., 2007), detailing his own, as well as crew members', post-flight allergic-type responses. Dr. Carpentier recalls an increase in eosinophil and basophil blood cell counts after the crew members were exposed to lunar dust, which may have indicated an allergic response.

Although no substantive evidence exists that astronaut performance was impaired by lunar dust (Wagner, 2006), one can imagine that if a crew member were "almost blinded" and had to "remain in the suit loop as much as possible because of the dust and debris floating around," the dust did have some impact on performance.

Dust from the lunar soil that was carried into the spacecraft during the Apollo missions proved to be a significant, intermittent problem. With the return to the moon and planned long-duration stays on the lunar surface, the dust toxicity and contamination problems are potentially much more serious than those that were experienced during the Apollo missions. Physical evidence also suggests that lunar dust could be a health hazard at a lunar outpost. Gravity at one-sixth that of the gravitational force of the Earth increases the time in which dust remains airborne, thereby increasing the probability that these dust particles will be inhaled.

Some examples of lunar dust grains are provided in figure 13-1.

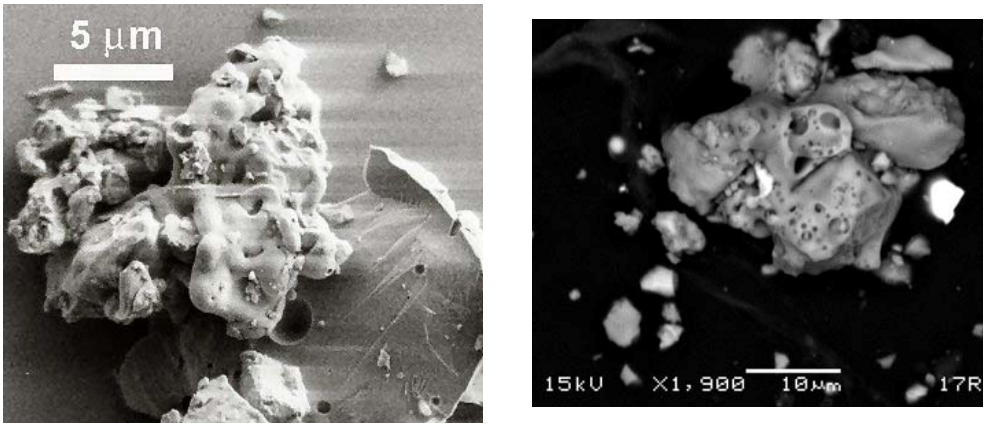

Figure 13-1. ***Examples of lunar dust grains.*** **– LEFT:** ***Scanning electron microscope (SEM) image of a typical lunar agglutinate. Note the sharp edges, reentrant surfaces, and microcraters. Smaller grains, which are less than 1 µm in diameter, are attached to this particle, and are also seen as loose grains in the upper portion of the image.*** **RIGHT:** ***SEM image of a lunar agglutinate fragment that was removed from the outer surface of Harrison Schmitt's EVA suit.***

Computer-based Simulation Information

This section is not applicable to this risk.

Risk in Context of Exploration Mission Operational Scenarios

Multiple, probable scenarios exist in which crew members could be exposed to lunar dust during both lunar sortie and lunar outpost missions. Further, there are opportunities for crew members to be directly exposed to lunar dust after they perform EVAs. Post EVA, lunar crew members will introduce into the habitat and lunar lander the dust that has collected on their spacesuits and boots. Cleaning of the suits between EVAs may also directly expose crew members to lunar dust. For crew members, changing of Environmental Control and Life Support System filters is yet another potential route of direct exposure to lunar dusts. These episodic periods of increased lunar dust exposure must be taken into account when long-term exposure limits are calculated. As missions become longer, the greater dose and/or duration of lunar dust exposure will increase the potential human health risk. When a crew returns to microgravity, if lunar dust is introduced into the crew return vehicle, there will be an increased opportunity for ocular exposure if particles of dust are floating throughout the cabin. EVAs cause dermal injuries when suits that are based on the current design are used, and the introduction of lunar dusts may enhance injuries that will be sustained from contact with the EVA suit. In addition, NASA is considering the use of a rover design that will allow shirtsleeve operation of the vehicle. Thus, the rover, which must be kept in an interior space to be entered without a spacesuit, may also bring dust into the habitat.

Conclusion

Our evidence base shows that prolonged exposure to respirable lunar dust could be detrimental to human health. Lunar dust is known to have a large surface area (i.e., it is porous), and a substantial portion is in the respirable range. The surface of the lunar dust particles is known to be chemically activated by processes ongoing at the surface of the moon. We predict that this reactivity will disappear on entry into the habitable volume; however, we do not know how quickly the passivation of chemical reactivity will occur, nor do we know how toxic the deactivated dust may prove to be. Although many Apollo astronauts seemed to tolerate lunar dust, their exposure times were brief and time (duration) exposure factors need to be determined. Other Apollo crew members and ground support personnel noted that the lunar dust was a sensory irritant. Finally, the size characteristics of the dust that actually was present in the atmosphere of the lunar lander have never been determined. Obtaining these data will help us understand the size distribution of the particles that are expected to be found in future lunar habitats. It is important to design experiments that will close or, at a minimum, narrow our knowledge gaps so that a scientifically defensible exposure standard can be set by NASA for protection of crew health.

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Exercise and Extravehicular Activity

Risk of Compromised EVA Performance and Crew Health Due to Inadequate EVA Suit Systems

Risk of Operational Impact of Prolonged Daily Required Exercise

Chapter 14: Risk of Compromised EVA Performance and Crew Health Due to Inadequate EVA Suit Systems

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Improperly designed EVA suits can result in the inability of the crew to perform as expected, and can cause mechanical and decompression injury. Suit developers must fully understand the impact of the suit design on crew performance and health to ensure properly designed mobility, pressures, nutrition, life support, etc. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

Although the Apollo EVA suits performed very well on the short missions for which they were designed, longer missions to the moon and Mars will require more robust suit designs. An integrated human testing program across multiple environments aims to correct or mitigate many of the problems with the Apollo EVA suits, thus maximizing human performance and efficiency while minimizing crew member health and safety risks on future missions.

Executive Summary

Constellation Program missions to the moon and Mars will include as many as 24 hours of EVA per crew member per week, which will involve the performance of exploration, science, construction, and maintenance tasks. The effectiveness and success of these missions is dependent on designing EVA systems and protocols that maximize human performance and efficiency while minimizing health and safety risks for crew members.

The Apollo EVA suits performed very well in the short-duration missions for which they were designed. However, the longer-duration missions, more frequent EVAs, and more varied EVA tasks that are anticipated during the CxP will require EVA suits and systems that are more robust than those used during the Apollo Program. Many of the problems that were encountered with the Apollo EVA suits (e.g., limited mobility and dexterity, high and aft center of gravity (CG), and other features requiring significant crew compensation) will need to be corrected or mitigated to optimize EVA objectives.

It is critical to understand the effects of EVA system design variables such as suit pressure, weight/mass, CG location, joint ranges of motion, and biomedical monitoring on the ability of astronauts to perform safe, efficient, and effective EVAs. To achieve this understanding, the EVA Physiology, Systems, and Performance (EPSP) Project is working with the CxP to develop and execute an integrated human testing program across multiple environments. This program will provide objective data that will enable informed design decisions, thereby ensuring a Constellation EVA system that optimizes crew member health, safety, efficiency, and performance.

This report describes the risks to crew health, safety, performance, and efficiency that an inadequate EVA suit system design would bring, and provides the evidence base to substantiate the importance of the risks.

Introduction

Fewer than 20 lunar EVAs were performed during the entire Apollo Program. Current architectures under consideration by the NASA Constellation Architecture Team-Lunar (CxAT-Lunar) could involve as many as 30,000 hours of lunar exploration EVA time. As demonstrated in figure 14-1, these plans represent an enormous increase in EVA hours in an extreme and challenging environment. No previous astronaut or spacesuit has performed more than three lunar EVAs, yet future astronauts and their EVA suits must be capable of performing as many as 76 lunar EVAs during a 6-month mission.

Providing the capability for humans to work productively and safely while performing an EVA involves many important, medically related considerations. Maintaining sufficient total pressure and oxygen partial pressure is vital not only to human health, but also to survival. Pre-breathe protocols must adequately reduce the amount of inert gas in astronauts' blood and tissues to prevent DCS (also known as "the bends") while minimizing the impact on crew efficiency. The EVA suit must be ventilated to remove expired carbon dioxide (CO_2), both perspired and respired water vapor, and metabolically generated heat. Since ventilation flow alone may not be sufficient to control core body temperature and prevent unwanted heat storage, cooling water is typically circulated through small tubes that are located in garments worn close to the skin. Heat influx also must be controlled, and the EVA crew member must be protected from harmful solar and other radiation. Nourishment and water must be available for ingestion, and accommodations must be provided for liquid and solid waste collection.

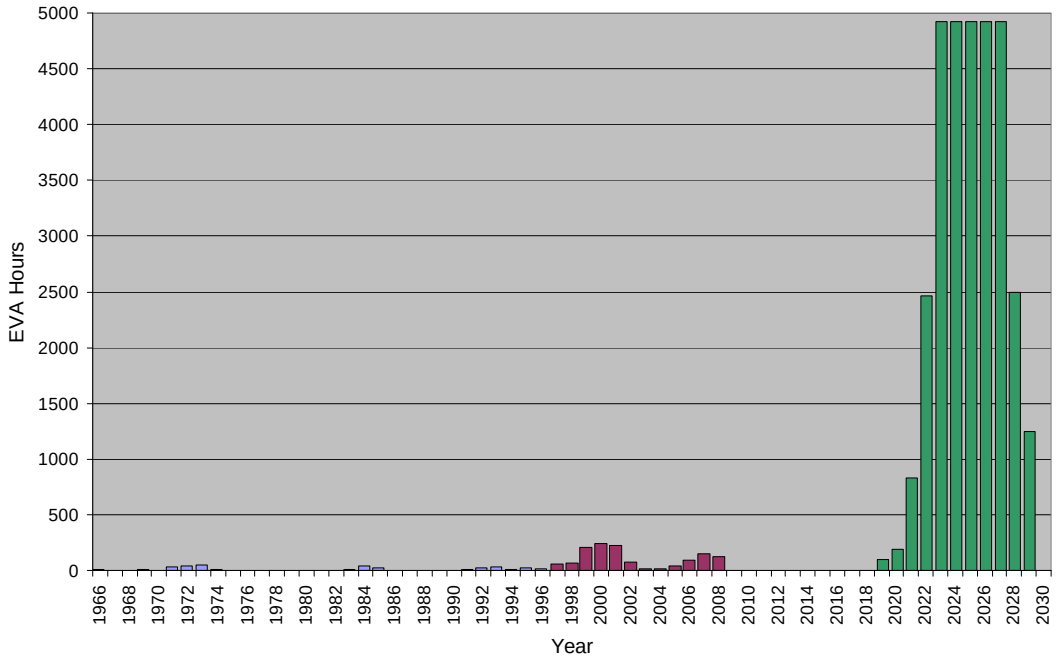

Figure 14-1. ***EVA estimates for current lunar architecture.***

Considerable evidence shows that the inadequate design of any aspect of an EVA suit system can have serious consequences. A large body of evidence in this area consists of astronaut first-hand experience and non-experimental observations (e.g., Category III and Category IV[23]). More recent evidence has been gathered in a rigorous, controlled manner in which subjects serve as their own controls from shirt-sleeved to suited conditions and across repeated measures trials in which a single parameter is varied (e.g., Category II). This report identifies and describes the various risks and associated evidence as follows:

- Risks to Crew Performance: EVA Suit Design Parameters
- Risks to Crew Performance, Health, and Safety: EVA Biomedical Monitoring and Consumables Management
- Risks to Crew Health: EVA Suit Design Parameters
- Risks to Crew Health: Decompression Sickness
- Risk to Work Efficiency: EVA Suit Design Parameters

[23]To help characterize the kind of evidence that is provided in each of the risk reports in this book, the authors were encouraged to label the evidence that they provided according to the "NASA Categories of Evidence."

- Category I data are based on at least one randomized controlled trial.
- Category II data are based on at least one controlled study without randomization, including cohort, case-controlled or subject operating as own control.
- Category III data are non-experimental observations or comparative, correlation and case, or case-series studies.
- Category IV data are expert committee reports or opinions of respected authorities that are based on clinical experiences, bench research, or "first principles."

Evidence

Risks to crew performance: extravehicular activity suit design parameters

Space Flight Evidence

Throughout the history of space flight, astronauts and cosmonauts have performed nearly 300 EVAs. However, only 14 of those EVAs have been conducted on the lunar surface in one-sixth gravity. Accordingly, the current understanding of suited human performance in partial-gravity environments is limited. A recent face-to-face summit with some of the Apollo astronauts provided valuable insight and yielded recommendations for the next-generation lunar EVA suit. Fourteen of the 22 surviving Apollo astronauts participated in the Apollo Medical Operations Project to identify Apollo operational issues that impacted crew health and performance. In the category of EVA Suit Operations using the shuttle/ISS EMU, recommendations centered on improving the functionality of the suit as well as improving human factors and safety features. The astronauts recommended increasing ambulatory and functional capability through increased suit flexibility, decreased suit mass, lower CG, and reduced internal pressure (Scheuring et al., 2007).

The following excerpt from Scheuring et al. (2007) describes the astronauts' view on the need for increased suit mobility: "EVA suit mobility was more of an issue in terms of surface locomotion and energy expenditure. The crews often felt they were fighting the resistance in the suit. This was fatiguing, especially in the thighs. The astronauts pointed out that the lunar surface is more similar to an ocean than a desert. The undulating surface posed a number of challenges, including ambulating against a suit that did not allow mobility at the hip. Normal human locomotion includes flexion at the hip and the Apollo A7LB {lunar surface EVA suit} had limited ability to bend the suit at the hip and to rotate within the suit. The crewmember had to bend forward from the knee joint, which demanded considerably more work load on the quadriceps muscles. Therefore, recommendations on mobility centered on adding hip mobility and improving knee flexibility. One comment summarized this point well, '*Bending the knee was difficult in the suit. We need a better [more flexible] knee joint*'."

The Apollo astronauts also strongly recommended improving glove flexibility, dexterity and fit. According to the crews, the most fatiguing part of surface EVA tasks was repetitive gripping. One crew member stated that "e*fficiency was no more than 10% of the use of the hand*" (Scheuring et al., 2007). The crew also sustained significant fingernail and hand trauma, as described in "Risks to crew health: EVA suit design parameters" below.

Ground-based Evidence

Physiologists and physicians are using various analog environments to study the effects of suit weight, mass, CG, pressure, biomechanics, and mobility on human performance. Test activities are designed to characterize performance during ambulation and exploration-type tasks such as ambulation on both level and inclined surfaces, ambulation while carrying a load, rock collecting, shoveling, and kneeling. Other studies examine recovering from a fall and simple exploration and construction tasks using hand tools and power tools. Data collected include metabolic rates, subject anthropometrics, time series motion capture, ground reaction forces (GRFs), subjective ratings of perceived exertion (RPEs) (Borg, 1982), and operator compensation using a relative subjective scale. The operator compensation scale, the gravity compensation and performance scale (GCPS), is modeled after the Cooper-Harper rating scale (Cooper and Harper, 1969) and is described in Appendix A.

The lunar analogs used include the Partial Gravity Simulator (Pogo) and Neutral Buoyancy Laboratory (NBL) at NASA JSC, parabolic flight, Desert Research and Technology Studies (D-RATS), the Haughton Mars Project (HMP), and NEEMO.

Results from early tests conducted on the Pogo have begun to characterize the metabolic cost, biomechanics, and subjective factors that are associated with ambulation and task performance in the Mark III Advanced Spacesuit Technology Demonstrator (MKIII), which is a prototype EVA suit that was designed for multi-axial mobility in planetary environments.

These tests have characterized the baseline metabolic cost of suited ambulation in lunar gravity across a wide variety of speeds, and have considered factors such as suit weight, inertial mass, suit pressure, and suit kinematic constraints and stability. Figure 14-2 shows the current understanding of how these factors contribute to the increased metabolic cost of suited ambulation in the MKIII suit (Gernhardt et al., in preparation (a)).

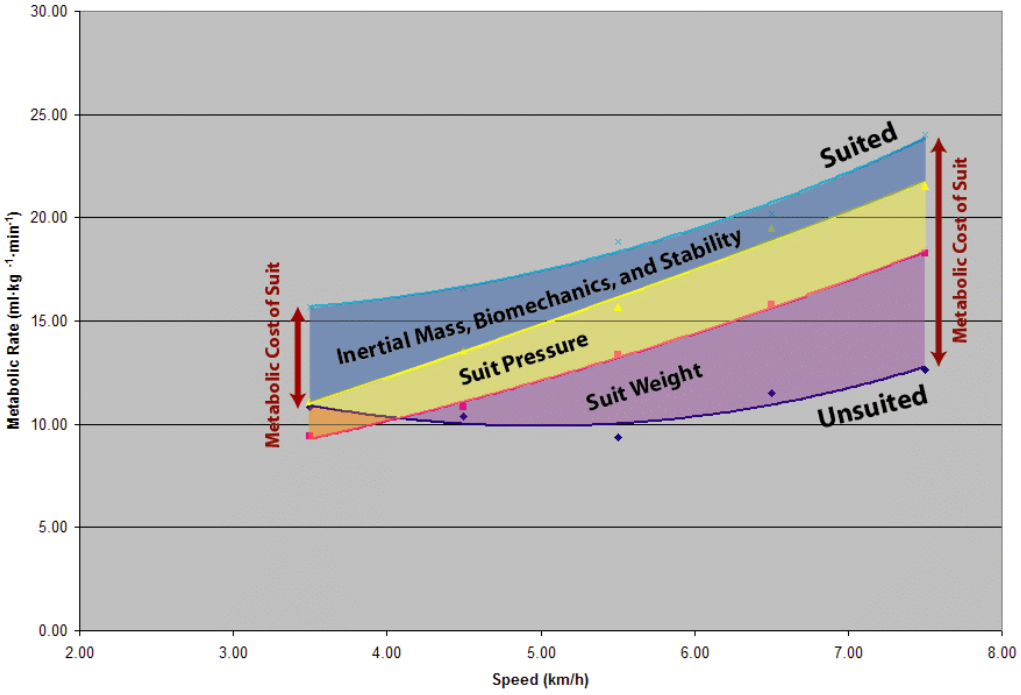

Figure 14-2. ***Suit design parameters that contribute to the metabolic cost of the suit.***

The parameter that has the largest impact on metabolic rate has been suit weight. Variations in suit pressure make little difference, but varying suit weight has led to significant differences in metabolic rate across speeds. Figure 14-3 shows how varying suit weight affects metabolic rate as a function of level ground ambulation speed (Gernhardt et al., in preparation (a)).

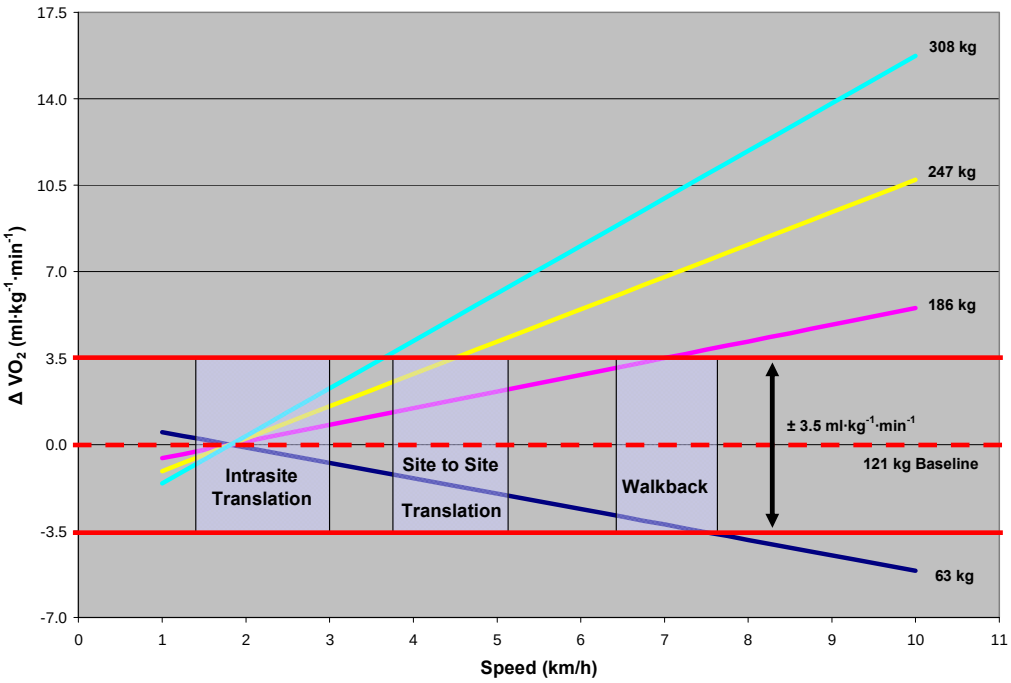

Figure 14-3. ***Effect of suit weight on metabolic rate across speed of ambulation.***

This is just one example of how lunar operational concepts will play a large role in determining requirements. If a crew member is only expected to walk slowly, the suit weight may not be a critical design parameter; but if a long (e.g., 10-km/6.2-mile) walkback contingency must be prepared for, the suit weight will be absolutely critical to mission success.

Based on the Pogo test results, a predictive equation for metabolic rate has been proposed that includes factors such as subject anthropometrics, locomotion speed, suit pressure, and suit weight. As more data are collected, this algorithm will be expanded into an EVA consumables calculator in which inputs on the subject, suit, and type and duration of tasks can predict a metabolic profile and the expected consumables usage. This algorithm is an example of a design tool that can help to develop suits that increase efficiency in crew health and performance based on different operational concepts.

In addition to ambulation, the effect of varying suit weight and pressure has been examined across a variety of exploration-type tasks, such as shoveling and picking up rocks. Figure 14-4 describes the metabolic rate and GCPS ratings for six subjects averaged over three different tasks (i.e., shoveling, picking up and moving rocks, and a construction task busy board) as a function of 1g-equivalent suit weight. Both the objective and the subjective ratings show the same trends, which surprisingly indicate that a heavier suit weight is associated with better performance. The GCPS quantifies the suit operator compensation that is required for optimal task performance, which is defined as being equivalent to 1g shirt-sleeved (i.e., unsuited) performance. Ratings of 1 to 3 indicate acceptable performance, 4 to 6 indicate that modifications are recommended for optimal performance, and 7 to 9 indicate that modifications are required; a rating of 10 indicates that the task cannot be performed under the current conditions. (See Appendix A for further explanation of the GCPS subjective assessment tool.)

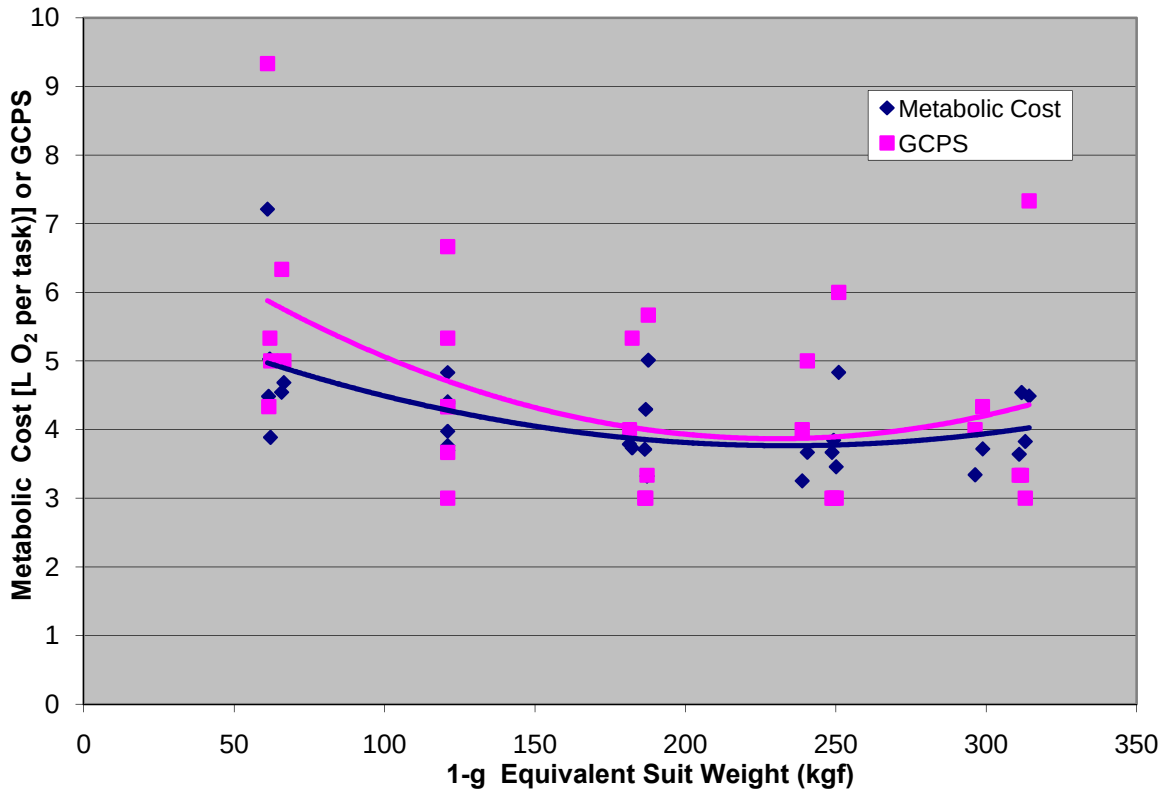

Figure 14-4. ***Effect of suit weight on metabolic rate and subjective GCPS ratings during exploration tasks*****.**

Biomechanical impacts of the suit are more difficult to differentiate; however, they may be critical to understanding skeletal muscle and bone loss in fractional gravity and for developing countermeasures against such losses. A key biomechanical finding relates to the GRF, which was higher in suited conditions than in unsuited conditions and also increased as suit weight increased. However, the GRFs were still lower than those that a crew member would normally experience on Earth. This suggests that EVA performance on the lunar surface may not provide sufficient loading to protect against bone loss, thus indicating the continued need for exercise countermeasures (Gernhardt et al., in preparation (a); in preparation (b)).

Recognizing that not all ambulation on the moon will be similar to that on a level treadmill, EPSP personnel have initiated studies to characterize the effects of incline and terrain on metabolic rate. Inclined walking trials have shown that the metabolic cost of the suit that is due to factors other than suit weight goes to almost zero, indicating an energy recovery component of the suit that is currently not well understood (Gernhardt et al., in preparation (c)).

Beyond the above stated parameters, the Apollo Program demonstrated that suit CG is an important variable that affects human performance. Recent studies have evaluated CG in the underwater environments at NEEMO and the NBL. These studies assessed crew performance of representative planetary exploration tasks using a single EVA suit weight with six different CG locations. A reconfigurable backpack that has repositionable weight modules was used to simulate perfect, low, forward, high, aft, and NASA baseline CG locations under the assumption of a 60-lb. suit, a 135-lb. Portable Life Support System (PLSS), and a reference 6-ft, 180-lb subject. Subjects used the GCPS rating tool to evaluate the CG locations. As shown in figure 14-5, subjects preferred (with lower GCPS score) the perfect, low, and forward CGs over the high, aft, or NASA baseline

(Crew and Thermal Systems Division (CTSD)) CGs (both high and aft, similar to the Apollo suit CG). These findings suggest that a conventional backpack PLSS may not be optimal and that alternative configurations should be considered (Jadwick et al., 2008).

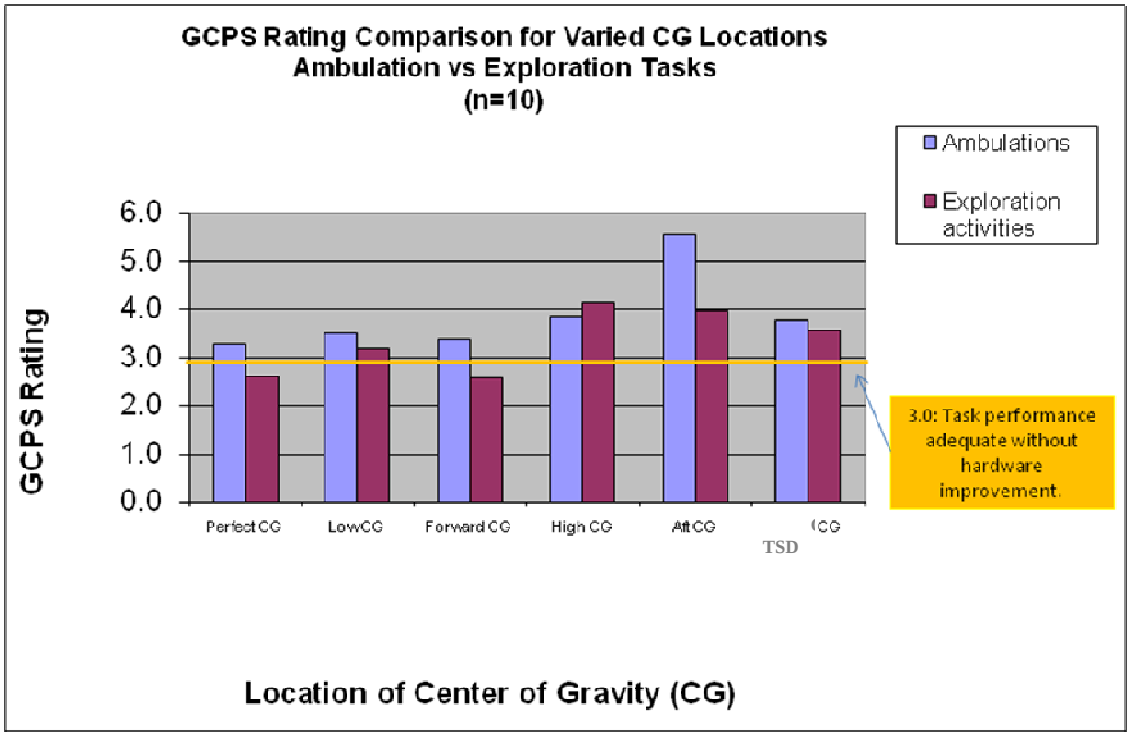

Figure 14-5. ***GCPS ratings for suit center of gravity.***

Risks to crew performance, health, and safety: extravehicular activity biomedical monitoring and consumables management

Overview

The physiologic cost of performing work in a pressure garment is significantly greater than that of performing the same work without a suit. High workloads result in energy expenditure and the production of heat, which, in turn, increase the usage rate of suit consumables. Accordingly, monitoring of crew physiologic parameters and consumables is critical. Flight surgeons must ensure that an astronaut is not working at levels that may lead to overheating or exhaustion, and EVA planners must be able to make real-time adjustments to crew activity to conserve consumables that are required for life support (Waligora and Horrigan, 1975; Waligora et al., 1975).

Space Flight Evidence

Energy expenditure (metabolic rate) was not measured during the Project Gemini EVAs. It was nonetheless clear that, in several cases, the astronauts worked at levels that were above the heat removal capability of the gas-cooled life support system (Waligora and Horrigan, 1975; Kelley et al., 1968). During the first U.S. EVA, astronaut Ed White found that opening and closing the hatch was much more difficult than planned and that he perspired enough to fog the helmet visor. Although the duration of the EVA was short, it took several hours for White to return to thermal equilibrium.

Thermal homeostasis of the crew member is crucial for safe and effective EVA performance. Heat storage above 480 Btu/hr leads to performance decrements, such as a loss of tracking skills and increased errors in judgment, and tissue damage begins at 800 Btu heat storage (Jones, 2007). The observations from the Gemini experience led to the development of a liquid cooling system that could accommodate high heat production in the suit from high EVA workloads. This liquid cooling garment (LCG) consists of a system of plastic cooling tubes that run along the inside of an undergarment that is worn inside the suit. The temperature of the coolant (water) running through the tubes regulates the amount of heat that is removed from the surface of the skin. The Apollo LCG had three temperature settings: minimum (69.8°F/21°C), intermediate (59°F/15°C), and maximum (44.6°F/7°C) (Waligora et al., 1975).

Astronaut energy expenditure rates during Apollo lunar surface EVAs ranged from 780 to 1,200 Btu/hr, as determined by three independent methods (Waligora et al., 1975). The lowest metabolic rates occurred while the astronauts drove and rode in the lunar rover vehicle, while the highest metabolic rates were observed during egress/ingress through the tight-fitting hatch of the lunar module, offloading and setup of equipment, drilling, and stowage of lunar samples. It is estimated that 60% to 80% of the heat that was generated with these workloads was dissipated through the LCG. The minimum and intermediate LCG settings were most commonly used; however, the maximum setting was frequently used during the high workload periods that were experienced during Apollo 15 and Apollo 17 EVAs (Waligora and Horrigan, 1975). In a simulation (figure 14-6) using a validated thermoregulatory model (41 Node Metabolic Man; Pisacane, et al., 2007), the relationship between heat storage and metabolic rate was examined as a function of LCG inlet temperature (tracings, showing 21°C (69.8°F) and 24°C(75.2°F)) (Kuznetz, 2004). These data suggest that at metabolic rates above ~1,200 Btu/hr, LCG inlet temperatures exceeding 21°C (69.8°F) may induce crew member heat storage rates above the 480 Btu/hr that lead to performance impairment. Although Apollo metabolic rates rarely exceeded 1,200 Btu/hr and the LCG inlet temperature minimal setting was 21°C (69.8°F), these data are instructive for the design of future lunar EVA suits, which may be used in situations in which crew metabolic rates exceed levels seen during Apollo.

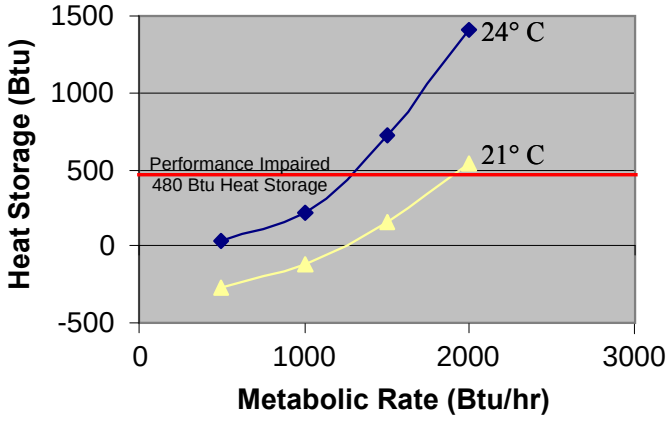

Figure 14-6. ***Heat storage based on metabolic rate and LCG inlet water temperature.***

It is important to note that although the metabolic rates experienced during the Apollo EVAs were lower than had been predicted before the missions, there were several cases in which the PLSS consumables were nearly depleted, according to the *Summary of Apollo G Mission Lunar Surface EMU Post Flight Thermal Analysis*

Results, Table E1 (MOD, unpublished internal report). During Apollo 14, Apollo 15, and Apollo 17, there were six cases in which less than 10% usable oxygen remained at the end of the EVAs. During Apollo 14, Apollo 16, and Apollo 17, there were seven cases in which 12% or less power remained (in one case, power was at < 4%), and four cases in which 11% or less usable feed water remained. Two crew members, on Apollo 15 and Apollo 16, completed their EVAs with only 4% and 2% remaining, respectively, of their CO_2 removal capability (lithium hydroxide (LiOH)).

Although each of the Apollo missions was limited to two or three EVAs, future lunar missions are expected to consist of three EVAs per week for up to 6 months. The increased number and frequency of exploration EVAs, coupled with labor-intensive construction and exploration tasks, will require a better understanding of energy requirements, heat dissipation technologies, and consumables management.

Nutrition, hydration, and waste management

The longer and work-intensive EVAs that are planned for future Exploration missions will also need to account for astronaut nutrition, hydration, and waste management. Specifically, dehydration is an issue that can lead to poor crew performance. The Apollo suit had a 15-oz drink bag; however, this amount of fluid is considered insufficient for crews that are performing surface EVA. Scheuring et al. (2007) provide several citations regarding the need for more water. As the authors write: "The astronauts strongly agreed the amount of liquid beverage contained in the suit needed to be increased for future crewmembers, including separate capabilities for plain water and non-caffeinated high-energy drink."

The delivery systems for nutrition and hydration need to be improved as well. One Apollo astronaut commented: "The fruit bar mounted inside the suit was sometimes problematic because you couldn't always get to it, but it's nice to have something solid to eat" (Scheuring et al., 2007). Similar issues have been reported with the current EVA suit, used for microgravity EVA in the Space Shuttle and ISS Programs. Furthermore, the time that is required to prepare the nutrition and hydration systems prior to conducting an EVA must be decreased. Filling and degassing the drink bag that is used in the current U.S. suit is time-consuming and contributes to the poor work efficiency index (WEI) of shuttle and ISS EVAs.

Additionally, the development of an improved in-suit urine collection device was recommended by the Apollo astronauts. In some cases during lunar surface EVAs, astronaut urine was not fully contained and resulted in skin irritation (Scheuring et al., 2007). Improved in-suit waste management systems will become critical in the event a crew is required to be suited for as many as 152 hours during a contingency return to Earth should the vehicle be unable to maintain pressure. Exposure to urine and fecal waste products for that length of time may lead to skin breakdown, cellulitis, and sepsis.

Biomedical monitoring

Flight surgeons and biomedical engineers (BMEs) in the Mission Control Center monitor astronaut physical parameters during EVAs to assess workload and performance. Real-time medical monitoring can provide emergency medical assistance in response to off-nominal situations. However, bioinstrumentation systems that were used in the Apollo Program and are being used in the Space Shuttle Program have been problematic. Scheuring et al. (2007) provide approximately 75 citations from the flight surgeon logs, BME logs, and medical mission debriefings that relate to issues associated with bioinstrumentation. These range from complaints of skin irritation due to the electrode paste to signal dropouts and sensor failure (Scheuring et al., 2007). Both Apollo and shuttle/ISS EVA crew members have expressed frustration with the cumbersome and time-consuming process of donning/doffing their biomedical sensor systems. Improvements to the biomedical sensor systems for future missions are therefore warranted.

Ground-based Evidence

At the request of the Constellation EVA Systems Project Office (formerly known as the Advanced EVA Office) management, a study was conducted to determine whether it is possible for a suited crew member to walk back to a terrestrial habitat in the event of a failed rover. As a starting point that is based on the Apollo Program and anticipated lunar surface operational concepts, it was assumed that 10 km (6.2 miles) would be the maximum EVA excursion distance from the lander or habitat. Results from this EVA Walkback Test (EWT) using the Pogo provide key insight into how human performance may be impaired by inadequate consumables and/or inadequate cooling.

For the EWT, six suited subjects were instructed to attempt to translate 10 km on a level treadmill at a rapid, but sustainable, pace using a self-selected gait strategy and speed. Prior to this test, the investigators expected that crew members could only complete half of that distance or that the total duration would exceed 3 hours. However, all of the crew members finished the test, and the mean time to complete 10 km was only 96 minutes. The metabolic work level for the entire test averaged 51% of VO_2pk [volume of oxygen consumption, peak], with a range of 45% to 61%. Physiological and consumables usage data are summarized in Table 14-1. RPEs (11.8 ± 1.57 (SD)) equated to a feeling between "light" (RPE=11) and "somewhat hard" (RPE=13) on the 6- to 20-point Borg RPE scale, which is used to gauge how much effort a person feels that he or she must exert to perform a task. Similarly, subjects averaged 3.5 ± 1.44 (SD) on the 10-point GCPS, indicating "fair" to "moderate" operator compensation was required to perform the task (Gernhardt et al., in preparation (b)).

Table 14-1. ***Summary Data for the Lunar 10-km Walkback Portion of the Test***

10k Walkback Summary Data (averaged across enter 10 km unless noted)		
	Mean	**SD**
Avg Walkback Velocity (mph)	3.9	0.5
Time to Complete 10 km (min)	95.8	13.0
Avg %VO_2pk	50.8%	0.3%
Avg Absolute VO_2 (1/min)	2.0	0.3
Avg Metabolic Rate (Btu/hr)	2,374.0	303.9
Max. 15-min-avg Metabolic Rate (Btu/hr)	2,617.2	314.6
Total Energy Expenditure (kcal)	944.2	70.5
Water used for drinking (oz)	~24–32	N/A
*Water used for cooling (lb.)	4.91	N/A
Oxygen Used (lb)	0.635	N/A
Planning/PLSS Sizing Data	**Walkback**	**Apollo**
Oxygen Usage (lb/hr)	0.4	0.15
Btu Average (Btu/hr)	2,374	932.8
Cooling Water (lb/hr)	3.1	0.98
Energy Expenditure (kcal/hr)	599	233

*Assumes thermally neutral case and sublimator cooling

Subjects' heat production rates ranged from 1,918 to 2,667 Btu/hour, and averaged 2,374 Btu/hour, a rate that would exceed the heat removal rates of the Apollo or space shuttle EVA suits. Core temperature measurements indicated an average rise (Δ) of 33.8°F/1°C from normal (98.6°F/37°C) across the entire test, although one subject's core temperature (103.6°F/39.8°C) peaked near a level of concern. Subjects unanimously reported cooling to be inadequate at the higher workloads (Gernhardt et al., in preparation (b)).

This limited cooling capacity will impede the improved efficiency that was observed at higher speeds. Efficiency of locomotion can be determined by the transport cost, which is expressed as oxygen consumption per kilogram per kilometer, and can be thought of as a human's "gas mileage." In suited conditions in lunar gravity, there was a clear trend of decreasing transport cost as speed increased. So while a crew member might expend more energy on a per-minute basis by traveling at faster speeds, the metabolic cost per kilometer would actually be less (Gernhardt et al., in preparation (b)).

Unfortunately, at speeds above 3 mph (figure 14-7) the heat production, which is shown on the right axis and the red tracing, begins to exceed the 2,000 Btu/hr cooling limit of both the Apollo and the shuttle EVA suits, resulting in increased core body heat storage. Without improvements in cooling for future suits, crew members performing lunar EVAs would not be able to exploit the increased efficiency (figure 14-7, on the blue tracing as decreasing oxygen transport cost) available at faster ambulation speeds. This would result in increased consumable requirements to cover the same distance (Gernhardt et al., in preparation (b)).

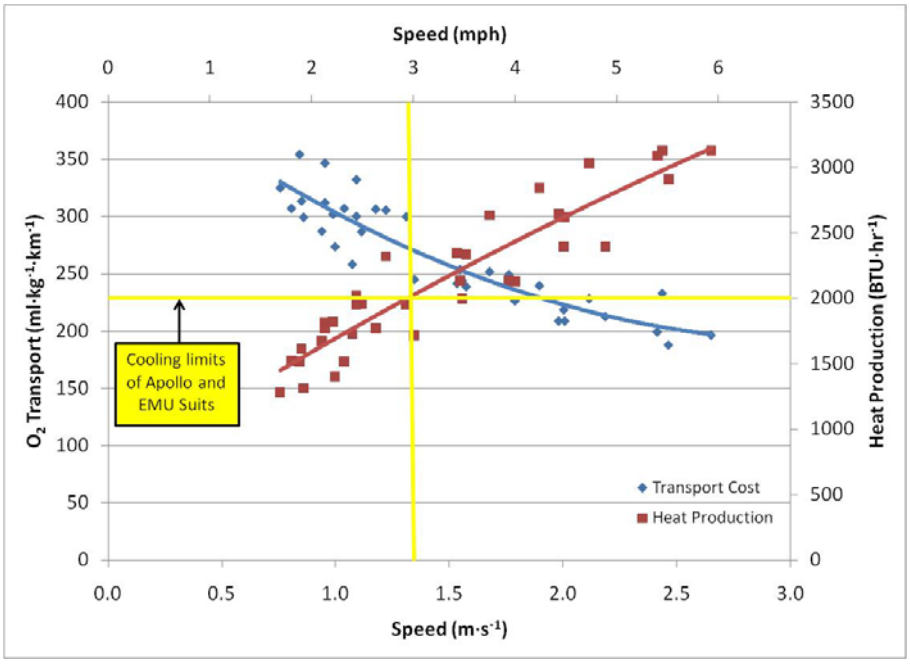

Figure 14-7. ***Relationship between transport cost and heat production for lunar suited ambulation.***

While life support consumables are an important consideration for EVA excursions, the 10-km Walkback also provided important insight into hydration and nutritional requirements for a task of similar duration or intensity. All subjects were provided with 32 oz of water in an in-suit drink bag, standard for use of the MKIII suit. Crew members consumed 50% to 100% of the water that was provided, and one crew member would have preferred to have an additional 20% of that volume available. In addition, the 10-km Walkback required an average of 944 kcal. All of the crew members felt that a nutritional item, either food (e.g., an energy bar or a gel) or a flavored electrolyte drink might improve their performance and/or endurance (Gernhardt et al., in preparation (b)). These observations were in accordance with the Apollo recommendations cited above.

Because the EWT was limited to 10 km on a level treadmill, additional studies were performed to understand how a more realistic simulation would affect the results. Factors such as incline/decline, lunar-like terrain, and real-time navigation will all contribute to the performance of a 10-km traverse. Results of these Pogo tests have indicated that inclined ambulation does increase metabolic rate, but at a rate that is much less than experienced in the 1g environment. To classify the effect of lunar terrain and navigation of human performance, subjects completed a series of 10-km traverses at the HMP site, which is an international interdisciplinary field research project centered on scientific study of the Haughton impact crater and surrounding terrain on Devon Island, Canada. The rocky polar desert setting and geologic features provide a good analog of the lunar surface for EVA translation and navigation studies. At HMP, unsuited subjects began at a location that was 10 km from the finish point and were instructed to return at a rapid, but sustainable, pace using a global positioning satellite (GPS) receiver for navigation and tracking speed and grade. Three separate starting points, each equidistant from the finish point, were defined, and the subjects completed each route once. The straight-line distance between starting and ending points was 9.91±0.22 km/6.16 ± 0.14 miles (mean ± SD), and the actual distance traveled was 10.61±0.61 km/6.59 ± 0.38 miles. Completion time averaged 126.5 ± 28.7 min, which was longer that the EWT average of 95.8 ± 13.0 min (Norcross et al., 2008).

Comparison between these field tests and speed/grade matched treadmill controls has provided a crude correction factor for terrain, suggesting that metabolic rates in the actual environment were an average of 56% higher than in controlled treadmill conditions. Further studies are needed to understand whether this increase would be as high in lunar gravity (Norcross et al., 2008).

Risks to crew health: extravehicular activity suit design parameters

Space Flight Evidence

A comprehensive analysis was recently completed of all musculoskeletal injuries and minor trauma sustained in flight throughout the U.S. space program (Scheuring et al., 2009). This study identified 219 in-flight injuries, of which 50 resulted from wearing the EVA suit, making this the second leading cause of in-flight injuries. The incidence rate of EVA injuries was 0.05 per hour for 1,087.8 hours of EVA activity. This equates to an incidence rate of 1.21 injuries per day, or 0.26 injuries per EVA. The following excerpts from this study are illustrative of the types of EVA-induced injury:

> "Hand injuries were most common among EVA crewmembers, often due to the increased force needed to move pressurized, stiff gloves or repetitive motion for task completion. Many astronauts described the gloves causing small blisters and pain across their metacarpophalangeal (MCP) joints. This could be due to dorsal displacement of the MCP joints against the glove in order to flex the fingers [Viegas et al., 2004]. While not mission impacting injuries, they can potentially distract an astronaut from important EVA tasks. Astronauts frequently develop onycholysis (separation of nail from nail bed) after Neutral Buoyancy Laboratory training sessions, and it is possible some of these injuries represent exacerbations of underlying ground-based injuries."

However, the authors later state that pre-flight conditions were not strong predisposing factors for these injuries.

> "Foot injuries also caused problems for EVA astronauts. One astronaut described an episode of 'excruciating, searing, knife-like pain' during an EVA. The astronaut attributed the pain to excess suit pressure bladder material inside the boot, but despite attempts at correcting the

> problem, the pain persisted with the development of a blister…Though the EVA was completed successfully, the astronaut described the pain from this injury as 'on the forefront of my mind'. Another astronaut had similar symptoms after his second EVA with resultant numbness and pain on the dorsum of his feet."

Pressure-associated erythema developed on the dorsal surfaces of each foot, and symptoms persisted throughout the mission and 2 to 3 weeks post-landing (Scheuring et al., 2009).

Nine of the 219 in-flight injuries were sustained by Apollo astronauts who were performing lunar surface EVAs. One Apollo astronaut suffered a wrist laceration from the suit wrist ring while working with drilling equipment, and another crew member sustained wrist soreness due to the suit sleeve rubbing repeatedly. One crew member injured his shoulder during a lunar EVA while attempting to complete multiple surface activities on a tight mission timeline. Unbeknownst to his flight surgeon, this crew member later took large doses of aspirin to relieve the pain. Many Apollo astronauts noted problems with their hands. One astronaut remarked: "EVA 1 was clearly the hardest … particularly in the hands. Our fingers were very sore." Another Apollo astronaut remarked that his hands were "very sore after each EVA"; while another astronaut stated that following the third lunar EVA, his MCP and proximal interphalangeal joints (knuckles) were so swollen and abraded from a poor-fitting glove and/or lack of inner liner or comfort glove that he is certain that a further EVA would have been very difficult if not impossible. Accordingly, it is no surprise that the Apollo astronauts were adamant that the glove flexibility, dexterity, and fit be improved (Scheuring et al., 2007).

Ground-based Evidence

To adequately prepare for mission EVAs, astronauts undergo extensive ground-based training at the NBL, which provides controlled neutral buoyancy operations to simulate the zero-g or weightless condition. Articles are configured to be neutrally buoyant by using a combination of weights and flotation devices so these articles seem to "hover" under water, thus enabling large, neutrally buoyant items to be easily manipulated much as they would be in orbit. The significant increase in EVA NBL training to support the construction and maintenance of the ISS led to an apparent increase in the incidence of symptoms and injuries experienced by crew members operating in the EVA suit.

A study that was conducted from July 2002 to January 2004 identified the frequency and incidence rates of symptoms by general body location and characterized the mechanisms of injury and effective countermeasures (Strauss, 2004). During this study, 86 astronaut-subjects were evaluated in the NBL during 770 suited test sessions. Symptoms were reported by the test subjects in 352, or 45.7%, of the sessions. Of these symptoms, 47% involved hands; 21% involved shoulders; 11% involved feet; 6% each involved arms, legs, and neck; and 3% involved the trunk. Hand symptoms were primarily fingernail delamination, which was thought to be secondary to excess moisture in the EVA gloves and axial loading of the fingertips (figure 14-8). There were also abrasions, contusions, and two cases of peripheral nerve impingements related to glove fit and hard point contact compressions. Shoulder symptoms were due to hard contact with suit components (figure 14-8) and strain mechanisms. Elbows were the most common area of pain or injury in the arms, as were knees in the legs. While most of the symptoms and injuries sustained during EVA training were "mild, self-limited, and controlled by available countermeasures," some "represented the potential for significant injury with short- and long-term consequences regarding astronaut health and interference with mission objectives." (Strauss, 2004)

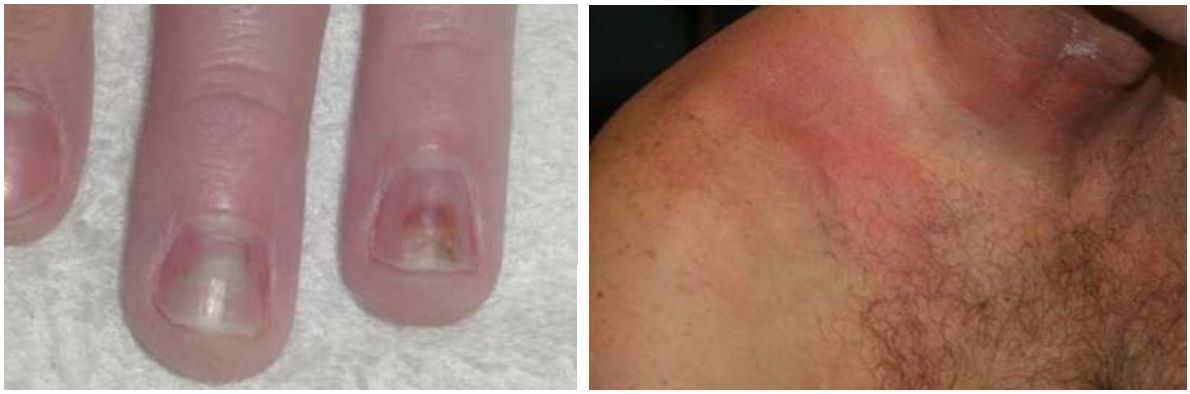

Figure 14-8. ***Fingernail and shoulder trauma sustained during EVA training*** **(Jones et al., 2006).**

A shoulder injury tiger team was created in December 2002 at NASA JSC to evaluate the possible relationship between shoulder injuries and EVA training at the NBL (Williams and Johnson, 2003). This team surveyed 22 astronauts who had participated in EVA training. In this group, 14 astronauts (64%) had experienced some degree of shoulder pain that they attributed to EVA training. A majority of these cases were classified as minor, resolving within 48 to 72 hours. However, two of the 14 subjects required surgical repair after injury. It was determined that the major risk factors leading to injury were: limited range of motion in the shoulder joint due to use of the "planar" hard upper torso (HUT) of the EVA suit, performing tasks in inverted body positions during NBL training, performance of overhead tasks, repetitive motions, the use of heavy tools, and frequent training sessions. Additional minor risk factors included suboptimal suit fit and lack of appropriate padding or load alleviation (Williams and Johnson, 2003; Jones et al., in review 2009). While the astronaut-tool-EMU simulation package may be neutrally buoyant as a whole, the astronaut is not weightless within the suit. In the inverted (head-down) position, gravity causes the astronaut to "fall into" the head of the spacesuit, pressing the shoulders into the HUT of the suit. This further limits the scapulothoracic motion of the shoulder (Viegas et al., 2004). Key elements in the risk mitigation of shoulder injuries that are associated with EVA training include redesign of the EMU shoulder joint or development of the next-generation suit for ISS EVA, reduction of high-risk NBL activities, optimization of suit fit, and continued emphasis on physical conditioning (Williams and Johnson, 2003).

During the 10-km EWT, subject discomfort levels were recorded, and a medical monitor examined the subjects for signs of suit-induced trauma at the completion of the test. In terms of discomfort, the mean rating was 1.5 ± 1.1 (SD), which is "very low" to "low" on the 10-point discomfort scale. The knee area and the feet/toes were the most frequent sites of discomfort during and after the test (figure 14-9). Fatigue and/or muscular tightness were reported most commonly in the quadriceps, thighs, gluteal muscles, and lower back (Gernhardt et al., in preparation (b)).

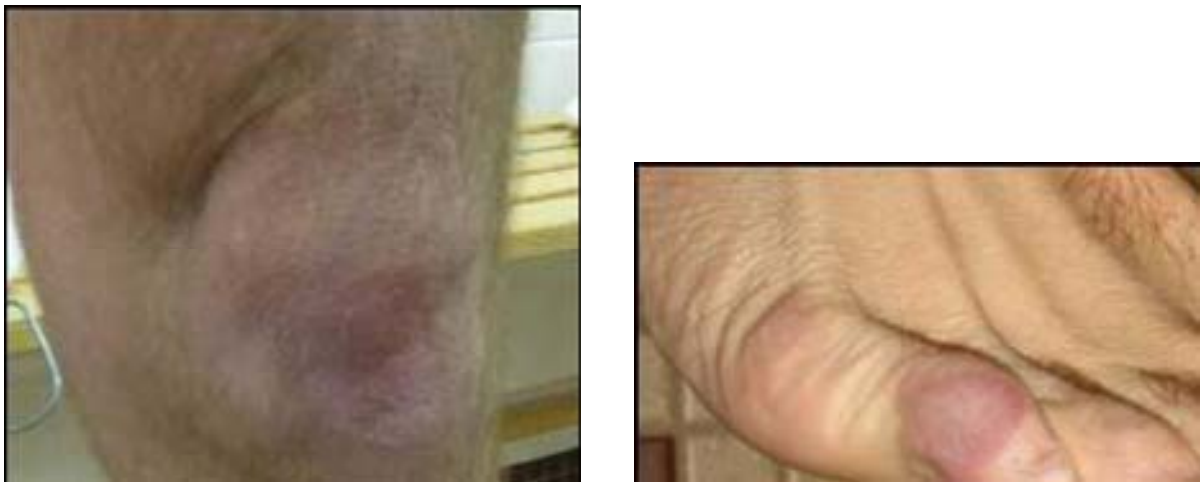

Figure 14-9. ***Knee and foot trauma sustained during 10-km EWT.***

Risks to crew health: decompression sickness

Overview

Decompression sickness represents a risk to the successful performance of EVAs as well as to the health and safety of the astronauts. Type I (pain-only) DCS symptoms can range from awareness in a joint or muscle to pain in which the performance of a task is affected. Symptoms of Type II (serious) DCS can include confusion, memory loss, headache, impaired vision, extreme fatigue, seizures, vomiting, shortness of breath, unconsciousness, paralysis, and, ultimately, death.

The risk of developing DCS is decreased by performing an oxygen pre-breathe to reduce the amount of inert gas (usually nitrogen) in the blood and tissues before a crew member is subjected to decompression in the spacesuit. Many factors influence the required duration of the pre-breathe protocol. During the Apollo missions, the environment inside the lunar module was 34.5 kPa (5.0 psia) and 100% oxygen. The absence of inert gas in the environment meant that pre-breathe was unnecessary to reduce DCS risk. However, concerns over flammability mean that Orion, Altair, and any surface assets during future lunar exploration will likely operate at 101 kPa (14.7 psia) and 20.8% oxygen; 70.3 kPa (10.2 psia) and 26.5% oxygen; and/or 55.2 kPa (8.0 psia) and 32% oxygen with the balance nitrogen. In any of these environments, the partial pressure of nitrogen will require some amount of oxygen pre-breathe prior to a crew member performing an EVA at 29.6 kPa (4.3 psia) to reduce the amount of inert gas that is dissolved in that crew member's blood and tissues.

The risk of DCS during EVAs performed during CxP missions will be quantified and mitigated using the same combination of mathematical decompression stress modeling, statistical analysis of relevant ground-based and space flight data, expert judgment, and rigorous validation of pre-breathe protocols using prospective ground-based hypobaric EVA simulation studies. Through this process, pre-breathe protocols will be developed that will reduce the DCS risk to within acceptable limits while minimizing the impact on crew work efficiency.

Protocols are designed to reduce the risk of DCS to within acceptable limits. The NASA *DCS Risk Definition and Contingency Plan* (1998) criteria specify acceptable limits as a total incidence of DCS $\leq$ 15% at a 95% CL, with < 20% Grade IV venous gas emboli (VGE) and 95% CL, and no Type II (serious) instances of DCS.

The 1/6g environment, the increased time to return to Earth in the event of serious DCS, and the more frequent EVAs planned for lunar surface missions may necessitate the development of new limits of acceptability for DCS risk for these missions.

Pre-breathe protocols are typically developed by experts using models of decompression stress and by considering relevant data from past experiences in ground-based studies and space flight. Before they are implemented in space flight, pre-breathe protocols are typically tested in ground-based hypobaric chamber EVA simulation studies to verify that the observed incidence of DCS and VGE are indeed within the agreed-to acceptable limits. Analysis of the ground-based data using Bayesian statistical methods ensures that a pre-breathe protocol is approved for use in space flight only when the incidence of DCS and VGE are within acceptable limits *and* the level of confidence in the estimate of true DCS and VGE risk is 95% or greater.

Space Flight Evidence

Two different spacesuits are currently used to perform EVAs from the ISS: the Russian Orlan and the U.S. EMU. Differences in operating pressures between the U.S. and Russian spacesuits have led to different EVA preparations. The Russian Orlan spacesuit system operates at 40.0 kPa (5.8 psia). By contrast, the U.S. EMU system operates at 29.6 kPa (4.3 psia) of oxygen, with traces of CO_2 and water vapor.

The Russian EVA preparation protocol includes a 30-minute oxygen pre-breathe in the Orlan spacesuit at a pressure of 73 kPa (10.6 psia) to partially wash out nitrogen from crew members' blood and tissues (Barer and Filipenkov, 1994). Literature from the Russian program shows that of approximately 114 EVAs that had been performed in the Russian spacesuit, including 18 EVAs from the ISS, crew members showed no signs of DCS (Malkin, 1994; Davis et al., 1977; Fulton, 1951).

Three different pre-breathe protocols may be used before performing an EVA in the U.S. EMU: an exercise pre-breathe, a 4-hour in-suit pre-breathe, or a campout pre-breathe. The protocols vary in effectiveness and, hence, in risk of DCS. Selection of a particular method depends on the particulars of the EVA, including the DCS risk, the timeline, and the operational risk. However, no symptoms of DCS have been reported to date by astronauts who have performed EVAs in the EMU spacesuits following any of the three pre-breathe protocols (Horrigan et al., 1997; Waligora and Pepper, 1995).

Ground-based Evidence

According to ground-based studies of the U.S. pre-breathe protocols, exercise pre-breathe is the method that has the lowest predicted risk of DCS. It has been tested extensively under laboratory conditions and meets the NASA *DCS Risk Definition and Contingency Plan* (1998) criteria of a total incidence of DCS $\leq$ 15% at a 95% CL, with < 20% Grade IV VGE and 95% CL, and no Type II (serious) instances of DCS.

The 4-hour in-suit pre-breathe protocol resulted from many years of experience with 4-hour in-suit pre-breathe testing. This was primarily gained from ground testing of suited subjects and crew members in preparation for altitude chamber runs. More than 300 such exposures have been completed with < 1.5% instances of DCS observed, with no Type II DCS. However this method has not been subjected to the same level of controlled laboratory evaluation as the exercise pre-breathe method.

When simulating U.S. pre-breathe protocols in ground-based studies using volunteers wearing regular clothing, the rate at which DCS symptoms developed was 17% to 26%. Given these data and the lack of any observed DCS symptoms during space flight using the same protocols, the conclusion can be drawn that the

risk of DCS occurring in actual weightless EVA conditions is significantly lower compared to ground simulation. Russian physiologists explain this by citing the inhibiting effect of the spacesuit and microgravity on nucleation mechanisms in human tissues. The hard shell of the spacesuit prevents a crew member from making abrupt movements during an EVA, thus decreasing amplitude/speed characteristics, lowering the intensity of cavitations, and lessening the possibility of developing gas bubbles in tissues. Moreover, removing the mass load and decreasing the muscular exertion when performing static or dynamic tasks in microgravity decreases the number of pre-EVA gas bubble formations. The effect of these factors leads to a decrease in the intensity of and the rate at which pathogenic gas bubbles develop in the body as a causative agent of DCS (Conkin et al., 1987; Kumar et al., 1993; Powell et al., 1993).

Ground-based Simulation Information

A physics-based tissue bubble dynamics model (TBDM) will be used in the development of pre-breathe protocols. The TBDM provides a time-varying index of theoretical physiological decompression stress, referred to as a Bubble Growth Index (BGI), which is based on variations in pressure and gas composition (Gernhardt, 1991). BGI is defined as the radius of a theoretical gas bubble, r, divided by the initial radius of the bubble. The TBDM models the rate of change of bubble radius (dr/dt) according to Equation 1. Thus, the predicted decompression stress (BGI) at time t can be calculated throughout the entire time course of any decompression profile.

$$\frac{dr}{dt} = \frac{\frac{\alpha D}{h(r,t)}\left[P_a - vt + \frac{2\gamma}{r} + \frac{4}{3}\pi r^3 M - P_{Total} - P_{metabolic}\right] + \frac{rv}{3}}{P_a - vt + \frac{4\gamma}{3r} + \frac{8}{3}\pi r^3 M} \quad (1)$$

where:

r = bubble radius (cm)
t = time (sec)
α = gas solubility ((mL gas)/(mL tissue))
D = diffusion coefficient (cm^2/sec)
h(r,t) = bubble film thickness (cm)
P_a = initial ambient pressure (dyne/cm^2)
v = ascent/descent rate (dyne/$cm^2 \cdot cm^3$)
γ = surface tension (dyne/cm)
M = tissue modulus of deformability (dyne/$cm^2 \cdot cm^3$)
P_{Total} = total inert gas tissue tension (dyne/cm^2)
$P_{metabolic}$ = total metabolic gas tissue tension

The TBDM's index of decompression stress, BGI, can be quantitatively related to the percentage of DCS risk using a logistic regression model. Previous analysis has shown the TBDM to provide good prediction of DCS risk (Gernhardt, 1991). For example, a logistic regression was performed using DCS and VGE data from NASA Bends Tests 1–7 (n=345, 57 DCS cases, 16.5% DCS, 41.4% VGE). Data that were derived from the pre-breathe staged decompressions, all with exercise at altitude, included data points at 70.3, 41.3, and 29.6 kPa (10.2, 6.0, and 4.3 psia), and did not include adynamic or exercise pre-breathe data. BGI provided signifi-

cant prediction of DCS and VGE data ($p < 0.01$). The Hosmer-Lemeshow Goodness-of-Fit statistic: p=.35 for DCS, p=.55 for VGE, indicates a good fit of the data (Abercromby, 2008). (Note: For the Hosmer-Lemeshow statistic, $p > .05$ rejects the hypothesis that there is a significant difference between the model predictions and the observed data.) A 360-minute half-time compartment was assumed.

Conclusion

The combination of space flight and ground-based experience points to a high degree of safety in both approaches being used to mitigate the risk of DCS. The U.S. approach to DCS risk management enables greater crew mobility than does the Russian approach due to lower pressure in the EMU spacesuit; however, the simpler and shorter Russian protocol is preferable in terms of work efficiency. Over time, these pre-breathe protocols will need to be streamlined to optimize both crew mobility and work efficiency.

Risks to work efficiency: extravehicular activity suit design parameters

The total WEI is defined as

$$\frac{\textit{EVA Time}}{\textit{(Total suit and airlock prep + pre-breathe + airlock depress, repress + post EVA)}}.$$

The current NASA EVA total WEI is 0.39 to 0.51. Constellation EVA Systems Project documentation contains requirements stating that EVA WEI shall be 3.0. Many factors contribute to WEI, including vehicle systems, suit systems, and operational procedures. Future EPSP studies will evaluate WEI based on current knowledge and concepts of operations, and will provide data to make recommendations to improve WEI. These studies will include: (1) an evaluation of suit components that may improve WEI (e.g., integrated biosensor systems that are quick don/doff; drink bags that require less preparation time); (2) development of improved pre-breathe protocols; (3) studies in lunar analogs that will evaluate the efficiency of different mission operations concepts and measure the trends in WEI over time; and (4) an evaluation of suit prototypes and the development of operational concepts to meet WEI requirements.

Computer-based Simulation Information

Computer-based simulation data are discussed above in the Decompression Sickness section.

Risk in Context of Exploration Mission Operational Scenarios

Extravehicular activity is a critical factor in the success of the construction, maintenance, scientific, and exploration aspects of every lunar architecture concept being considered by the CxAT-Lunar team. Current plans call for each crew member to perform up to 24 hours of EVA per week for missions lasting up to 6 months. This corresponds to as many as 624 hours of EVA per crew member in a single mission. As described in the Evidence section of this chapter, the risks that are associated with any inadequacies that exist in current EVA suit designs – particularly with respect to suit-induced trauma – will be greatly amplified by such frequent EVAs.

Current CxAT-Lunar mission architectures include small pressurized rovers (SPRs) as a core element of the surface mobility system. The implications of SPRs on crew health, safety, productivity, and efficiency are potentially enormous. The availability of a pressurized safe-haven within 20 minutes at all times to provide DCS

treatment, SPE protection, and on-site treatment of or medication for an injured crew member would significantly reduce many of the risks associated with planetary exploration. Furthermore, because crew members would be inside the SPRs during most surface translations, the overall number of in-suit EVA hours to achieve the same (or greater) science/exploration return would be reduced. The possibility of performing single-person EVAs with a second crew member inside the SPR would further reduce total EVA hours during the lunar architecture to the same order of magnitude as during ISS construction. As a result, the number of cycles on the EVA suits would be decreased, thereby increasing the life of each EVA suit and reducing EVA risk for crew members.

Conclusion

The CxP will be more dependent on EVA excursions away from a pressurized habitat or vehicle than any program in the history of NASA. EVAs will be required to conduct planned scientific expeditions, assemble structures, perform nominal maintenance, and intervene and solve problems outside of the vehicle that cannot be solved either robotically or remotely. The ultimate success of future Exploration missions is dependent on the ability to perform EVA tasks efficiently and safely in these challenging environments.

With lunar missions planned for up to 30 times more EVA hours than during the Apollo era, exploration missions to the moon and Mars will present many new challenges with regard to crew health, safety, and performance. To date, our understanding of human health and performance parameters in partial-gravity environments is limited to observations of, and lessons learned from, Apollo-era astronauts who performed EVAs on the lunar surface. Since the Apollo Program, and using lessons learned from microgravity EVAs aboard the space shuttle and ISS, new prototype suits have been in development for future space exploration activities. However, to date there has been limited quantification of the physiological and biomechanical variables associated with suited activities in unit and partial gravity. The integrated human testing program that is under way at NASA will help to better characterize the impacts to crew health and performance of the various parameters that are involved in EVA suit design.

Collaborative work is also under way to enable the development of suit technologies that enhance crew comfort and efficiency; provide for optimal nutrition, hydration, and waste management; and reduce suit-induced trauma and fatigue. These efforts will provide objective data to enable informed requirements and the design of Constellation suit systems that will provide sufficient protection and life support for nominal zero-G and surface activities, as well as survival for contingency operations.

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Appendix A: Gravity Compensation and Performance Scale[24]

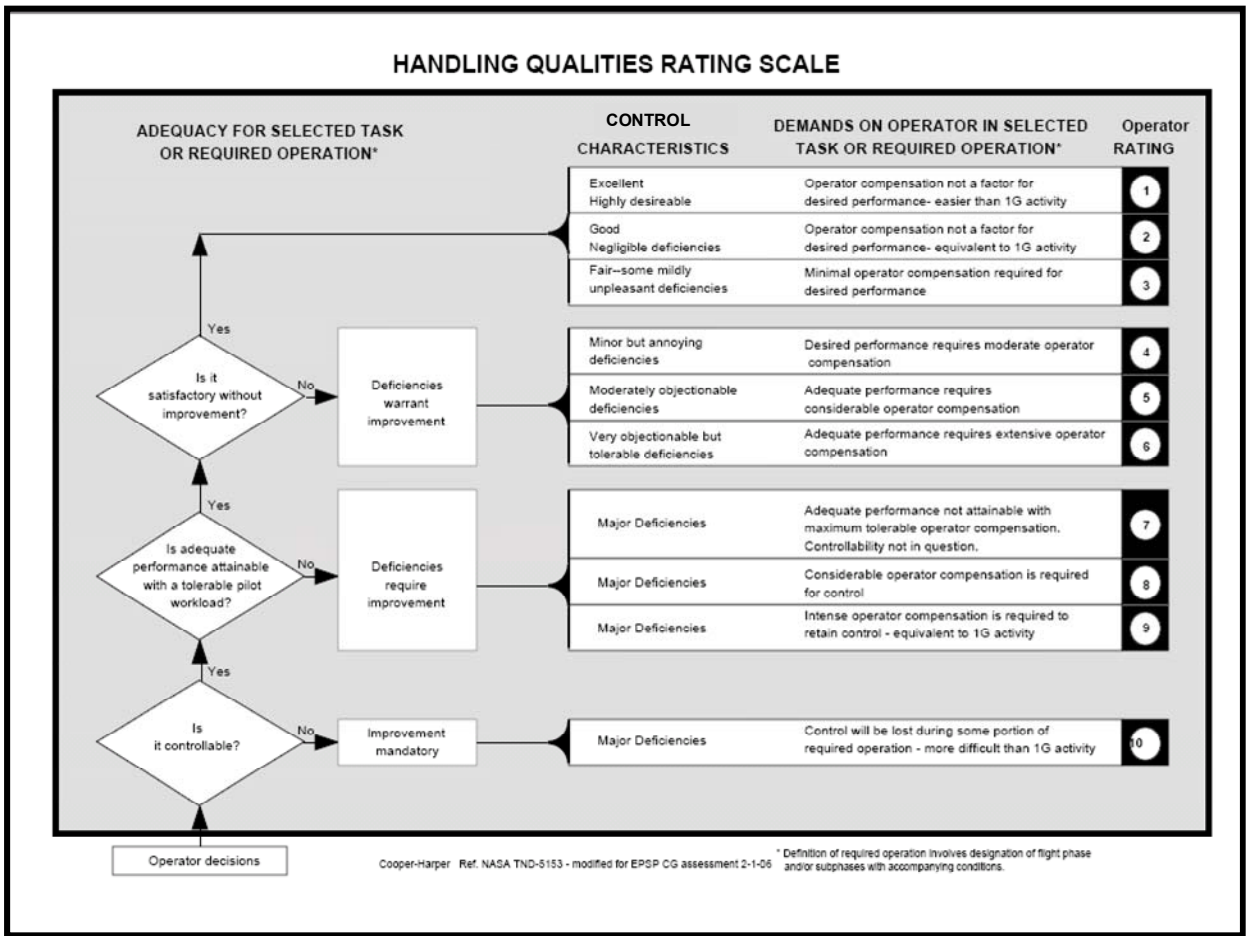
The Cooper-Harper scale, which has been in wide use since the late 1960s, permits quantification of pilot perceptions of aircraft handling characteristics. Most of the participants in EPSP studies are astronauts, many of whom are pilots and familiar with the use of this scale; however, the scale itself assumes a certain level of consistency in both pilot skills and specifications of the desired aircraft performance. In the development of next-generation EVA suits for Exploration missions, NASA requires controlled evaluations of varied suit concepts across an ambitious range of activities. These evaluations must be performed by astronauts or test subjects whose skills are limited to microgravity and/or simulated partial-gravity environments – far from equivalent to the skilled pilot population for whom the Cooper-Harper scale was originally designed.

EVA suit development for lunar and martian surface operations will require a wide range of evaluations encompassing tasks as varied as habitat building, traversing rocky terrain, core sampling, shoveling, and, potentially, rescuing an incapacitated crew member. In addition, suit concepts vary widely in mass, weight, CG, and pressure, and each must be evaluated across this range of tasks. NASA does not currently have rigorous performance measures for such tasks, and the EPSP Project personnel have begun the process of characterizing human-suit system performance under a variety of conditions and suit concepts using available analog facilities. Due to the many limitations of using the Cooper-Harper scale under these circumstances, scientists in the EPSP Project adapted the Cooper-Harper scale to reflect handling/controllability characteristics of task performance in reduced-gravity environments when compared relative to one's own shirt-sleeved performance of the same task in 1g. This modified scale, the GCPS, is shown on the following page. Using this scale, a rating of 2 during a suited experimental trial is perceived by the subject to be equivalent to his/her unsuited performance of the same task in 1g, thereby providing a quantitative rating of desired task performance in the suit.

As an example, a subject who is performing a shoveling task while wearing a suit that has a high-and-aft CG may rate the task performance as a 5 because the selected CG setting requires considerable effort/compensation compared to performing the same task unsuited with nominal CG. This new tool is useful for comparing multiple subjects' ratings of operator compensation that is required to perform a variety of simulated surface exploration tasks across a wide range of suit concepts, configurations, and gravity levels.

[24]Modified from the Cooper-Harper scale.

GRAVITY COMPENSATION AND PERFORMANCE SCALE (GCPS)



Chapter 15:
Risk of Operational Impact of Prolonged Daily Required Exercise

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Muscle atrophies in microgravity and strength decreases. Currently, significant daily time is scheduled to crew exercise. Making the exercise more efficient may allow similar beneficial effects to be achieved more simply, and in shorter time, which would provide more crew time for operational support. Benchmarking crew strength requirements, and testing exercise equipment and regimens against these benchmarks, will promote the development of more efficient, yet equally safe, exercise regimens. – *Human Research Program Requirements Document*, HRP-47052, Rev. C, dated Jan 2009.

Exercise is performed in space to promote musculoskeletal, cardiovascular, and psychological health. Research efforts seek to optimize exercise hardware, prescriptions, and physiological performance targets to support the provision of activities promoting health and fitness without compromising crew time or operations.

Executive Summary

After the submission of the risk Evidence Reports to the IOM for review in 2008, the program determined that the tasks that are within this risk were already covered by the HRP Program Requirements Document (PRD) Requirement 6.4. In Revision C of the PRD, therefore, the requirement was rewritten to better express this fact: "Each HRP research element must focus the research on producing countermeasures and technologies that fit within the extremely limited resource envelopes anticipated for the exploration mission. An example is the reduction in time dedicated to exercise prescriptions. Present exercise prescriptions present a large burden on the overall mission timeline." In addition, the risk was deleted from the list of risks in the newer PRD Revision C version, and the exercise time that is required to maintain measured aerobic capacity will be optimized as part of the activities that are associated with the risk of reduced physical performance capabilities due to reduced aerobic capacity. In addition, the exercise volume that is required to maintain fitness and performance will be further optimized through the activities that are associated with the risk of impaired performance errors due to reduced muscle mass, strength, and endurance. Despite the deletion of the risk of operational impact of prolonged daily exercise from newer versions of the PRD, a brief summary of the issues that are associated with this risk is included in this chapter.

The only countermeasure that is used consistently to date in the U.S. human space program to counteract the skeletal muscle atrophy and loss of muscle strength and endurance that is associated with microgravity exposure is physical exercise. On the ISS, each U.S. crew member is scheduled to exercise for as many as 2.5 hours per day for 6 days per week. This almost daily time commitment is significant and represents a potential risk to the accomplishment of other mission operational tasks. While no evidence exists that the currently required exercise regimen has negatively impacted mission operations, future missions would benefit from optimized exercise protocols that provide needed outcomes in a shorter time period, thus allowing crew members more time in which to complete mission operations. The development of a benchmark for the requisite level of crew strength and endurance is required to accomplish this objective. Once this benchmark is developed, exercise hardware and safe exercise regimens with equivalent or improved benefits that reduce the time that is dedicated to daily physical exercise must be created. Such efforts should have a high priority, particularly if operational time requirements for future missions are predicted to increase substantially over current levels.

Introduction

For long-duration missions aboard the ISS, U.S. crew members have been required to complete a 2.5-hour 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 hours were devoted to resistive exercise on the interim resistive exercise device (iRED) and a further approximately 1 hour was devoted to either the Treadmill with Vibration Isolation System (TVIS) or the Cycle Ergometer with Vibration Isolation System (CEVIS) or a combination of the two. On days when crew members were scheduled to conduct operations outside the ISS (i.e., EVAs), they were not scheduled for exercise, since EVAs typically require a significant amount of the duty day (6 to 7.5 hours) and strenuous physical effort. Thus, the exercise session that was normally scheduled was waived for crew members who were participating in an EVA.

The current suite of U.S. 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. To our knowledge, the current exercise time requirements have

not negatively impacted mission operations, but such a risk exists, particularly if the time that is needed to complete future daily mission operations increases above that of present levels.

Evidence

As far as we are aware, no published scientific or anecdotal evidence exists that demonstrates that the exercise time that is scheduled for ISS crew members has negatively impacted the accomplishment of mission objectives. The long daily sessions of scheduled exercise do represent a risk to the accomplishment of other tasks, however, particularly within the confines of the flight rules that define the crew duty day that are available for all scheduled activities. In brief, crew members are scheduled daily for an 8-hour sleep period, leaving a 16-hour duty day. That duty day is divided into a post-sleep period with time for personal hygiene and a morning meal, a midday meal, and a pre-sleep period with further time for an evening meal and other activities. Time for daily planning conferences, private medical conferences, and other activities is also scheduled. Generally, the rest of the 16-hour duty date is allocated to mission operations (6.5 hours) and exercise (2.5 hours). Thus, the potential exists for competition between scheduled mission tasks and exercise sessions.

Computer-based Simulation Information

No computer-based simulation pertaining to this risk is available.

Risk in Context of Exploration Mission Operational Scenarios

Without knowledge of the details of Exploration mission operational scenarios, assessing the level of risk that prolonged periods of daily exercise might represent is difficult. However, since the time that is scheduled for exercise cannot be used for other purposes within the confines of duty day limitations, if duty day restrictions for Exploration missions do not differ significantly from those that are imposed for ISS crew members, the combined time that will be available in which to complete daily mission objectives and exercise will be only about 9 hours. Thus, the time that is spent for daily exercise sessions will decrease by an equivalent amount to the time that is available in which to complete mission operational tasks.

Conclusion

Prolonged daily exercise sessions compete with the time that is available for mission operations and thus represent a potential risk to the timely completion of mission objectives. Key gaps exist in our knowledge concerning the level of skeletal muscle strength and endurance that should be maintained by crew members during long-duration space flight and how to optimize exercise hardware and protocols to achieve and maintain that maintenance level. Research is needed to define a skeletal muscle performance benchmark and to develop exercise hardware and regimens that will allow the benchmark to be met and sustained for future human space flight missions.

Appendices

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Acronyms and Abbreviations

A

ACE	advance composition explorer
ACES	advanced crew escape suit
AFT	Advanced Food Technology [Project]
AGARD	Advisory Group for Aerospace Research and Development
AGS	Alternating Gradient Synchrotron
ALARA	as low as reasonably achievable
ANARE	Australian National Antarctic Research Expeditions
ARI	Army Research Institute
APA	American Psychiatric Association
ApoE	Apolipoprotein E
ARS	acute radiation syndrome
ASG	Astronaut Spouses Group
ASTP	Apollo-Soyuz Test Project
AT	*ataxia telangiectasia*
ATM	*ataxia telangiectasia* mutated
AU	astronomical unit

B

B/F/B	breakage-fusion-bridge
BALF	bronchoalveolar lining fluid
BEIR	Biological Effects of Ionizing Radiation
BFO	blood-forming organ
BGI	Bubble Growth Index
BHMS	Boeing Human Modeling System
BHP	Behavioral Health and Performance [Element]
BME	biomedical engineer

C

C	carbon control
C&W	caution and warning
CAD	coronary artery disease
CAU	cockpit avionics upgrade
CBA	carcinoma-bearing animal
CDC	Centers for Disease Control
CEVIS	Cycle Ergometer with Vibration Isolation System
CG	center of gravity
CHD	coronary heart disease
C.I.	confidence interval
CL	confidence level
CM	command module [Apollo]
CME	coronal mass ejection
CMO	crew medical officer
CNS	central nervous system
CO_2	carbon dioxide
COSTEP	comprehensive suprathermal and energetic particle analyzer
CTA	conditioned taste aversion
CTAS	Center TRACON Automation System
CTSD	Crew and Thermal Systems Division
CVD	cardiovascular disease
CxAT-Lunar	Constellation Architecture Team-Lunar
CxP	Constellation Program

D

D-RATS	Desert Research and Technology Studies
DCS	decompression sickness
DCX	doublecortin
DDREF	dose and dose-rate effectiveness factor
DNA	deoxyribonucleic acid
DNA-PK	DNA-dependent protein kinase
DSB	double strand break
DSM-IV-TR	*Diagnostic and Statistical Manual Fourth Edition* Text Revision
DT	dual task

E

EAR	excess absolute risk

EEG	electroencephalogram
ELR	excess lifetime risk
EMU	extravehicular mobility unit
EPA	Environmental Protection Agency
EPSP	EVA Physiology, Systems, and Performance [Project]
ERR	excess relative risk
ESM	equivalent system mass
EVA	extravehicular activity
EWT	EVA Walkback Test
ExMC	Exploration Medical Capabilities [Element]

F

F/W	fatigue/weakness
FAA	Federal Aviation Administration
fc	foot-candles
FDA	Food and Drug Administration
Fe	iron
FGB	functional cargo block
FR	fixed ratio
FSO	Family Support Office

G

GCPS	gravity compensation and performance scale
GCR	galactic cosmic ray
GI	gastrointestinal
GOES	geostationary operational environmental satellite
GPS	global positioning satellite
GRF	ground reaction force
GRT	grammatical reasoning task
GSD	geometric standard deviation

H

HACCP	hazard analysis and critical control point
HBP	Human Behavior and Performance
He	helium
HF	human fibroblast
HHC	Human Health and Countermeasures [Element]
HIDH	Human Integration Design Handbook
HMP	Haughton Mars Project
HPA	hypothalamic-pituitary-adrenal
HPBL	human peripheral blood leukocyte
HPP	high-pressure processing
HPRT	hypoxanthine-guanine phosphoribosyltransferase
HRP	Human Research Program
HUT	hard upper torso
HZE	high-Z high-energy

I

I/O	industrial and organizational
IARC	International Agency for Research on Cancer
ICD-10	*International Classification of Diseases-10*
ICE	isolated, confined, and extreme
ICRP	International Commission on Radiation Protection
ICRU	International Commission on Radiation Units
IMM	integrated medical model
IMS	Inventory Management System
IOM	Institute of Medicine
IP	internet protocol
IQ	intelligence quotient
IR	irradiated
iRED	interim resistive exercise device
IRP	Integrated Research Plan
ISIS	Intelligence Spacecraft Interface Systems
ISS	International Space Station
IVA	intravehicular activity

J

JHPEE	*Journal of Human Performance in Extreme Environments*
JSC	[NASA] Johnson Space Center

K

KSS	Karolinska Sleepiness Scale

L

LADTAG	Lunar Airborne Dust Toxicology Assessment Group
LCG	liquid cooling garment
LDTRP	Lunar Dust Toxicity Research Project

LEO	low-Earth orbit
LET	linear energy transfer
LiOH	lithium hydroxide
LM	lunar module [Apollo]
LSS	life span study

M

MCP	metacarpophalangeal
MER	Mars exploration rover
MeV/n	mega electron volts per nucleon
Mg	magnesium
MIDAS	Man-machine Integration Design and Analysis System
MKIII	Mark III Advanced Spacesuit Technology Demonstrator
MOD	Mission Operations Directorate
MOLA	Mars orbiter laser altimeter
MPSL	Mars Phoenix scout lander
MST	memory search task
mSv	milli-Sievert

N

NAAQS	National Ambient Air Quality Standard
NAS	National Academy of Sciences
NBL	Neutral Buoyancy Laboratory
NCRP	National Council on Radiation Protection and Measurements
Ne	neon
NEEMO	NASA Extreme Environment Mission Operations
NEO	neuroticism, extroversion, and openness to experience
NFT	neurofibrillary tangle
NIMH	National Institute of Mental Health
NOAA	National Oceanographic and Atmospheric Agency
NOLS	National Outdoor Leadership School
NRC	National Research Council
NSBRI	National Space Biomedical Research Institute
NSRL	NASA Space Radiation Laboratory
NTSB	National Transportation Safety Board

O

O	oxygen
OER	oxygen enhancement ratio
Op Psy	Operational Psychology

P

PAC	premature atrial contraction
PAO	Public Affairs Office
PAWS	Performance Assessment Workstation
PBS	Public Broadcasting System
PCI	Personality Characteristics Inventory
PDF	probability distribution function
PEL	permissible exposure limit
PHF	paired helical filament
PLSS	Portable Life Support System
Pogo	Partial Gravity Simulator
PRD	Program Requirements Document
PSA-NCAM	polysialic acid form of neural cell adhesion molecule
PVC	premature ventricular contraction
PVT	psychomotor vigilance task

Q

QMSFRG	quantum multiple scattering fragmentation

R

RBE	relative biological effectiveness
RDA	Recommended Daily Dietary Allowance
REI	rear entry ILC Dover suit
REID	risk of exposure-induced death
REM	rapid eye movement
ROS	reactive oxygen species
RPE	rating of perceived exertion
RSP	respiratory support pack

S

SD	standard deviation
SEM	scanning electron microscope standard error of mean
SGR	*Small Group Research*
SGZ	subgranular zone
SHE	Syrian hamster embryo

SHFH	Space Human Factors and Habitability
Si	silicon
SIR	standard incidence ratio
siRNA	small interfering ribonucleic acid
SMM	shared mental model
SOBP	spread-out Bragg peak
SOD	superoxide dismutase
SOHO	solar and heliospheric observatory
SPE	solar particle event
SPR	small pressurized rover
SSA	Social Security Administration
SSB	single-strand break
STRES	simulated training requirements effectiveness report
Sv	Sievert
SWA	slow wave activity
SWS	slow wave sleep

T

2D	two-dimensional
3D	three-dimensional
TBDM	tissue bubble dynamics model
TEPC	tissue-equivalent proportional counter
TIB	time in bed
TiO2	titanium dioxide
TK	triose-kinase
TLD	thermoluminscent dosimeter
TOD	top of descent
TRACON	Terminal Radar Approach Control
TSP	total suspended particles
TVIS	Treadmill with Vibration Isolation System

U

UGID	upper gastrointestinal distress
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation
USAF	United States Air Force
USDA	United States Department of Agriculture
UTT	unstable tracking task
UV	ultraviolet

V

VAS	Visual Analog Scale
VGE	venous gas emboli
VO_2pk	volume of oxygen consumption, peak

W

WAFAL	Water and Food Analytical Laboratory
WEI	work efficiency index
WHO	World Health Organization
WinSCAT	space flight cognitive assessment tool for Windows

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