Infection Prevention and Control During Prolonged Human Space Travel

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Prolonged human spaceflight to another planet or an asteroid will introduce unique challenges of mitigating the risk of infection. During space travel, exposure to microgravity, radiation, and stress alter human immunoregulatory responses, which can in turn impact an astronaut’s ability to prevent acquisition of infectious agents or reactivation of latent infection. In addition, microgravity affects virulence, growth kinetics, and biofilm formation of potential microbial pathogens. These interactions occur in a confined space in microgravity, providing ample opportunity for heavy microbial contamination of the environment. In addition, there is the persistence of aerosolized, microbe-containing particles. Any mission involving prolonged human spaceflight must be carefully planned to minimize vulnerabilities and maximize the likelihood of success.

Keywords. infection prevention; infection control; space medicine; aviation medicine; astronaut.

The US National Aeronautics and Space Administration (NASA) is currently planning for prolonged human spaceflight. It is estimated that a mission to and from Mars will take a minimum of 520 days, the crew will be 360 million kilometers from Earth, there will be a 20-minute one-way communication delay from this distance [24], and there may be no way to return to Earth until the mission is completed. Clearly space travel creates a unique challenge of preventing and controlling infection. In addition to the physiological effects of microgravity on humans, exposure to solar and cosmic radiation, the stress of being in a confined setting, and the myriad of changes observed in microorganisms in this unique environment all add to the complexity of this endeavor (Figure 1).

Crucian and Sams wrote, “it cannot yet be firmly concluded that a clinical risk related to immune dysregulation actually exists for exploration-class spaceflight” [1]. Nevertheless, in microgravity, potential microbial pathogens demonstrate enhanced expression of virulence factors [2–5], more rapidly enter into log-phase growth in liquid media [6, 7], and may increase biofilm formation [8]. At the same time, there is dysregulation of the human immune system during space travel, which may increase risk of infection [9–11], including reactivation of herpesviruses [12]. In addition, anaerobic colonic flora is diminished with a commensurate increase in aerobic bacteria such as Pseudomonas and Staphylococcus aureus [13, 14] and there is a greater abundance of S. aureus, along with Enterobacteriaceae, on the skin [13] and in the upper airway [14]. Numerous conditions that are conducive to the spread of infection exist within the confines of a containment vessel such as the International Space Station. Transmission of microbial flora among astronauts, including some multidrug-resistant pathogens, has been demonstrated [13, 15–20]; microbes survive in free-floating condensate [21]; and symptom-based management of medical conditions [22] may be carried out by individuals who may not have medical or nursing degrees and must confer with earthbound physicians at Mission Control. Based on postflight medical debriefs, there were 29 infectious disease
incidents (ie, fever/chills [8], fungal infection [5], flu-like illness [3], urinary tract infection [4], aphthous stomatitis [3], viral gastroenteritis [2], subcutaneous skin infection [2], and other viral disease [2]) among approximately 742 crew members who have flown 106 space shuttle flights [23].

This review explores the challenges of preventing and controlling infections and suggests potential countermeasures. The opinions expressed are those of the author. It is hoped that the article will engender greater collaboration among the infection control, infectious diseases, and space science communities.

INFECTION PREVENTION CHALLENGES

The Astronaut

The immune system undergoes a number of changes during space travel [9, 10], including impaired wound healing [25], inhibition of leukocyte blastogenesis and altered leukocyte distribution [26–28], altered monocyte and granulocyte function [28–30], impaired leukocyte proliferation following activation [31], altered cytokine production patterns [26], abrogated bone marrow responsiveness to colony-stimulating factors [32, 33], altered T-cell intracellular signaling [34], inhibition of natural killer cell activity [35], inhibition of delayed-type hypersensitivity [36, 37], and apparent Th2 potential bias shift [10]. Although the effects of spaceflight on human gut flora have not been studied extensively, changes in the human microbiome have been demonstrated, with reduced density of anaerobic flora and increased density of aerobic gram-negative bacteria and staphylococci on the skin and in the upper airway and colon [14]. Additionally, stress associated with space travel in a confined environment may induce changes in the intestinal microbiome that are unrelated to microgravity, and this may impact immune function [38, 39].

The Microbe

In microgravity, bacteria demonstrate enhanced growth patterns in liquid media [6], reflecting a shortened lag phase and enhanced exponential growth [7]. Additionally, bacteria demonstrate enhanced virulence [2–5]; higher minimal inhibitory concentrations to various classes of antimicrobial agents [40–42], which is at least partly due to thickening of the microbial cell wall [43, 44]; increased conjugal transfer rates [45]; increased production of quorum-sensing molecules such as N-acyl homoserine lactone [46]; enhanced virulence, leading to increased mortality in animal infection models [47]; increased biofilm formation [48]; and increased survival within macrophage [4]. For additional information on the effect of microgravity on microbes, see Horneck et al [49].

The Spacecraft or Space Habitat

The internal environment of a spacecraft or space station can become heavily contaminated with microbes [50], and free-floating condensate has been found to harbor numerous bacteria, fungi, and even protozoa [21]. Microgravity affects the aerobiology of the aerosols that are created from a cough or sneeze or during speech. Particles remain airborne until they are inspired, swallowed, contact an otherwise absorbable surface, or are ideally promptly removed by an air filtration system. The presence of these aerosols affects the risk of person-to-person transmission of viruses such as influenza [51–53] and even bacteria such as S. aureus [54, 55].

PREFLIGHT COUNTERMEASURES

Interventions for mitigating the risk of infection prior to space travel are described in this section (Table 1).

The Astronaut

A robust vaccination program that includes tetanus/diphtheria/acellular pertussis (Tdap), measles/mumps/rubella (MMR), influenza, pneumococcal, meningococcal, and hepatitis A and B vaccines should be implemented. Because of increased reactivation of herpesviruses, which has been noted in past space missions [12], varicella zoster virus vaccine should be given. In the unlikely event that an astronaut is unknowingly carrying Salmonella, typhoid vaccine should be considered to reduce the risk of transmission.
Health screening, including a complete dental exam, should be standard practice. Screening for tuberculosis with an interferon gamma release assay [56] should be conducted. Because S. aureus [49] has been transmitted astronaut-to-astronaut in space [13, 18], robust screening of astronauts for both methicillin-susceptible and methicillin-resistant S. aureus carriage should be done, to include nares, throat, and rectal sampling [57, 58] using techniques with enhanced sensitivity and that involve a molecular method [59]. An algorithm using quantitative nasal cultures may identify those at high risk for persistent S. aureus carriage [60]. S. aureus [61, 62] carriers should be decolonized using serial screening cultures after completion of a decolonization regimen to ensure that carriage has been eradicated [63]. Screening for human immunodeficiency virus (HIV) should be done. Also, screening of astronauts for latent endemic fungal infections such as coccidiomycosis and histoplasmosis should be considered to minimize the risk of reactivation [64]. Screening for Strongyloides and possibly other parasitic infections that may be endemic to the astronauts’ home countries should be considered. Screening multiple stool samples for Salmonella carriage should also be considered [65].

Pretravel infection control education that includes hand hygiene and cough etiquette and a review of the modes of
microbial transmission and attendant mitigation strategies should be provided. An infection control manual should be reviewed prior to travel and kept on board. The manual should include instructions regarding symptom-based isolation precautions, aseptic technique for insertion and maintenance of inserted medical devices, and similar information. Training for aseptic insertion of intravenous and bladder catheters should also be provided. Additionally, focus groups consisting of astronauts with past space travel experience and human factors engineers should meet to discuss barriers to performing hand hygiene and the ideal location of waterless hand-hygiene product dispensers [66]. As part of the current Health Stabilization program, astronauts are isolated from others in the community for a period of time greater than the incubation period for most common viral upper respiratory tract, gastrointestinal, viral, and bacterial infections. Isolation begins 7 days before launch.

It is unclear whether all foodstuffs should be irradiated with gamma radiation for prolonged space missions. Prolonged ingestion of sterile food alters the colonic microbiome, and the microbes in food that become part of the colonic flora likely serve an important homeostatic function for the immune system. On the other hand, irradiation prolongs shelf-life and potential contamination with microbes that cause gastrointestinal illness are a concern. As such, gamma irradiation of selected food should be undertaken as is currently done. Deliverables to the containment vessel should be gamma-irradiated or undergo other sterilizing procedures.

The Spacecraft or Space Habitat
Ideally, the breathable air within a spacecraft or space habitat is filtered with a high-efficiency particulate air (HEPA) filter and humidity controlled. However, energy requirements for existing filters has made the use of such an air-handling system prohibitive. Consideration should be made for positive or neutral pressure within the containment vessel to reduce the risk of airborne microbes entering the containment vessel after docking if technically feasible. Additionally, consideration should be made for the bathroom to be under negative or neutral pressure compared with that of the living quarters in the containment vessel. The water storage and distribution system should be manufactured using noncorrosive material that has limited organic carbon to minimize biofilm formation. Antibiofouling coatings and materials should be developed to further mitigate propagation of microbes in the water system. Of course, these materials must not introduce any potential toxicity to the astronauts. Potable water should be pasteurized or undergo catalytic oxidation, which is the current method of disinfection. Redundancy for additional protection from waterborne microbes should include point-of-use submicron filters. Foot-pedal–operated potable water outlets will minimize the risk of touch contamination and transmission of pathogens [67]. Coating surfaces within the spacecraft should be made of a nonleaching, nonporous antimicrobial material [68], providing these materials do not introduce toxicity to the astronauts despite prolonged exposure through contact or aerosolization. Other design considerations should be reviewed such as temperature and humidity control and waste processing [69]. Alternatively, if a low-power portable ultraviolet light unit is developed and proven effective, it could be used to reduce microbial contamination of environmental surfaces [70].

Other Risks
Animals, which pose a risk of zoonotic infection to astronauts [71, 72], should undergo pretravel screening to minimize the risk of disease transmission [73] or, as is currently the case, should be pathogen-free animals. Policies and procedures that are carefully reviewed by veterinary experts in zoonoses should be in place, to include care of animals (eg, glove use when handling animals or when in potential contact with animal waste), handling animal waste, and housing.

COUNTERMEASURES DURING SPACE TRAVEL

Interventions for mitigating the risk of infection during space travel are described in this section (Table 2) Astronauts with signs or symptoms of respiratory tract infection should wear surgical masks to mitigate risk of transmission to other astronauts [74]. Cough etiquette should be adhered to, especially by those with upper respiratory tract symptoms when unmasked, for example, while eating. Consideration should be made for non-ill astronauts to wear fit-tested N-95 respirators if a companion astronaut has signs or symptoms of a respiratory tract infection and the causative pathogen is known to be transmitted by small aerosol particles [51–53]. Although alcohol-based hand-hygiene products are recommended for most earthbound healthcare settings [66, 75, 76], these products cannot be used in space because the alcohol would contaminate the drinking water supply through the humidity condensate. Therefore, the most effective waterless, nonalcohol-based hand-hygiene product for space travel (ie, potentially harmful vapors from the product can be removed by the air-handling system), such as benzalkonium chloride–based products, should be used. Chlorhexidine-based cloths [77], or possibly other cloth-based, nonalcohol-containing, US Food and Drug Administration–approved products, which are currently used in some school settings, should be considered based on efficacy and safety.

The spacecraft or space habitat should be equipped with both nonsterile and sterile gloves, as well as topical (for skin or ocular use), oral, and intravenous antimicrobial agents. In addition, equipment for intravenous or bladder
Table 2. Countermeasures during Spaceflight

<table>
<thead>
<tr>
<th>Currently Done by US National Aeronautics and Space Administration</th>
<th>Not Done but Recommendeda</th>
<th>Not Done but Considerab</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Astronaut</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Surgical mask and cough etiquette</td>
<td>• Source control (ie, surgical mask worn) by astronauts with upper respiratory infection</td>
<td>• Chlorhexidine daily mouth rinseb</td>
</tr>
<tr>
<td>• Fit-tested N95 respirator for other astronauts if respiratory illness caused by a pathogen that can be spread by small aerosol particle</td>
<td>• Diagnostic testing capabilities for common viral and bacterial pathogens</td>
<td>• Probiotic ingestion</td>
</tr>
<tr>
<td>• Waterless hand-hygiene product</td>
<td>• Glove use handling animals or if potential contact with animal waste</td>
<td>• Portable ultraviolet light machine to disinfect surfaces</td>
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<tr>
<td>• Germicidal wipes for cleaning high-touch, inanimate objectsb (eg, toileting device)</td>
<td>• Intravenous catheter infection prevention engineering controls (eg, chlorhexidine sponge dressingb)</td>
<td></td>
</tr>
<tr>
<td>• Gloves and gown for contact with potentially infectious material</td>
<td>• Electric toothbrush use</td>
<td></td>
</tr>
<tr>
<td>• Antimicrobial agents (topical [skin and ocular], oral, intravenous)</td>
<td>• Safety cabinet for sterile preparation of intravenous medications</td>
<td></td>
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<tr>
<td>• Intravenous catheter insertion equipment</td>
<td>• Sensor in bathroom; visual/audio cues if no hand hygiene performed</td>
<td></td>
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<tr>
<td>• Cutaneous antiseptic for minor surgeryb</td>
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<tr>
<td>• Vitamin D supplementation</td>
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<tr>
<td>• Regular exercise program</td>
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<tr>
<td><strong>Containment vessel</strong></td>
<td></td>
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<tr>
<td>• Intermittent quantitative sampling of air and potable water</td>
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A table listing countermeasures during spaceflight, with columns for items currently done, not done but recommended, and not done but considered. The table includes various preventive measures such as surgical masks, hand hygiene products, and regular exercise.

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Catheterization that includes infection prevention engineering controls should be available [78, 79]. A cutaneous antiseptic to cleanse minor wounds, prep skin prior to insertion of an intravenous catheter, or be used during minor surgeries should be included. Astronauts routinely take a vitamin D supplement, which may enhance immune function [80] and reduce risk of reactivation of herpesviruses [81], and this practice should continue. Use of a powered toothbrush [82], or possibly use of a daily mouth rinse with chlorhexidine, may reduce risk of periodontal disease and should be considered [83]. However, as with daily use of cutaneous antiseptics, the unintended consequences of long-term use must be considered. Germicidal wipes for cleaning high-touch inanimate objects, such as the toileting device, are necessary. Toileting devices that come in contact with an astronaut’s skin should be cleaned after each use. Hand-hygiene compliance is important, particularly after a bowel movement, prior to food preparation, and similar activities. Input from human factors engineers will ensure ease of use of available products, thereby increasing compliance. Consideration could be made for a sensor in the bathroom with visual and/or audio cues to alert an astronaut who did not perform hand hygiene after using the bathroom facility [84]. Routine cleaning of the inanimate environment with a germicidal wipe is important, as outlined in a preflight infection control manual and currently performed on the International Space Station. Intermittent, quantitative air and water sampling should continue to be done to alert crew of defects in mitigation strategies.

Regular exercise, which has been integrated into astronaut activity on the International Space Station, may improve immune function during spaceflight [85]. Ingestion of Lactobacillus reduces the bioburden of aerobic enteric flora [14] and, in addition to immunomodulatory effects [86], may reduce risk of infection [87]. In addition, intravaginal Lactobacillus administration reduces risk of recurrent urinary tract infections [88]. Thus, use of probiotics should be considered if found to be safe during prolonged human exposure to microgravity. Recent research has demonstrated that colonizing the skin and nares with extracellular serine protease (Esp)-producing S. epidermidis selectively inhibits S. aureus nasal colonization and biofilm formation [89]. As such, a somewhat far-reaching countermeasure would involve colonizing astronauts’ nares prior to travel with ESP-producing S. epidermidis.

An unmet need that is currently being investigated is for astronauts to have access to equipment needed to detect microbial pathogens-causing infections in order to direct appropriate therapeutic interventions and mitigate transmission risk. Challenges include testing for common viruses and bacteria, ease of use, durability of reagents, and output that does not require incubation.

**UNANSWERED QUESTIONS**

- Will prolonged spaceflight lead to changes in the risk of infections based on altered human immune function and bacterial physiology that were predicted by preflight studies?
• What is the best antimicrobial coating for the containment vessel surfaces and water distribution and storage systems? This coating should be broad-spectrum, long-acting, and nonleachable, with a minimal likelihood of resistance developing among exposed microbes and no toxicity to humans despite prolonged exposure.
• What is the most effective, acceptable antiseptic agent to be used for hand hygiene during space travel?
• Does the benefit of gamma-irradiated food outweigh the potential detrimental effect on colonic microbial diversity and colonization resistance?
• What diagnostic testing should be used during space travel? Enhanced diagnostic abilities during prolonged spaceflight, far beyond current symptom-based diagnoses, will be essential. Such testing must be clarified for instances when the above-noted countermeasures did not prevent such illnesses.
• Why do microbes become more virulent in microgravity? How and why does the human immune system change under conditions found in space? A better understanding of these changes is of seminal importance and may afford us greater insight into our own evolution and lead us to unique therapeutic interventions not otherwise realized through experimentation on Earth.

CONCLUSION

Serious infections during space travel have been limited to date; many infections have been superficial skin infections (D. L. Pierson, personal communication). However, plans for human space travel lasting nearly 2 years are currently being discussed at NASA. At the same time, ongoing studies on the International Space Station and elsewhere [90] are attempting to assess the impact of prolonged human spaceflight on the immune system. If clinically significant immune dysfunction is documented, this, along with alterations in bacterial physiology during spaceflight, will create challenges to successful human missions. Attention to basic infection prevention and control practices should help to reduce the risk posed to astronauts. Research funding should be available to address transduction dynamics of microbes in microgravity and other unanswered questions. It is hoped that the present review offers some suggestions to mitigate such potential risk.

SEARCH STRATEGY AND SELECTION CRITERIA

References for this review were identified through searches of PubMed for articles published from January 1971 to June 2012, by use of the terms “microgravity,” “space travel,” “infection control,” “immune function,” “infection prevention,” “Lactobacillus,” “vaccination,” “Staphylococcus aureus” screening and decolonization,” “Salmonella” detection,” “latent tuberculosis detection,” “hand hygiene,” “zoonoses,” “prevention of gingivitis,” “vitamin D and immune function,” and “prevention of Legionnaires’ disease.” Articles resulting from these searches and relevant references cited in those articles were reviewed. Articles published in English were included.

NOTES

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