EXPLORATION CLASS MISSIONS AND RETURN: EFFECTS ON THE IMMUNE SYSTEM

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ABSTRACT

Immune responses have been shown to be altered when humans, animals and cell cultures are exposed to space flight conditions. It is clear that, although there have been some issues regarding infection on short-term space flights, alterations in the immune system have not been a "show-stopper" for space flight missions to date. However, as very long-term multi-year exploration class missions are contemplated, the potential for space flight-induced alterations of the immune system to have major impact on crew health and success of the mission increases. The increased concern is due to exposure to new conditions such as novel forms of radiation, and the isolation of the crew from the ability to obtain rapid relief and rescue due to health problems. If, during space flight, immune capacity is diminished while bacterial growth and virulence is enhanced, and antibody efficacy is altered, a difficult situation could arise. If an ineffective antibiotic is transported for use by the crew, there will be no replacement readily available during an exploration class mission. Additionally, radiation exposure combined with a suppressed immune system could facilitate tumor development after return to earth. In order to protect crews and assure the success of exploration class missions, studies must be undertaken in space, as well as on earth using ground-based analog models, to fully establish the risk and to develop countermeasures to prevent or minimized unwanted outcomes.

INTRODUCTION

It is clear that immune responses are dramatically altered after space flight (Space Studies Board, 1998; Sonnenfeld et al., 2003). Multiple experiments, including human, animal and tissues cultures studies, have demonstrated that a variety of immune responses are altered after exposure to space flight conditions during actual flight experiments or during experiments using ground-based analog models that re-create some of the conditions of space flight (Space Studies Board, 1998; Sonnenfeld et al., 2003). Among the immune responses that have been shown to be affected by space flight conditions are: leukocyte blastogenesis (division of white blood cells required to start immune responses), cytokine production, leukocyte subset analysis, natural killer cell activity and delayed hypersensitivity skin tests (Space Studies Board, 1998; Sonnenfeld et al., 2003).

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Although it is clear that the immune response changes during and after space flight, the biomedical significance of these changes is still not fully established (Space Studies Board, 1998; Sonnenfeld et al., 2003). There have been reports of changes in resistance to infection during space flight, with the development of a urinary tract infection in one case (Space Studies Board, 1998; Sonnenfeld et al., 2003). In the Apollo program, problems with development of respiratory tract infections in crews led to the development of the Crew Health Stabilization program countermeasure of decreased interaction of crews with other people on the ground still in use today (Space Studies Board, 1998; Sonnenfeld et al., 2003). Additionally, it is now clear that latent viruses, such as Epstein-Barr virus, are reactivated in space flight crews (Pierson et al, 2005; Shearer et al., 2005; Stowe et al., 2001). Studies using the hindlimb unloading model of rodents some space flight conditions have shown that hindlimb unloading of mice has resulted in decreased resistance to infection with bacteria and viruses (Sonnenfeld et al., 2003). Therefore, the potential for space flight conditions inducing changes in the immune systems yielding altered resistance to infection and/or tumors certainly exists. However, it is also clear that decreased resistance to infection or tumors has not been a "show-stopper" to date for the space flight program (Space Studies Board, 1998; Sonnenfeld et al., 2003). In almost every case, crews have been able to function normally without serious incident.

However, we are now facing a new era of space flight, i.e. the development of exploration class missions. Exploration of space beyond low earth orbit has the possibility of changing the conditions of the flight environment to create greater risk.

THE EXPLORATION CLASS MISSION ISSUES

As we now move towards exploration class missions beyond low earth orbit, we face new scenarios then what has been seen before during space flight missions (Table 1). We will face new types of radiation that have never b been encountered before by humans in space or, if they have been encountered, humans have never been exposed to them in space for the length of time they will face in the future (Space Studies Board, 1996).

Additionally, crews will be away from earth for a more extended period of time, with limited chances for very rapid rescue, return or re-supply (Board on Health Science Policy, 2001). This means a scenario could develop where if an infection developed and an antibiotic

Table 1. Potential New Risks for Exploration Class Missions

1) New forms of radiation
2) Crew isolation with no chance of rapid rescue or treatment
3) Altered immune system with potential altered virulence of pathogens

was taken to which the organisms was resistant, there would be limited opportunity to provide a different antibiotic or to rapidly return the individual to earth for additional treatment. Additionally there have been unconfirmed reports of antibiotics not working as effectively in space as on the ground (Space Studies Board, 1998).

An additional challenge that may be faced was made clear by some modeling experiments on earth (Nickerson et al., 2001, 2004; Wilson et al., 2002). In these experiments, bacteria were grown in clinostat-derived tissue culture models that replicated some space flight conditions such as low shear. These experiments clearly demonstrated that growth in those conditions altered both the growth rates of the bacteria and the expression of virulence factors (Nickerson et al., 2001, 2004; Wilson et al., 2002). Therefore, a possible scenario could develop where a bacteria or virus that is part of the normal microbial components of human microbial flora (that normally does not cause a problem for the host) could have enhanced growth and virulence in space, not respond well to the available antibiotics, and the astronaut host for this bacteria could have a space-flight impaired immune response (that would not have a negative effects under normal conditions). The possibility for a very serious infectious disease problem that could threaten both the health of the astronaut and the success of the mission is obvious!

We must be prepared to both detect and deal with this problem. There are several steps that should be taken (Table 2). We must carry out experimentation in appropriate space flight models on the ground and in space to fully identify the risk. We must know what changes happen to infectious agents and to the host immune system under the conditions we will encounter in exploration class missions.

We must know how to test whether the host is compromised. This involves development of standards for immunological parameters that need to be tested for astronauts on a routine basis. This testing needs to be carried out on the ground before flight to establish base lines and on a regular basis before and after the mission. We must assure that the standard testing can actually be carried out in space both on the exploration vehicles and on the ground on the Moon or Mars. Only then can we see if the host's immune defenses are compromised.

We must also assure that we are prepared to deal with violations of standards induced by space flight conditions. This would involve understanding the growth and virulence characteristics of microorganisms that could be potential pathogens under space flight conditions. Additionally, there is a great need for testing of antibiotics and antivirals to ensure that they actually function as they are designed under space flight conditions. We must also assure that countermeasure are developed that will ameliorate or eliminate any negative effects of the space flight environment on the immune system. In case of antimicrobials or lack of provision of the appropriate antimicrobials, be must be sure that the crews are as immuncompetent as possible throughout their space flight missions.

Table. 2. Challenges for the Future

1) Establishing risk
2) Establishing immunological standards
3) Determining what research is required to deal with any issues that are identified as a result of violation of standards during flight.

CONCLUSION

Only by vigilance and preparedness can we avoid unexpected deleterious effects of exploration class space flights on the immune system and, therefore, the health of the crews. A high level of preparedness will be required to assure the health and survivals of exploration class mission crews and the successful completion of exploration class missions.

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