

<b>Fiscal Year:</b>	FY 2005	<b>Task Last Updated:</b>	FY 11/23/2004
<b>PI Name:</b>	Pierson, Duane L Ph.D.		
<b>Project Title:</b>	Incidence of Latent Virus Shedding During Space Flight-DSO 493		
<b>Division Name:</b>	Human Research		
<b>Program/Discipline:</b>	HUMAN RESEARCH		
<b>Program/Discipline--Element/Subdiscipline:</b>	HUMAN RESEARCH--Operational and clinical research		
<b>Joint Agency Name:</b>	<b>TechPort:</b>	No	
<b>Human Research Program Elements:</b>	(1) <b>HHC:</b> Human Health Countermeasures		
<b>Human Research Program Risks:</b>	(1) <b>Immune:</b> Risk of In Mission Impacts, Adverse Health Events or Long-Term Health Impacts due to Altered Immune Response		
<b>Space Biology Element:</b>	None		
<b>Space Biology Cross-Element Discipline:</b>	None		
<b>Space Biology Special Category:</b>	None		
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<b>Zip Code:</b>	77058	<b>Congressional District:</b>	22
<b>Comments:</b>			
<b>Project Type:</b>	Flight	<b>Solicitation / Funding Source:</b>	96-OLMSA-01
<b>Start Date:</b>	04/01/1999	<b>End Date:</b>	08/01/2008
<b>No. of Post Docs:</b>	0	<b>No. of PhD Degrees:</b>	
<b>No. of PhD Candidates:</b>	0	<b>No. of Master' Degrees:</b>	
<b>No. of Master's Candidates:</b>	0	<b>No. of Bachelor's Degrees:</b>	
<b>No. of Bachelor's Candidates:</b>	0	<b>Monitoring Center:</b>	NASA JSC
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<b>Flight Program:</b>			
<b>Flight Assignment:</b>	In flight development phase (data collection has begun)		
<b>Key Personnel Changes/Previous PI:</b>			
<b>COI Name (Institution):</b>	Mehta, Satish K. Ph.D. ( Enterprise Advisory Services Inc. )		
<b>Grant/Contract No.:</b>	None		
<b>Performance Goal No.:</b>			
<b>Performance Goal Text:</b>			

Task Description:	<p>The reactivation of latent herpesviruses will increase health risks for crewmembers on ambitious long-duration NASA missions, such as those on the International Space Station and planetary exploration missions. Spaceflight conditions—stress and decreased cellular immunity—favor reactivation of herpesviruses. We previously reported that reactivation of Epstein-Barr virus (EBV) in crewmembers was associated with spaceflight. The number of copies of EBV DNA from saliva samples taken during space shuttle flights was about 10-fold higher than before and after spaceflight. These studies, performed on short-term spaceflights (~12 days), also supplied evidence that EBV reactivation progresses as the duration of flight increases. We have also shown increased reactivation and shedding of cytomegalovirus (CMV) in astronauts during flight. These conditions may increase the risk that the virus will be transmitted to crewmembers that do not have antibodies to it and could develop an active CMV infection. Recent data from our laboratory have shown reactivation of varicella-zoster herpesvirus (VZV) in astronauts during short-term spaceflights. Primary VZV infection (chickenpox, or varicella) leads to latent infection in cranial nerves and dorsal root and autonomic ganglia, from which the virus can reactivate to produce shingles (zoster). VZV reactivation during spaceflight thus poses a significant health risk to crewmembers. VZV reactivation after orofacial surgery has been seen clinically as delayed facial palsy and detected in the laboratory as virus DNA in saliva or as an increased antibody response. To determine the frequency of reactivation of latent viruses, latent virus shedding, and clinical disease after exposure to the physical, physiological, and psychological stressors associated with space flight The proposed research addresses a potentially important medical risk to astronauts, and will clearly and directly benefit their health by providing scientific knowledge that can be used to define the risk and develop appropriate countermeasures. If we show that the viral (EBV or VZV) DNA that we find in astronauts' saliva represents the shedding of infectious virus, we will have shown that during space flight, astronauts have a significant risk of contracting diseases caused by these viruses (VZV in particular), and of spreading the virus. If we show that increased viral reactivation is associated with changes in the circadian rhythm of astronauts' salivary cortisol and dehydroepiandrosterone (DHEA), and that those changes are associated with changes in crew members' immune response, we will have provided evidence for a mechanism by which stress before and during space flight could increase virus reactivation. If we find that the likelihood of viral reactivation and the abundance of infectious virus increase on long-duration missions, we will have shown that the risk of crew members' health and performance being affected by viral reactivation is an important consideration on long-duration missions.</p>
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	<p>Earth benefits: · Information gained from experiments performed on Space Shuttle missions will be essential for development of countermeasures for long-duration missions. · This molecular approach for monitoring viruses may be rapid and reliable tool for early detection of stress and diminished immunity. · This technology may provide clinically relevant data for management of patients suffering from chronic and acute stress. · Viral surveillance may lead to early intervention to minimize adverse health effects of acute/chronic stress.</p>
Task Progress:	<p>Two studies were completed in the year 2003-2004:</p> <ol style="list-style-type: none"> <li>1. EBV flight experiment: Epstein-Barr Virus Shedding by Astronauts During Space Flight (Journal of Brain Behavior and Immunology, Inpress 2004) ABSTRACT Patterns of Epstein-Barr virus (EBV) reactivation in 32 astronauts and 18 healthy age-matched control subjects were characterized by quantifying EBV shedding. Saliva samples were collected from astronauts before, during, and after 10 space shuttle missions of 5 to 14 d duration. At one time point or another, EBV was detected in saliva from each of the astronauts. Of 1398 saliva specimens from 32 astronauts, polymerase chain reaction analysis showed that 314 (23%) were positive for EBV DNA. Examination by flight phase showed that 29% of the saliva specimens collected from 28 astronauts before flight were positive for EBV DNA, as were 16% of those collected from 25 astronauts during flight and 16% of those collected after flight from 23 astronauts. The mean number of EBV copies from samples taken during the flights was 417, significantly greater (<math>p &lt; 0.05</math>) than the copies from the preflight (40) and postflight (44) phases. In contrast, the control subjects shed EBV DNA with a frequency of 3.7% and mean number of EBV copies of 40 per mL of saliva. Ten days before flight and on landing day, titers of antibody to EBV viral capsid antigen were significantly (<math>p &lt; 0.05</math>) greater than baseline levels. On landing day, urinary levels of cortisol and catecholamines were greater than their preflight values. In a limited study (<math>n = 5</math>), plasma levels of substance P and other neuropeptides were also greater on landing day. Increases in the number of viral copies and in the amount of EBV-specific antibody were consistent with EBV reactivation before, during, and after space flight.</li> <li>2. VZV flight experiment: Stress-Induced Sub-clinical Reactivation of Varicella Zoster Virus in Astronauts (Journal of Medical Virology, 2004) ABSTRACT Varicella zoster virus (VZV) becomes latent in human ganglia after primary infection. VZV reactivation occurs primarily in elderly individuals, organ transplant recipients, and patients with cancer and AIDS, correlating with a specific decline in cell-mediated immunity to the virus. VZV can also reactivate after surgical stress. The unexpected occurrence of thoracic zoster two days before space flight in a 47-year-old healthy astronaut from a pool of 81 physically-fit astronauts prompted our search for VZV reactivation during times of stress to determine whether VZV can also reactivate after non-surgical stress. We examined total DNA extracted from 312 saliva samples of 8 astronauts before, during and after space flight for VZV DNA by polymerase chain reaction: 112 samples were obtained 234 to 265 days before flight, 84 samples on days 2 through 13 of space flight, and 116 samples on days 1 through 15 after flight. Before space flight, only one of the 112 saliva samples from a single astronaut was positive for VZV DNA. In contrast, during and after space flight, 61 of 200 (30%) saliva samples were positive in all 8 astronauts. No VZV DNA was detected in any of 88 saliva samples from 10 healthy control subjects. These results indicate that VZV can reactivate subclinically in healthy individuals after non-surgical stress.</li> </ol>
Bibliography Type:	Description: (Last Updated: 03/24/2020)
Articles in Peer-reviewed Journals	Pierson DL, Stowe RP, Phillips TM, Lugg DJ, Mehta SK. "Epstein-Barr virus shedding by astronauts during space flight." Brain Behav Immun. 2005 May;19(3):235-42. <a href="#">PMID: 15797312</a> , May-2005
Articles in Peer-reviewed Journals	Mehta SK, Cohrs RJ, Forghani B, Zerbe G, Gilden DH, Pierson DL. "Stress-induced subclinical reactivation of varicella zoster virus in astronauts." J Med Virol. 2004 Jan;72(1):174-9. <a href="#">PMID: 14635028</a> , Jan-2004

Articles in Peer-reviewed Journals	Ling PD, Lednicky JA, Keitel WA, Poston DG, White ZS, Peng R, Liu Z, Mehta SK, Pierson DL, Rooney CM, Vilchez RA, Smith EO, Butel JS. "The dynamics of herpesvirus and polyomavirus reactivation and shedding in healthy adults: a 14-month longitudinal study." J Infect Dis. 2003 May 15;187(10):1571-80. Epub 2003 Apr 30. <a href="#">PMID: 12721937</a> , Jan-2004
Presentation	Mehta, S.K.; Smith, T.D., Lugg D.J.; Phillips, T.M.; Ott, C.M.; Donovan, K.M.; Klemes, P.; Pierson , D.L. "Reactivation of Latent Herpes Viruses in Antarctica. " Aerospace Medical Association 75th Annual Scientific Meeting May 2-6, 2004, Anchorage, Alaska. May-2004
Presentation	Mehta, S.K.; Laudenslager, M.L.; Robinson-Whelen, S.; Stowe, R.P.; Cohrs, R.J.; Ott, C.M.; Pierson, D.L. "Latent Herpes Virus Reactivation in Aquanauts" Conference on Space Habitation Research and Technology Development 01-07-04 Jan-2004
Presentation	Pierson, D.L.and Mehta, S.K. "Stress-Induced Subclinical Reactivation of Varicella-Zoster Virus (VZV) in Astronauts " Bioastronautics Investigators Workshop, Galveston, TX Jan-2003
Presentation	Mehta S.K.; Cohrs R.J.; Lugg D.J.and Pierson D.L. "Herpesvirus Reactivation Associated with Spaceflight " 14th IAA Humans In Space Symposium - Living in Space: Scientific, Medical and Cultural Implications. The Banff Centre in Banff, Alberta, Canada May-2003