

<b>Fiscal Year:</b>	FY 2008	<b>Task Last Updated:</b>	FY 02/26/2009
<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>	Shuttle/ISS		
<b>Flight Assignment:</b>	STS ; ISS In flight development phase (data collection has begun)		
<b>Key Personnel Changes/Previous PI:</b>			
<b>COI Name (Institution):</b>	Mehta, Satish Ph.D. ( Enterprise Advisory Services Inc. )		
<b>Grant/Contract No.:</b>	None		
<b>Performance Goal No.:</b>			
<b>Performance Goal Text:</b>			

	<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.</p>
<b>Task Description:</b>	<p>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</p> <p>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> <p>See also <a href="https://">https://</a></p>
<b>Rationale for HRP Directed Research:</b>	
<b>Research Impact/Earth Benefits:</b>	<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>
<b>Task Progress:</b>	<p>Varicella zoster virus (VZV) causes varicella (chickenpox) after which virus becomes latent in ganglia along the entire neuraxis. Virus reactivation produces zoster (shingles). Infectious VZV is found in vesicles of patients with zoster and varicella, but virus shed in the absence of disease has not been documented. VZV DNA was previously detected in saliva of astronauts during and after spaceflight, a uniquely stressful environment in which cell mediated immunity (CMI) is temporally dampened. The decline in CMI to VZV associated with zoster led to the hypothesis that infectious VZV would also be present in the saliva of astronauts subjected to stress of spaceflight. Herein, not only was the detection of salivary VZV DNA associated with spaceflight validated, but also infectious virus was detected in saliva from 2 of 3 astronauts. This is the first demonstration of shed of infectious VZV in the absence of disease. J. Med. Virol. 80:1116-1122, 2008</p> <p>Fifty-four patients with herpes zoster were treated with valacyclovir. On treatment days 1, 8, and 15, pain was scored and saliva examined for varicella-zoster virus (VZV) DNA. VZV DNA was found in every patient the day treatment was started and later disappeared in 82%. There was a positive correlation between the presence of VZV DNA and pain and between VZV DNA copy number and pain (<math>P&lt;.0005</math>). VZV DNA was present in 1 patient before rash and in 4 after pain resolved and was not present in any of 6 subjects with chronic pain or in 14 healthy subjects. Analysis of human saliva has potential usefulness in the diagnosis of neurological disease produced by VZV without rash. The Journal of Infectious Diseases 2008;197:654-7</p> <p>This task addresses the need to understand the effects of spaceflight on human immunity. This task directly addresses the risks associated with infectious diseases since all of the latent viruses studied are infectious disease risks. VZV is a specific risk to the astronaut age group. In addition, the risks associated with decreased immunity during spaceflight has been hampered from the beginning in the technical difficulties that prevent inflight analyses. The viral reactivation task allows assessment of immune status (especially cell-mediated immunity) during the flight phase by collection of saliva during space flight.</p>
<b>Bibliography Type:</b>	Description: (Last Updated: 03/24/2020)
<b>Articles in Peer-reviewed Journals</b>	<p>Satyaprakash AK, Tremaine AM, Stelter AA, Creed R, Ravanfar P, Mendoza N, Mehta SK, Rady PL, Pierson DL, Tying SK. "Viremia in acute Herpes zoster." Journal of Infectious Diseases. 2009 Jul 1;200(1):26-32. PubMed <a href="#">PMID: 19469706</a>, Jul-2009</p>
<b>Articles in Peer-reviewed Journals</b>	<p>Zhang Y, Rohde LH, Emami K, Hammond D, Casey R, Mehta SK, Jeevarajan AS, Pierson DL, Wu H. "Suppressed expression of non-DSB repair genes inhibits gamma-radiation-induced cytogenetic repair and cell cycle arrest." DNA Repair (Amst). 2008 Nov 1;7(11):1835-45. <a href="#">PMID: 18703169</a>, Nov-2008</p>
<b>Articles in Peer-reviewed Journals</b>	<p>Crucian BE, Stowe RP, Mehta SK, Yetman DL, Leal MJ, Quiarte HD, Pierson DL, Sams CF. "Immune status, latent viral reactivation, and stress during long-duration head-down bed rest." Aviation, Space, and Environmental Medicine. 2009 May;80(5 Suppl):A37-44. PubMed <a href="#">PMID: 1947616</a>, May-2009</p>

Articles in Peer-reviewed Journals	Cohrs RJ, Mehta SK, Schmid DS, Gilden DH, Pierson DL. "Asymptomatic reactivation and shed of infectious varicella zoster virus in astronauts." J Med Virol. 2008 Jun;80(6):1116-22. <a href="#">PMID: 18428120</a> , Jun-2008
Articles in Peer-reviewed Journals	Mehta SK, Tying SK, Gilden DH, Cohrs RJ, Leal MJ, Castro VA, Feiveson AH, Ott CM, Pierson DL. "Varicella-zoster virus in the saliva of patients with herpes zoster." J Infect Dis. 2008 Mar 1;197(5):654-7. <a href="#">PMID: 18260763</a> , Mar-2008
Articles in Peer-reviewed Journals	Mehta SK, Crucian B, Pierson DL, Sams C, Stowe RP. "Monitoring immune system function and reactivation of latent viruses in the Artificial Gravity Pilot Study." J Gravit Physiol. 2007 Jul;14(1):P21-5. <a href="#">PMID: 18372687</a> , Jul-2007
Articles in Peer-reviewed Journals	Stowe RP, Yetman DL, Storm WF, Sams CF, Pierson DL. "Neuroendocrine and immune responses to 16-day bed rest with realistic launch and landing G profiles." Aviat Space Environ Med. 2008 Feb;79(2):117-22. <a href="#">PMID: 18309909</a> , Feb-2008
Articles in Peer-reviewed Journals	Mehta SK, Pierson DL. "Reactivation of latent herpes viruses in cosmonauts during a Soyuz taxi mission." Microgravity - Science and Technology 2007 Sep;19(5-6):215-8. <a href="http://dx.doi.org/10.1007/BF02919485">http://dx.doi.org/10.1007/BF02919485</a> , Sep-2007
Articles in Peer-reviewed Journals	Mehta SK, Laudenslager ML, Stowe RP, Crucian BE, Sams CF, Pierson DL. "Multiple latent viruses reactivate in astronauts during Space Shuttle missions." Brain Behav Immun. 2014 Oct;41:210-7. Epub 2014 Jun 2. <a href="http://dx.doi.org/10.1016/j.bbi.2014.05.014">http://dx.doi.org/10.1016/j.bbi.2014.05.014</a> ; PubMed <a href="#">PMID: 24886968</a> , Oct-2014
Articles in Peer-reviewed Journals	Mehta SK, Laudenslager ML, Stowe RP, Crucian BE, Feiveson AH, Sams CF, Pierson DL. "Latent virus reactivation in astronauts on the International Space Station." npj Microgravity. 2017 Apr 11;3(1):11. <a href="http://dx.doi.org/10.1038/s41526-017-0015-y">http://dx.doi.org/10.1038/s41526-017-0015-y</a> , Apr-2017
Articles in Peer-reviewed Journals	Rooney BV, Crucian BE, Pierson DL, Laudenslager ML, Mehta SK. "Herpes virus reactivation in astronauts during spaceflight and its application on Earth." Front Microbiol. 2019 Feb 7;10:16. Review. eCollection 2019. <a href="https://doi.org/10.3389/fmicb.2019.00016">https://doi.org/10.3389/fmicb.2019.00016</a> ; PubMed <a href="#">PMID: 30792698</a> ; PubMed Central <a href="#">PMCID: PMC6374706</a> , Feb-2019
Books/Book Chapters	Pierson DL, Mehta SK, Stowe RP. "Reactivation of Latent Herpes Viruses in Astronauts." in "Psychoneuroimmunology. 4th edition." Ed. R. Ader. Amsterdam ; Boston : Elsevier/Academic Press, c2007. vol II, p. 851-868., Aug-2007
Books/Book Chapters	Mehta SK, Pierson DL. "Artificial Gravity and the Immune System Function." in "Artificial gravity." Ed. G. Clement, A. Buckley. Hawthorne, Calif. : Microcosm Press ; New York : Springer, c2007., Sep-2007
Patents	US patent application 61/087,045. US patent application # 61/087,045 was filed on August 7, 2008. Aug-2008 Pierson DL. "Methods for diagnosis of Varicella zoster virus infection."