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Risk of severe COVID-19 infection in International Space Station astronauts despite routine pre-mission measures

To the Editor:

In the article "SARS-CoV-2 Pandemic Impacts on NASA Ground Operations to Protect ISS Astronauts,"[1] recently published in the *Journal of Allergy and Clinical Immunology: In Practice*, Makedonas et al addressed current medical tests and clinical monitoring procedures that ensure the health and safety of National Aeronautics and Space Administration astronauts, including a prelaunch quarantine (to decrease infectious disease risk), the issue of immune system dysregulation during the mission, and post-mission astronauts' vulnerability to infectious disease as well as post-mission quarantine protocols. They also highlighted the risk associated with poor COVID-19 prognosis in immunocompromised individuals such as postflight astronauts. Although the article by Makedonas et al can be considered a significant contribution to the field of space medicine in the COVID-19 pandemic era, it has a major omission. We believe that the authors are overly focused on postflight issues, whereas the cardinal issue is severe infection during the mission, as addressed in recent publications.[2,3] In this commentary, we provide evidence indicating that even with the most reliable pre-mission screening and quarantine strategies, astronauts with a latent (hidden, inactive, or dormant) SARS-CoV-2 infection can inadvertently be sent to space. Although according to some early studies, the rate of asymptomatic infections was as high as 81%,[4] a meta-analysis that included 13 studies involving 21,708 individuals reported asymptomatic presentation in 17% of the population.[5] Accordingly, when there is a dormant infection in these individuals, not only they are unaware of the infection, it is likely that they could successfully pass all prelaunch medical tests. The findings of new studies clearly support the key idea discussed in our article, "Can Reactivation of SARS-CoV-2 Decrease the Chance of Success of Future Deep Space Missions?"[2]. Regarding reactivation, a recent study[6] showed that among 109 patients, 29 experienced reactivation (27%), and seven of these were symptomatic (24%). Given this consideration, during a long-term space mission, when the immune system starts to weaken, the dormant infection may progress to a severe infection. This issue is of paramount importance because it directly affects the chance of success of any mission. Further studies are warranted to clarify the different aspects of this issue.

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Conflicts of interest: The authors declare that they have no conflicts of interest.
Received for publication May 15, 2021; accepted for publication May 17, 2021.

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https://doi.org/10.1016/j.jaip.2021.05.043

Reply to "Risk of severe COVID-19 infection in International Space Station astronauts despite routine pre-mission measures"

To the Editor:

We thank Mortazavi et al[1] for their interest in our article.[2] In their commentary, the salient point raised is that risk for SARS-CoV-2 reactivation during spaceflight is a concern that was unaddressed in our original article.

The point of the article was to share how the National Aeronautics and Space Administration (NASA) adjusted protocols to reduce risk for returning astronauts during the initial stages of the pandemic. Returning astronauts manifest a defined pattern of immune dysregulation, and the early-pandemic crews returned through a unique set of vehicle transfers (International Space Station [ISS] to Houston, via Kazakhstan) making clinical care a unique challenge. The article details all of the protocols put in place to protect crewmembers who are perceived to be more vulnerable to a serious prognosis if infected immediately after landing. The protocols span various operational impacts, including limiting contacts, adjusting postflight schedules, and for the first returning crew, monitoring of immune status before release from quarantine.

The commentary authors speculate that SARS-CoV-2 infection is challenging to detect ("hidden, inactive, or dormant"), and therefore an astronaut may launch to space with an asymptomatic but active infection that would worsen owing to immune compromise during flight. In fact, our article did not address protections for launching crewmembers; it was specific to returning crewmembers. The launch and landing clinical care scenarios are very different, and even more so because most American astronauts will now launch from US soil on a *SpaceX Dragon* capsule. Nevertheless, the commentary supposition is interesting and certainly worth considering. NASA protocols, including some specific for SARS-CoV-2, are designed to protect crews before launch. They should mitigate to the maximum extent possible the risk for an astronaut launching with an asymptomatic