Aerospace Medicine Clinic

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You're the NASA Flight Surgeon for an International Space Station (ISS) mission during the first year of the COVID-19 pandemic. Your crew are among the last unvaccinated individuals to travel to ISS prior to the release of mRNA vaccines. Thanks to NASA and International Partners cooperation, preflight quarantine was successful, and your crew is safely aboard the ISS with no active medical issues.

The world's first mRNA vaccines were released a month ago, and during your most recent weekly Private Medical Conferences (PMCs) with your crew (the telemedicine version of a clinic visit), you receive several questions about the possibility of sending COVID-19 vaccines to ISS on the next cargo resupply vehicle. As rationale for requesting on-board vaccination, your crew cite the relative immunosuppression experienced by long-duration spaceflight crews[3] and their risk of developing COVID-19 during the immediate postflight period.

1. What changes in immunology have been seen in long-duration spaceflight that would concern you about crew susceptibility to COVID-19?
   A. Reduction in T-cell CD4 and CD8 function.
   B. Subclinical neutropenia.
   C. Reactivation of EBV, CMV, and VZV in flight.
   D. Relative pancytopenia.
   E. Lack of band neutrophils.

ANSWER/DISCUSSION

1. A. Reduction in T-cell CD4 and CD8 function. The concern that possible degradation of immune system correlates during spaceflight could worsen COVID-19 prognosis prompted additional immunologic investigation in crewmembers returning during the first year of the pandemic. Spaceflight-related T-cell changes were shown to resolve between 7–10 d postflight based on multiparametric flow cytometry of blood samples[7]; these changes have been documented elsewhere[6] and are considered to be subclinical. Reactivation of latent viruses in spaceflight has been documented,[8] but this is indirectly related to the question, which pertains to the immune system's ability to mount a cell-mediated response to a new virus; SARS-CoV-2 is not considered to have latent or reactivation features at this time. B, D, and E have not been documented in spaceflight.

Wanting to advocate for your crew's concerns and interested in preventing postflight COVID-19 to the extent possible, you consult your pharmacy team to better understand the feasibility of transport and stowage logistics. You learn there is ultra-cold (–20°C) stowage space available on the next cargo vehicle that could support flying up vials of the Moderna COVID-19 vaccine, and the pharmacy team thoroughly reviews the detailed Moderna vaccine administration information.

2. Based on known spaceflight pharmacology and Moderna mRNA vaccine constraints, which of the following statements does NOT apply to theoretical use of the Moderna vaccine in spaceflight?
   A. Medications requiring ultra-cold stowage must maintain documented temperature recording logs, from initial terrestrial packing to vehicle-loading and ultimately unpacking aboard ISS.
   B. Vibrational effects of launch, which can lead to foaming of liquid medications, coupled with the lack of air-fluid separation levels in microgravity, make it difficult to aspirate liquid medications into syringes, potentially requiring additional vials to provide "buffer" volume.
   C. Moderna multidose vials contain 10 doses of vaccine with some buffer volume, thus 1 vial is sufficient for fully vaccinating 5 crewmembers with 2 doses each.
   D. Shaking or vibration, as on a launch vehicle, of Moderna mRNA vaccine should be minimized, rendering the ultimate effectiveness of the vaccine unknown.
   E. Moderna mRNA vaccine expires after 6 mo at –20°C, 30 d refrigerated, and 12 h after vial puncture, and cannot be re-refrigerated.

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ANSWER/DISCUSSION

2. C. One vial is not sufficient for fully vaccinating five crewmembers, as only half the vial would be used and need to be discarded after first dose administration. This is because it cannot be re-refrigerated or refrozen once brought to room temperature and/or pierced.[5] Preventing temperature excursions during transport is paramount for medications requiring ultra-cold storage, especially considering the transport and launch of spaceflight cargo occur at warmer latitudes (i.e., Texas, Florida). As a result of these handling constraints, refreezing, re-refrigerating, or agitating mRNA vaccine product is not advised.[1] Vibrational effects of launch vehicles on liquid medications has been shown to result in excessive foaming.[4] Multiple ISS crews have filmed demonstrations of the challenges and solutions to overcoming lack of air-fluid separation levels for adequate liquid medication aspiration and administration in microgravity.[2]

You realize the need to also consider expected side effects after administration, especially after the second dose. You turn to the FAA policy, which recommends DNIF for 48 hrs after vaccine administration, and review possible adverse reactions.

3. Knowing your crew are expected to respond appropriately to emergencies 24/7 aboard ISS, how could you potentially apply this information to in-flight astronauts?
   A. Vaccinate all crew simultaneously, as the cumulative risk of a severe adverse reaction for fully vaccinating five crewmembers is still sufficiently low (<1%).
   B. Consider staggering doses by 48 h between crewmembers.
   C. Ensure the correct quantities of supplies are present to address adverse reactions, such as anaphylaxis in a remote environment.
   D. B and C only.
   E. A, B, and C.

ANSWER/DISCUSSION

3. D. While the risk of allergic reaction with the Moderna vaccine is indeed <1% (1 in 400,000 per dose),[5] this does not negate the need to follow appropriate medical practice by ensuring the presence of a treatment or reversal agent for adverse reactions, particularly in a remote environment with limited resources. While the FAA Office of Aerospace Medicine policy provides guidance regarding side effects of vaccination for fliers,[10] it was not written with on-orbit ISS crewmembers in mind. Theoretically, the spirit of this policy may support staggering doses between half the crew by 1 wk to minimize operational risk to crew and ISS (e.g., ideally vaccinating half the crew on a Friday evening before a weekend, and the second half of the crew the following Friday, giving each group 48 h of relatively minimal responsibilities and sufficient recovery time).

However, staggering doses as proposed above would require additional vials given the limitation that a vial must be discarded 12 h after puncture. Wastage of this valuable resource would be significant since one vial would be used for 2–3 first doses, with the remainder of the vial contents rendered unusable (7–8 unused doses). As an Aerospace Medicine specialist with training in population health, you begin to feel uncomfortable with the ramifications of the request when you realize that the required logistics would result in more wasted doses than used doses.

4. You decide to request a formal Medical Ethics consult for additional support. What ethical aspects are considered in their response?
   A. Responsible resource stewardship (i.e., current supply-to-demand ratio of available vaccine for actively vulnerable individuals on Earth vs. those aboard ISS).
   B. Amount of taxpayer funds invested in astronaut selection, training, and health maintenance, as well as the need to protect this investment by preventing potential long-term sequelae of COVID-19 that could be medically disqualifying.
   C. Whether this intervention will change the already-established landing and postflight precautions.
   D. A & C only.
   E. All of the above.

ANSWER/DISCUSSION

4. E. These are all considerations that ultimately resulted in the Ethics consultant recommending not to pursue on-board vaccine administration, balancing key medical ethics principles of beneficence, nonmaleficence, and justice.[9] Further supporting this decision was the fact that prior ISS landings during the pandemic were successfully executed with proper precautions, without transmission of SARS-CoV-2 to returned crewmembers.

You break the news to your crew that the vaccine request will not be fulfilled and cite the work above. They understand the rationale and are appreciative of the thorough investigation.

AEROMEDICAL DISPOSITION

Your crew remain healthy aboard ISS for another several months before landing preparations begin. Johnson Space Center has enacted Post-Flight COVID Countermeasures (PFCC) for each landing since the pandemic onset. These include pre-landing quarantine, PCR testing, and proper PPE precautions for all personnel directly supporting landing operations and interacting with returning crew. You enforce PFCC during your landing operations and the immediate postflight period, with no cases of SARS-Cov-2 transmitted to your crew.

You wait the recommended 7 d post-landing prior to administering the first dose of mRNA vaccine. This allows for presumptive return to preflight baseline of T-cell function for optimal immune system response; it also avoids any confounding between symptoms that are part of the expected postflight physiological response and symptoms of infection or vaccine side effects. This measure also preserves any immune-related research data taken in the first week postflight. Your crew tolerates their first dose of mRNA vaccine with no complications, followed by the second dose at the recommended timeframe, completing their initial series of vaccination against SARS-CoV-2.

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Erratum

Mayes RS, Keirns CJ, Hicks AG, Menner LD, Lee MS, Wagner JH, Baltzer RL. *USAFSAM Aeromedical Consultation Service Medical Risk Assessment and Airworthiness Matrix.* Aerosp Med Hum Perform. 2023; 94(7):514–522.

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In the above article, the authors missed errors in the Methods section, p. 517, left-hand column, first full paragraph, eighth sentence and in the equations about two-thirds of the way down the page. The sentence in question says "For instance, an "occasional" event would occur once every 10,000 (10^{-4}) to 100,000 (10^{-5}) h." It should read "…an "occasional" event would occur once every 10,000 (10^{4}) to 100,000 (10^{5}) h." In the equations, the denominators show as, respectively, 10^{-5} and 10^{-4} (see highlight in the equation below).

$$1-\left[1-\left(\frac{1}{10^{-5}}\right)\right]^{365.25*24} = 0.0839$$

$$1-\left[1-\left(\frac{1}{10^{-4}}\right)\right]^{365.25*24} = 0.5838$$

These are incorrect. The denominators should simply be 10^{5} and 10^{4}, respectively.

The authors apologize for these mistakes.