

Rash Spaceflight Associated CLIFF Peer Review

1. *Strength of evidence presented in CLIFF in modeling the characteristics and mission impact of this medical condition within the spaceflight environment?*

Score: 2

Grading Scale:

4 - Confident

3 - Somewhat confident

2 – Neutral

1 – Somewhat unconfident

0 – Not confident

2. How confident are you that these data accurately represent the spaceflight environment?	Tables 1, 2 Composite Incidence and Level of Confidence	Table 3, 4 BC/WC Loss of Crew and probability	Table 4 - Clinical Phase 1, 2 durations Table 5 – CP 2 Loss of Crew	Table 4 – RTDC % Table 6 – RTDC Loss of Crew	Table 4 – Loss of Crew Life % Table 7 – Loss of Crew Life, Loss of Crew	Table 8 – TI
Score	3	2	3	1	3	3

Comments and limitations:

1. **General comments.** Skin rashes have been reported frequently during spaceflight, perhaps more commonly than would be expected. Some authors believe that this may be a result of immune system dysregulation, and others have noted that vasodilation in microgravity may be a factor. It is also true that maintaining standard levels of hygiene is more difficult in space and may contribute to this condition. As a result, “spaceflight-related skin rashes” was added to the medical condition list as a phenomena separate from allergic, bacterial, viral or fungal skin eruptions. It might be expected that skin rashes are under-reported as some may be quite minor and not require treatment. It is also difficult to distinguish between the various types of rashes from the available literature, whether they are infectious in origin versus spaceflight-related (idiopathic). The best case is considered to be mild to moderate and uncomplicated skin rash that responds to topical treatment. while the worst case is moderate to severe skin rash, covering an extensive area and that requires more than 5-7 days of topical treatment, requires a course of oral or IV medications, or is refractory to treatment.

2. **Incidence.** The composite incidence rate was derived from two LSAH data reports; however, the raw data that was used is not available. Therefore, incidence data was derived from a previous

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IMM CLIFF entitled "Skin Rash." Per the IMM CLIFF, skin infections, petechiae, hyperemia (allergic reaction), dry skin and herpes zoster were not included in case counts for this condition and thus would fit the new case definition. During spaceflight, determination of the etiology of a skin rash is difficult; therefore, categorization of this condition is problematic. In addition, mild skin rashes may go unreported and many will likely resolve without intervention, leading to an under-estimation of the true incidence. The best case/worst case probabilities used data from a previous IMM CLIFF in which 3 of 26 events fell under the worst case definition. There is almost a total lack of studies that would help determine the untreated worst case clinical duration. The other clinical phase durations are supported by terrestrial evidence, and I am in agreement with their calculation. Using subject matter expert opinion a value of "1%" for RTDC for treated worst case was assigned to reflect that this would be an extremely unlikely event. For untreated worst, a wide range of values was given because of the lack of data to support a more definitive number. Loss of crew life is not expected for this condition. The probability density curve that was derived appears to be a reasonable representation of the data presented.

3. Clinical phase data. I am in agreement with the clinical phase 1 duration entered in this CLIFF. This data was compiled by a team of expert clinicians, and I was involved in the discussions leading to the calculation of the clinical phase duration. CP2 was supported by terrestrial evidence.

4. Task impairment. The analysis was performed and reviewed by a separate team of expert clinicians. I am aware of the methods that were used but did not directly participate in the discussions.

5. Dependence on mission phase or duration of mission. This medical condition is not dependent on mission phase.

6. Limitations

- There may be some overlap between spaceflight-associated skin rashes and other CLIFF conditions relating to skin eruptions or infections.
- Under-reporting for this condition could have occurred during past space missions due to subtle rashes that were not of clinical consequence. This may result in underestimation of the incidence.
- The authors did not have access to the original LSAH data and thus there was a dependence on already published sources.
- After extensive literature searches performed by the editors for this condition, no studies were found that informed hospitalization rates, likely a result of this condition's mostly benign consequences.
- The authors to this CLIFF did not have access to the original LSAH data and thus there was an implied dependence on already published sources.
- Given a paucity of data, subject matter expertise was used to assign values for worst case RTDC probabilities.

Reviewed by:

David C. Hilmers