

Allergic Reaction (Mild to Moderate) 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: 3

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	3	3	3

Comments and limitations:

1. General comments. This CLIFF characterizes mild to moderate allergic reactions during spaceflight. It considers mild type I IgE mediated allergic reactions that could be caused by a wide variety of substances that may be carried on board such as medications and experiment materials or inhaled allergens that might be airborne. This CLIFF does not consider delayed type hypersensitivity or serum sickness type reactions. The most severe form of allergic reaction, anaphylaxis, is covered in another CLIFF. There have been reports of allergic reactions during spaceflight, almost all of them mild. It should be noted that exploration missions will likely carry a much wider range of medications than has been carried in the past. Thus, the likelihood of an allergic reaction to pharmaceuticals may be underestimated by using historical data to estimate future incidence. In addition, it is hypothesized that space-related immune dysregulation may increase the probability of allergic reactions. The best case is considered to be an allergic reaction that is quickly relieved by one dose of oral medication. The worst case is a more severe allergic reaction, able to be treated with oral medication but requires multiple doses and a longer duration of treatment.

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2. Incidence. There have been 15 events recorded during 45.49 years of spaceflight that can be classified as mild-moderate allergic reactions. There have been no updates to the LSAH database since the IMM CLIFF was written; therefore, the incidence of 0.3292 events per person year has remained the same. Analog and terrestrial studies are not felt to be of the same applicability as the spaceflight data. The best case/worst case percentages (93%/7%) are based on the spaceflight dataset that showed 14 of the 15 events fitting the best case definition and 1/15 satisfying the worst case definition. The clinical phase durations, Return to Definitive Care (RTDC) and loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. Given the relatively mild symptoms associated with this condition, the RTDC and loss of crew life probabilities are all zero. 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 as allergic reactions can occur at any time.

6. Limitations

- The spaceflight environment may result in immune dysregulation which may affect the incidence and outcomes of allergic reactions among astronauts during spaceflight. Thus, the incidence could be underestimated.
- This CLIFF only considers type I IgE mediated reactions. It does not consider types II-IV (cytotoxic, immunocomplex, and cell-mediated) reactions.
- Exploration missions will likely carry a much wider range of medications than has been carried in the past. Thus, the likelihood of an allergic reaction to pharmaceuticals may be underestimated by using historical data to estimate future incidence.
- The best case scenario definition of "allergic reaction quickly relieved by one dose of oral medication" is not ideal for calculation of WC/BC probability since symptoms of allergic reactions such as rashes would rarely disappear within a couple hours. In reality, these mild to moderate allergic reactions would be treated with more than one dose of medication pending resolution of symptoms. Therefore, there is no terrestrial data found on WC/BC probability.

Reviewed by:

David C. Hilmers