

Anaphylaxis 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	3	3	3	3	3

Comments and limitations:

1. General comments. This CLIFF describes anaphylaxis during spaceflight. Anaphylaxis for purposes of this CLIFF includes both anaphylactic (IgE-mediated) and anaphylactoid (non-IgE mediated) reactions. Both can be acute, life-threatening, events that can lead to shock and death. There have been no reports of anaphylaxis in space. The risk of anaphylaxis during spaceflight is ameliorated by pre-flight testing of astronauts for common antigens, the absence of some common terrestrial triggers such as insect bites, and a controlled environment. However, it is hypothesized that space-related immune dysregulation may increase the probability of anaphylaxis. The most likely sensitizing antigens for a crewmember would be on board medication and tracers and markers used in life sciences experiments. The best case is considered to be an anaphylactic event that responds to initial treatment with 1-2 doses of epinephrine while the worst case is anaphylactic shock requiring supportive care.

2. Incidence. Since there are no reports of anaphylaxis during spaceflight, terrestrial studies were used to determine the composite incidence. A large epidemiologic terrestrial study (the

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Rochester Epidemiology Project) informed the incidence calculation. As there appears to be some differences between genders, separate distributions were made for males and females. The best case/worst case percentages (69/31%) are based on terrestrial data indicating that 69% of patients with anaphylaxis were discharged from the emergency department while 31% required hospitalization. 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. 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 anaphylaxis can occur at any time.

6. Limitations

- There is only general terrestrial population data available to determine incidence and outcomes.
- Terrestrial data has limited applicability. The risk of anaphylaxis during spaceflight is ameliorated by pre-flight testing of astronauts for common antigens, the absence of some common terrestrial triggers such as insect bites, and a controlled environment. For example, Hymenoptera are the second leading cause of anaphylaxis in all age groups on earth. This exposure will not be relevant in space, so the overall incidence may be overestimated.
- The spaceflight environment may result in immune dysregulation which may affect the incidence and outcomes of anaphylaxis among astronauts during spaceflight. Thus, the incidence could be underestimated.
- The use of large terrestrial studies such as the Rochester Epidemiology Project which have high numbers of subjects and small standard deviations can lead to overconfidence in the estimation of spaceflight incidence.

Reviewed by:

David C. Hilmers