

Reactive Airway 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	2	3	3	3	2	3

Comments and limitations:

1. General comments. This CLIFF characterizes reactive airway disease (RAD) that might arise from exposure to irritants during spaceflight. RAD can cause bronchoconstriction similar to asthma but results from exposure to irritants. RAD should be distinguished from occupational asthma as RAD is usually a single event without a prolonged exposure. The symptoms (cough, chest tightness, wheezing, burning sensation) and treatment of RAD are similar to those of an acute asthma exacerbation but without the underlying pathology. Treatment consists of bronchodilators and corticosteroids through the inhaled, oral or IV routes. The incidence is dependent on the possible irritants that are carried onboard, and the risk of an exposure can be controlled by engineering and operational safeguards. There may be significant overlap with other conditions such as toxic exposures and allergic reactions that can cause cough and shortness of breath. There are 3 reported events during spaceflight that could fit the condition definition, but the events are not well-described. The best case is considered to be reactive airway that responds to inhalers and/or steroids without requiring hospitalization. The worst case is reactive airway requiring hospitalization, but not requiring intubation. Intubation is covered in another CLIFF dealing with respiratory failure.

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2. Incidence. There have been 3 events reported during spaceflight that could be categorized as reactive airway through the year 2013, including both Russian and US crewmembers. There is no LSAH data available since that time to further refine this estimate. The incidence was obtained using the 3 events and the number of total person-years (80.79) in space through 2013. The best case/worst case probabilities used data from 2 terrestrial studies that showed that 2-3.77% of patients with acute asthma exacerbations needed to be hospitalized. From this data an estimate of 3% was made. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence and the case definitions, and I am in agreement with their calculation. RTDC used hospitalization as a surrogate and is therefore 0% for BC and 100% for worst case. Loss of crew life is assumed to be 0% for the best cases by condition definition (excludes cases leading to intubation). A study showed that there is a very small (0.1%) but non-zero risk of death from an acute asthma exacerbation. Intubation is excluded as it is the subject of a separate CLIFF. 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 reactive airway disease may occur during any time during the mission. However, it may be more likely during times of routine maintenance and performance of scientific experiments since exposures may be more frequent during those times.

6. Limitations

- The incidence is dependent on the possible irritants that are carried onboard, and the risk of an exposure can be controlled by engineering and operational safeguards. It is difficult to estimate an overall incidence of reactive airway as it varies mission to mission, depending on the possible irritants.
- There may be significant overlap with other CLIFFs such as respiratory failure, toxic exposures and allergic reactions that can cause cough and shortness of breath. For example, “respiratory failure” is a broad term that includes the need for nasal cannula oxygen which is likely to be the case in any asthma patient requiring hospitalization.
- Some of the calculations used data for acute asthma and occupational asthma which are related but distinct from reactive airway.
- There is a paucity of data to inform the untreated cases Loss of crew life probability and CP2 durations.
- Data on “reactive airway” incidence, treatment and outcome are limited. Therefore, asthma exacerbation was used as a proxy to provide data.

Reviewed by:

David C. Hilmer