Streptococcal Pharyngitis 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.** Inflammation or infection of the throat or peritonsillar area is called pharyngitis. It is a common complaint on earth and about 90% of cases are due to causes other than bacterial, such as irritation or viruses. Most bacterial pharyngitis is caused by group A streptococcus (GAS) but other strains of streptococci and a number of other bacteria can be the cause of pharyngitis, as well. GAS is of particular concern because if left untreated it can lead to rheumatic heart disease (although less commonly in adults) or post-infectious glomerulonephritis. There are no currently available vaccines against GAS. There have been 11 reported cases of pharyngitis during spaceflight, but the etiology of these cases is unknown. This CLiFF covers streptococcal pharyngitis. All other non-streptococcal pharyngitis etiologies are included in ICL 82 Upper Respiratory Infection. Since some cases of pharyngitis, including GAS-related ones, may cause few symptoms, they may go unreported, whether in space or on earth. The best case is considered to be uncomplicated streptococcal pharyngitis that resolves spontaneously while the worst case is a peritonsillar abscess requiring IV antibiotics and possible incision/drainage.

2. **Incidence.** As mentioned above, there have been 11 cases of pharyngitis reported during spaceflight. However, no cultures were done to determine their etiology, and the data can not be used to calculate composite incidence. There are two terrestrial studies that were used to derive age-adjusted incidence rates of GAS pharyngitis based on the historical ages of flown astronauts. A proportion of 20% was used to adjust the incidence rate of unspecified pharyngitis reported in one of the studies, reflecting the relative proportion of acute pharyngitis that is bacterial. This may result in an over-estimate since some cases of bacterial pharyngitis are not due to GAS. Since some cases of pharyngitis, including GAS-related ones, may cause few symptoms, they may go unreported which could lead to a small underestimate of the true value. The best case/worst case probabilities used data from a review article on pharyngitis that reported peritonsillar abscess in fewer than 1 percent of patients treated with antibiotics. The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. The surrogate for RTDC in this case was hospitalization which may be an overly conservative estimate of the need for RTDC since IV antibiotics will be available onboard the space craft. Loss of crew life was assumed to be zero in all cases. Worst cases would lead to shock/sepsis which 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 infections can occur during any time during the mission. The disease is contagious and it is possible that the incidence among other crew members would increase if one person was infected.

6. **Limitations**

- All non-strep pharyngitis infections are found in ICL 82 - upper respiratory infections. This CLiFF specifies GAS pharyngitis; however, some infections that are assumed to be GAS are actually other types of strep or other non-strep bacteria.
- The current definition states that the best case is uncomplicated streptococcal pharyngitis that resolves spontaneously. This implies that it resolves without treatment. Since most cases of uncomplicated GAS are treated with oral antibiotics or IM injections, it should be clarified to state that, in the best case, the pharyngitis resolves with oral or IM antibiotics.
- The worst case is progression to peritonsillar abscess (PTA). However, only 20% of PTA's are caused by GAS. Thus, these may not fall within the definition of GAS-pharyngitis. Parsing out data of pharyngitis and PTA's that are specific to GAS was difficult and thus limits the accuracy of the findings. Similarly, as a PTA is not the worst case for an upper respiratory infection, it should be noted that a PTA caused by other types of bacteria are not included within the scope of any CLiFF.
- It is unknown how the space environment affects the incidence and transmission of GA; however, we believe that the possible increased susceptibility caused by immune

modulation in the space environment is probably less than the decreased susceptibility given the age and health of astronauts.

- There is little data to support UTWC estimates as it would be unethical to study untreated worst cases.
- PTA could lead to death if left untreated, but the intermediate stage would be sepsis/shock which is the subject of another CLiFF. Thus, Loss of crew life was assumed to be zero.

Reviewed by:

David C. Hilmers