

## Bacterial Skin Infections 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<br>Composite Incidence and Level of Confidence | Table 3, 4<br>BC/WC<br>Loss of Crew and probability | Table 4 -<br>Clinical Phase 1, 2 durations<br><br>Table 5 – CP 2 Loss of Crew | Table 4 – RTDC %<br><br>Table 6 – RTDC Loss of Crew | Table 4 – Loss of Crew Life %<br><br>Table 7 – Loss of Crew Life, Loss of Crew | Table 8 – TI |
| Score                                                                                      | 3                                                          | 2                                                   | 3                                                                             | 3                                                   | 2                                                                              | 3            |

### Comments and limitations:

**1. General comments.** Skin infections are a common complaint on earth that also have been reported fairly frequently during spaceflight. The etiology of skin infections can be from a wide range of bacteria, viruses, and fungi. Viral infections are the subject of a separate CLIFF. Bacterial skin infections, the subject of this CLIFF, can affect all layers of the skin and can also be deep, forming abscesses or furuncles that can go into the subcutaneous tissue. Superficial infections usually respond well to treatment but deeper infections may require incision and drainage. Cellulitis is an acute bacterial infection of the skin and subcutaneous tissue. It is most commonly caused by streptococci and staphylococci. It may present with pain, fever, rapidly spreading erythema, regional lymphadenopathy, and edema. Treatment is with appropriate antibiotics and analgesics, as indicated. Deep infections may result in pockets of pus that need to be drained. Untreated cellulitis can progress to sepsis and septic shock which is the subject of a separate CLIFF. Many astronauts have remarked that their wounds healed more slowly while on orbit. Infections may be caused by the direct effects of microgravity on immunity or characteristics of the cabin environment, such as moisture, airborne contaminants, and condensate. Hygiene may also suffer during spaceflight which can predispose to bacterial infections. The best case is a bacterial skin infection that resolves

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without treatment, or treatment with topical or a single course of oral antibiotics. The worst case is defined as a moderate or severe bacterial skin infection requiring a second course of oral antibiotics, a course of intramuscular or intravenous antibiotics, or that is refractory to treatment. A condition that is included is furuncles or boils, which may need to be drained. The definitions do not specifically address this case. Necrotizing fasciitis is a separate condition and covered under another CLIFF.

**2. Incidence.** Because of the unique environment associated with living and working in space, it was felt that spaceflight data would best inform the incidence for this condition. There have been reports of 17 skin infections in space without a specific etiology. It has been reported elsewhere that 62% of skin infections in space are from bacterial causes. This adjustment was made to the total number of reported cases to calculate the incidence. It is likely that very minor bacterial infections have not been reported in the past which could lead to an underestimation of the true incidence. The best case/worst case probabilities used data from a terrestrial paper showing an antibiotic treatment failure rate of 12%. The definition causes some problems here as some bacterial infections which cause small abscesses may only require drainage and may not need antibiotics at all. 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 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 but bacterial infections may be slightly more likely to occur during periods of high physical activity such as during daily exercise or during EVA's. Some skin infections such as impetigo are highly contagious. It would be expected that the incidence would rise amongst the crew once one member of the crew is infected.

### 6. Limitations

- It is likely that very minor bacterial infections have not been reported in the past which could lead to an underestimation of the true incidence.
- The incidence calculation was modified based on an a report that 62% of skin infections in space were of bacterial origin (Marshburn paper). It would be preferable to use the original data that informed the estimate in the analysis directly, rather than to assume a fixed proportion.
- The definition causes some problems as some bacterial infections which cause small abscesses may only require drainage and may not need antibiotics at all. This is not addressed in the definition.
- The best case/worst case split was complicated because "failure rate" of antibiotics likely encompasses second line therapy, which is included within the "worst case" for the condition.
- Some skin infections such as impetigo are highly contagious. It would be expected that the incidence would rise amongst the crew once one member of the crew is infected.

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- There may be some overlap with other CLIFFs, particularly when the etiology of the infection is not clear. For example, untreated cellulitis can progress to sepsis and septic shock which is the subject of a separate CLIFF.

Reviewed by:

David C. Hilmer