

Skin Infections – Viral/Fungal 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 LOC and probability	Table 4 - Clinical Phase 1, 2 durations Table 5 – CP 2 LOC	Table 4 – RTDC % Table 6 – RTDC LOC	Table 4 – Loss of crew life % Table 7 – Loss of crew life LOC	Table 8 – TI
Score	3	2	2	3	3	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, fungi, and parasites. Bacterial skin infections are the subject of a separate CLIFF. Viral and fungal skin infections, the subject of this CLIFF, generally only affect the superficial layers of the skin. They may be persistent and may not respond well to treatment. However, while bothersome, they generally are not associated with significant morbidity or mission impact. Examples of viral skin infections include HSV (causing perioral or labial lesions), HPV (causing warts), molluscum contagiosum, and viral exanthems such as from EBV. Viral exanthems of childhood such as from chickenpox, rubella and measles, are not common in adults and are mitigated by vaccinations. This CLIFF does not cover sexually transmitted diseases such as genital warts (HPV), HIV, and genital herpes as they may be covered in future CLIFFs and are thought to be highly unlikely. Herpes zoster infection (shingles) and mouth ulcers are also the subject of other CLIFFs. Fungal infections may include tinea corporis, tinea pedis, tinea cruris, tinea capitis, candidal skin infections, and skin infections from endemic mycoses. Humid environments and poor hygiene can contribute to increased incidence and severity of fungal skin infections. 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

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can predispose to viral and fungal infections. Treatment consists of topical or oral anti-virals (such as acyclovir) or anti-fungals (such as terbinafine). In some cases, IV medications may be indicated. The best case is a mild viral or fungal skin infection, that resolves without treatment, or minimal treatment with topical or a single course of oral antivirals or antifungals. The worst case is defined as a moderate to severe viral or fungal skin infection that could require a second course of antivirals/antifungals, or could be refractory to treatment.

2. Incidence. There is a paucity of evidence related to viral or fungal infections during spaceflight. There are reports of rash, but these are not broken down by etiology. There are reports from Apollo 14 and 15 of 4/6 crewmembers and a number of close contacts contracting candida skin infections but there have been no cases documented on subsequent missions. The best flight data available indicates that there have been 17 documented skin infections of all types during spaceflight. The etiology of skin infections includes bacterial, viral, fungal, and parasitic causes. Existing data does not show the breakdown of these infections by etiology. The previous IMM CLIFF refers to Barratt's textbook as stating 62% of skin infections have been bacterial. The primary reference for this statistic has not been determined. Clinically, however, this is a reasonable breakdown. The risk of parasitic skin infections in the spaceflight environment is thought to be extremely low and is disregarded. Thus, the other 38% of skin infections are assumed to be viral or fungal. This was applied to the known 17 skin infections documented during spaceflight to obtain the incidence. It is likely that very minor viral and fungal infections have not been reported in the past which could lead to an underestimation of the true incidence. The best case/worst case probabilities were based on the clinical cure rate of topical terbinafine from a Cochrane review of topical antifungal treatment for tinea cruris and tinea corporis. It showed a 74.6% cure rate (best case) and a 25.4% failure rate (worst case). The clinical phase durations, RTDC and Loss of crew life probabilities are supported by terrestrial evidence, and I am in agreement with their calculation. RTDC and Loss of crew life probabilities are assumed to be 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 but fungal infections may be slightly more likely to occur during periods of high physical activity such as during daily exercise or during EVA's. Some viral skin infections are associated with infectious diseases. It would be expected that the incidence would rise amongst the crew once one member of the crew is infected.

6. Limitations

- The previous IMM CLIFF refers to Barratt's textbook as stating 62% of skin infections have been bacterial. The primary reference for this statistic has not been determined. Clinically, however, this is a reasonable breakdown.
- It is likely that very minor viral/fungal infections have not been reported in the past which could lead to an underestimation of the true incidence.

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- Some viral skin infections are associated with infectious diseases. It would be expected that the incidence would rise amongst the crew once one member of the crew is infected. There may be some overlap with other CLIFFs such as those dealing with allergic reactions and bacterial skin infections, particularly when the etiology of the infection is not clear.
- Fungal infections may be slightly more likely to occur during periods of high physical activity such as during daily exercise or during EVA's.
- Sexually transmitted infections were not included because they may be included separately in a later version. In addition, STI's are unlikely to occur because of pre-flight screening and, presumably, lower rates of sexual activity during spaceflight.
- There is a paucity of data concerning untreated viral and fungal skin infections.

Reviewed by:

David C. Hilmers