



# **Anaphylaxis, Intra-abdominal Infections, Skin Lacerations, and Behavioral Emergencies: A Literature Review of Austere Analogs for a Near Earth Asteroid Mission**

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## **ACRONYMS**

CRP	C-reactive protein
CMO	crew medical officer
EMT	Emergency Medical Technician
EVA	extravehicular activity
ExMC	Exploration Medical Capability
HRP	Human Research Project
ISS	International Space Station
NOLS	National Outdoor Leadership School
NEA	Near Earth Asteroid
SBO	small bowel obstruction
SMEMCL	Space Medicine Exploration Medical Conditions List
WBC	white blood cell

# 1. INTRODUCTION

As space exploration is directed towards destinations beyond low-Earth orbit to more distant objectives, such as exploring a Near Earth Asteroid (NEA) or Mars, the consequent new set of medical risks will drive requirements for new capabilities and more resources to ensure crew health. The Space Medicine Exploration Medical Conditions List (SMEMCL) has been developed by the Exploration Medical Capability (ExMC) element of the Human Research Program (HRP) to address the risk of “unacceptable health and mission outcomes due to limitations of in-flight medical capabilities”.<sup>1</sup> It itemizes 85 evidence-based clinical requirements for eight different mission profiles and identifies conditions warranting further research and technology development. These eight Design Reference Missions are:

1. Orion to International Space Station (ISS) Transfer: 4 crewmembers (3 males, 1 female), 3 days, no extravehicular activities (EVAs).
2. Lunar Sortie: 4 crewmembers (3 males, 1 female), 14 days, 4 EVAs/crewmember.
3. Lunar Outpost: 4 crewmembers (3 males, 1 female), 6 months, 90 EVAs/crewmember.
4. ISS Contingency Return: Illness or injury occurring on the ISS, which necessitates contingency return from the ISS back to Earth, and requires en route medical care.
5. Lunar Sortie Contingency Return: Illness or injury occurring during a Lunar Sortie mission, which necessitates a contingency return from the Lunar surface back to Earth and requires en route medical care.
6. Lunar Outpost Contingency Return: Illness or injury occurring during a Lunar Outpost mission, which necessitates a contingency return from the Lunar surface back to Earth and requires en route medical care.
7. 144-Hour Depressurization Return: Illness or injury occurring during a contingency return from a Lunar mission, assuming a depressurized cabin and crewmembers in full pressurized suits for up to 144 hours.
8. NEA: 3 crewmembers (2 males, 1 female), 395 days, 30 EVAs/crewmember.

Each condition is given a clinical priority for each mission profile as follows:

- 2 – Shall: The condition must be addressed by the medical system.
- 1 – Should: If resources are available, it is desirable for the condition to be addressed by the medical system.
- 0 – Not Addressed: The condition will not be addressed by the medical system.

Four medical conditions from the SMEMCL—intra-abdominal infections, skin lacerations, anaphylaxis, and behavioral emergencies—were selected by the author as a starting point for analyzing all the conditions on the SMEMCL. A systematic literature review was performed to understand how these conditions are treated in austere, limited-resource, space-analog environments. In this paper, such austere environments refer to high-altitude and mountain environments, submarines, military deployments, Antarctica, isolated wilderness environments, in-flight environments, and remote, resource-poor, rural environments. These austere environments serve as analogs to spaceflight because of their shared characteristics such as limited medical resources, delay in communication, confined living quarters, difficulty with resupply, variable time to evacuation. Treatment of these four medical conditions in austere,

limited-resource environments provides insight into medical equipment and training requirements for exploration-class missions.

## 2. METHODS

For the purposes of this publication, long-duration, exploration conditions were considered using the NEA mission profile. Only four conditions were chosen to initiate an analysis which was smaller in scale than considering every condition on the SMEMCL. Higher priority conditions were selected, which were deemed “shall” address on the SMEMCL: anaphylaxis, intra-abdominal infections, skin lacerations, and behavioral emergency. A more thorough follow-up analysis would consider the remaining conditions on the SMEMCL.

Literature searches were performed using keywords in PubMed, Scopus, Cinahl, National Technical Reports Library, and PsychINFO. Keyword searches were as follows:

- 1) (antarctic\*[ti] OR polar[ti] OR resource[ti] OR arctic[ti] OR astronaut\*[ti] OR wilderness[ti] OR submarine\*[ti] OR "Antarctic Regions"[Mesh] OR "Astronauts"[Mesh] OR "Space Flight"[Mesh] OR "United States National Aeronautics and Space Administration"[Mesh] OR mountaineering[mesh] OR altitude[mesh] OR wilderness medicine[mesh] OR wilderness[mesh] OR "Arctic Regions"[Mesh] OR "naval Medicine"[Mesh] OR "developing countries"[mesh] OR "poverty"[mesh]) AND (anaphyla\*[ti] OR "anaphylaxis"[mesh])
- 2) (antarctic\*[ti] OR polar[ti] OR resource[ti] OR arctic[ti] OR astronaut\*[ti] OR wilderness[ti] OR submarine\*[ti] OR "Antarctic Regions"[Mesh] OR "Astronauts"[Mesh] OR "Space Flight"[Mesh] OR "United States National Aeronautics and Space Administration"[Mesh] OR mountaineering[mesh] OR altitude[mesh] OR wilderness medicine[mesh] OR wilderness[mesh] OR "Arctic Regions"[Mesh] OR "naval Medicine"[Mesh] OR "developing countries"[mesh] OR "poverty"[mesh]) AND (emergen\*[tiab]
- 3) OR acute[tiab] OR "First Aid"[Mesh] OR "Emergency Treatment"[Mesh] OR "Triage"[Mesh]) AND (peritonitis[tiab] OR appendicitis[tiab] OR "intra-abdominal infection"[tiab] OR "intra-abdominal infections"[tiab] OR "cholecystitis"[mesh] OR "Gastroenteritis"[Mesh] OR "Peritonitis"[Mesh] OR ("Bacterial Infections and Mycoses"[Mesh] OR "Virus Diseases"[Mesh]) AND "Abdomen"[Mesh]))
- 4) (antarctic\*[ti] OR polar[ti] OR resource[ti] OR arctic[ti] OR astronaut\*[ti] OR wilderness[ti] OR submarine\*[ti] OR "Antarctic Regions"[Mesh] OR "Astronauts"[Mesh] OR "Space Flight"[Mesh] OR "United States National Aeronautics and Space Administration"[Mesh] OR mountaineering[mesh] OR altitude[mesh] OR wilderness medicine[mesh] OR wilderness[mesh] OR "Arctic Regions"[Mesh] OR "naval Medicine"[Mesh] OR "developing countries"[mesh] OR "poverty"[mesh]) AND (sutures[mesh] OR tissue adhesives[mesh] OR lacerat\*[ti] OR "lacerations"[mesh] OR bandages[mesh] OR sutur\*[ti] OR dermabond[ti] OR "steri-strip"[ti] OR "steristrip"[ti])

- 5) (antarctic\*[ti] OR polar[ti] OR resource[ti] OR arctic[ti] OR astronaut\*[ti] OR wilderness[ti] OR submarine\*[ti] OR "Antarctic Regions"[Mesh] OR "Astronauts"[Mesh] OR "Space Flight"[Mesh] OR "United States National Aeronautics and Space Administration"[Mesh] OR mountaineering[mesh] OR altitude[mesh] OR wilderness medicine[mesh] OR wilderness[mesh] OR "Arctic Regions"[Mesh] OR "naval Medicine"[Mesh] OR "developing countries"[mesh] OR "poverty"[mesh]) AND (suicid\*[ti] OR homicid\* OR psychosis[ti] OR psychotic[ti] OR "Suicide"[Mesh] OR "Homicide"[Mesh] OR "Psychotic Disorders"[Mesh] OR "Panic Disorder"[Mesh]) AND (emergen\*[tiab] OR acute[tiab] OR "First Aid"[Mesh] OR "Emergency Treatment"[Mesh] OR "Triage"[Mesh])

In the absence of comprehensive clinical research, such as trials or cohort studies, secondary literature such as systematic reviews and expert opinion such as clinical guidelines were used. Austere environments—described previously—were analyzed in regards to their similarity to spaceflight.

### 3. RESULTS

#### 3.1 Anaphylaxis

The first condition selected from the SMEMCL was anaphylaxis. Anaphylaxis is an acute, life-threatening, multi-organ response to an allergen that results in symptoms such as difficulty breathing and low blood pressure. The lifetime prevalence of anaphylaxis is estimated to be 2% to 4%.<sup>2</sup> Foods and medications cause most identifiable cases of anaphylaxis. Frequent food triggers in U.S. populations include peanuts, tree nuts, and shellfish;<sup>3</sup> drugs such as beta-lactams, neuromuscular blocking agents, fluoroquinolones, and monoclonal antibodies are the most common medication triggers.<sup>4</sup> Approximately 0.01% of cases are estimated to be idiopathic.<sup>5</sup> An inflammatory cascade caused by degranulation of IgE-mediated mast cells leading to anaphylaxis can be caused by most substances, even after repeated and uneventful exposure.<sup>6</sup> The anaphylactic reaction is characterized by flushing, urticaria, angioedema, wheezing, laryngospasm, abdominal cramps, diarrhea, hypotension, or shock.<sup>7</sup>

In austere environments, the treatment of anaphylaxis is not well researched due to its rare incidence, sudden onset, and drastic course—it is not amenable to randomized control studies. However, available evidence and expert wilderness medicine consensus support immediate administration of epinephrine by both trained medical and nonmedical personnel, particularly if medical evacuation is hindered by harsh environments or geographical location.<sup>8</sup>

In a case-series of eight patients with known anaphylactic reactions to *Hymenoptera* stings, National Park Service rangers with up to 110 hours of Emergency Medical Technician (EMT)-Basic training were able to administer epinephrine injections in the field with no adverse outcomes.<sup>9</sup> Similarly, the National Outdoor Leadership School (NOLS) database recorded two cases of anaphylaxis in 20 years (2.5 million participant-days) that were administered epinephrine and 149 cases of acute allergic reactions (not categorized as anaphylaxis) that were administered antihistamines. NOLS instructors, who had no formal medical training beyond

basic EMT training, administered these medications, and no deaths were reported among these patients.<sup>8</sup>

Arrhythmias, stroke, and myocardial infarctions have been reported as adverse effects of epinephrine administration for anaphylaxis.<sup>10</sup> However, literature demonstrates that these reactions were in elderly patients with known cardiac disease or occurred because of medication overdose. A Colorado youth developed ventricular dysrhythmia and myocardial ischemia after receiving a tenfold increased dose by EMTs.<sup>8,11</sup> Because of this incident, the Wilderness Medical Society recommends auto-injectors or prepackaged medication kits to decrease this risk.<sup>8</sup> Since anaphylaxis is life-threatening, there is no absolute contraindication to administering epinephrine.

A more common complication from epinephrine use in EpiPen (ActiveAide, Redwood Falls, MN) form is digital auto-injection, where the wrong end of the EpiPen is depressed and the finger is injected with epinephrine, potentially resulting in digital ischemia. However, a recent 6-year retrospective cohort study of accidental digital epinephrine injections reported to emergency departments and local Poison Control Centers (N= 127) demonstrated very few local and systemic effects; most cases required observation with complete resolution of symptoms.<sup>12</sup> No lasting symptoms were observed in the 23% that did receive treatment with vasodilators, suggesting that auto-injection of epinephrine is safe for spaceflight.

In summary, the mainstay of treatment for true anaphylaxis is rapid recognition of symptoms and administration of epinephrine and other synergistic medications, most of which are already included in current medical kits for other conditions: antihistamines, albuterol, intravenous fluids, and steroids. Wilderness literature has shown that anaphylaxis prevalence to be 0.01% to 2% depending on etiology.<sup>7</sup> Although rare, the consequences of untreated anaphylaxis are life-threatening.

## **3.2 Intra-abdominal Infections**

The second condition selected from the SMEMCL was intra-abdominal infections which are further delineated into appendicitis, diverticulitis, and cholecystitis.

### **3.2.1 Appendicitis**

Appendicitis is the most commonly documented surgical condition in austere environments as shown in submarine and Antarctic populations.<sup>13</sup> The lifetime prevalence of appendicitis in the United States has been estimated at 8.6% for men and 6.7% for women.<sup>14</sup> This incidence decreases with age. Increased incidence was observed in Australian polar expeditions, which was hypothesized to be linked to immunosuppression.<sup>15</sup> Although astronauts are predicted to have a low likelihood of developing appendicitis based on an average age of 45, spaceflight immunosuppression might increase their risk.<sup>13,16-18</sup>

When surgery is not available in an austere environment, appendicitis may be medically managed with antibiotics, analgesics, and intravenous fluids. The documented success rate of medical management of appendicitis ranges between 88% to 100%,<sup>19</sup> even in cases with

perforated viscera; however, the highest documented success rates of medical management were achieved when therapy was initiated within 6 hours of suspected diagnosis.<sup>20</sup> The recurrence rates after medical management of appendicitis in these studies were 5% to 38% within 17 months.<sup>19</sup>

Several more studies have reviewed medical management of appendicitis, which provides input into alternate treatment strategies in austere environments. Sakorafas posited that medical management is appropriate in many cases of suspected appendicitis without signs of frank peritonitis, and stated that this approach would be best applied in areas with poor health services or lacking operative capabilities.<sup>21</sup> In a 2006 prospective, multicenter, randomized control trial in which patients were randomized to surgical versus medical treatment, only 12% of patients ultimately required operation in the first 24 hours; the incidence of perforation was 5% in both groups, and the recurrence risk was 3% to 25%.<sup>22</sup> A separate study reported a recurrence rate of 37%.<sup>21,22</sup> However, in the event of recurrence, Styrud showed in a prospective, multicenter, randomized control trial that antibiotic therapy could be used a second time. Those who presented with late recurrence were likely to have a mild clinical course.<sup>23</sup>

A former report shows anesthesia and surgical morbidity associated with emergency appendectomy is sevenfold that of non-operative management for age- and gender-matched populations.<sup>21</sup> In selecting appropriate candidates for medical management, early, mild disease has been shown to respond best to antibiotic therapy. Antibiotic therapy is still the recommended management in cases of complicated appendicitis involving phlegmon or abscess formation.<sup>22</sup>

Though white blood cell (WBC) count and C-reactive protein (CRP) are often used as markers of infection, WBC count is not a reliable diagnostic tool, particularly if an individual is immunosuppressed. Repeated CRPs may be used to monitor severity of infection, although this may not be reliable in perforated or gangrenous appendix.<sup>24</sup>

Prophylactic appendectomies, which remove a normal appendix to prevent possible appendicitis before an expedition, have been proposed in an effort to mitigate the risk of appendicitis. The Antarctic research expeditions of Russia, China, Chile, Argentina, France, and the United Kingdom have intermittently required prophylactic appendectomies of their participants. Australian program Antarctic expeditions have consistently required Australian physicians wintering over in Antarctica to undergo prophylactic appendectomies since 1950. Other project members have inconsistently been required to undergo appendectomy. A non-physician project member did develop appendicitis requiring evacuation but was not evacuated, thereby resulting in his death. Since that occurrence, the Australian program began to require prophylactic appendectomies, which reduced the incidence of appendicitis from 43/1,000,000 person-days to 4.07/1,000,000 person-days.<sup>25</sup> It is possible that the incidence of appendicitis after appendectomy resulted from stump appendicitis, but the reports are not clear enough to delineate the exact cause of their abdominal pain.

Small bowel obstruction (SBO) is the most concerning complication associated with appendectomies. In the urban setting, open appendectomies have been reported as being associated with a 1.5% prevalence of SBO up to 15 years following initial surgery, and requiring

surgical intervention.<sup>26</sup> Lifetime prevalence is expected to be lower after prophylactic appendectomies because the appendix is not inflamed. A recent review of risk factors for post-laparotomy adhesions showed the rate of adhesion-related re-admissions from 4,445 laparoscopic appendectomies to be 1.3%,<sup>27</sup> which was relatively unchanged compared to the open appendectomy SBO incidence of 1.4%. It is unclear whether these cases ultimately required surgical intervention because adhesion-related re-admission was the end-point of the studies reviewed, not surgical intervention. Furthermore, no data on the complication rates of operative appendectomies in analog environments were available.

### **3.2.2. Diverticulitis**

Diverticulitis is more common in the fourth to fifth decade of life, affecting one-third of the United States population over age 45.<sup>7</sup> Complicated diverticulitis is defined as diverticular disease involving abscess formation or perforated viscus. In the past, this was often treated surgically, either with partial colonic resection or with percutaneous drainage of the abscess. Recent studies have shown good results with conservative management.<sup>28</sup>

In the absence of data from analog environments, all available literature was reviewed. In a single-institution, retrospective review of patients admitted for diverticulitis, 136 patients over a 13-year period were found to have perforated viscus and the vast majority of these (91%) were successfully managed non-operatively—even those with severe disease (defined by moderate to large free air or large abscesses).<sup>28</sup> Although this study did have patients that ultimately underwent elective resection for their diverticular disease, this was less than half (48%) of the study group. A greater than 90% success rate of non-operative intervention for acute diverticular disease has been cited in other studies as well and further stratified into 95% non-operative success rate in mild disease<sup>29</sup> and 93% success rate in 511 patients for diverticular disease without abscess or perforation.<sup>30</sup>

In a survey of 379 Dutch gastroenterologists and surgeons, 90% reported that they manage mild disease with simple bowel rest and no antibiotics,<sup>31</sup> whereas U.S. cases have been shown to successfully be treated only with single-agent, oral antibiotic therapy.<sup>32</sup> A recent systematic review of management of diverticulitis concluded that the heterogeneity of patients with colonic diverticular disease dictated that treatment should be tailored on an individual basis.<sup>33</sup>

### **3.2.3. Cholelithiasis**

In the United States, acute cholecystitis is traditionally treated with early laparoscopic cholecystectomy. A recent review of 7,103 laparoscopic cholecystectomies showed the postoperative incidence of SBO to be 0.2% up to 5 years following surgery.<sup>27</sup> However, some literature exists to support delayed operative intervention, as it is widely practiced outside the United States. In a retrospective chart review of nine Japanese hospitals, delayed laparoscopic cholecystectomy (defined as greater than 7 days from initial presentation) had a higher rate of intra-operative complications compared to open cholecystectomy but overall similar post-operative complication rates.<sup>34</sup>

The safety of performing laparoscopic or open cholecystectomy in an austere environment was investigated in a recent retrospective study performed in Afghanistan<sup>35</sup>. The technical complication rate of laparoscopic cholecystectomy was 3.9%, higher than those reported in other developing and developed countries; none of the major operative complications (three bile leaks and one duodenal perforation) were detected intra-operatively, requiring further interventions after the initial surgery.<sup>35</sup> This study was limited by unequal treatment groups (102 patients received laparoscopic cholecystectomy whereas 35 received open cholecystectomy) and suboptimal surgical conditions related to operator experience, peri-operative resources (e.g., endoscopic retrograde cholangiopancreatography), and physical environment. Good outcomes with laparoscopic compared to open cholecystectomy were reported in a separate prospective, nonrandomized, study of 45 patients in resource-poor Yemen; however, these procedures were performed by experienced general surgeons.<sup>36</sup>

An alternative to laparoscopic cholecystectomy practiced in the West Indies is mini-laparotomy cholecystectomy, which has been reported to have a conversion rate of only 4% in a study of 476 patients.<sup>37</sup> The mean incision length was 4.8 cm with a mean operating time of 31 minutes, and wound infection was the only postoperative complication, seen in less than 10% of patients. However, a randomized trial comparing mini-laparotomy to open cholecystectomy in 60 patients showed no significant difference in complications between the two options.<sup>38</sup> This study did not have many subjects and was not performed in an austere environment.

### **3.3 Skin Lacerations**

The third condition selected was skin lacerations, which may coexist with other forms of soft tissue trauma, underlying occult infection, or may be complicated by form, depth, or joint space involvement. In an effort to simplify definitions, only isolated skin lacerations are considered in this section.

One of primary end-goals of any wound management is avoiding infection. Assuming any of the coexisting injuries are absent, the management of lacerations necessitates hemorrhage control, wound exploration, anesthesia, irrigation, debridement, and, if indicated, wound closure, antibiotic administration, and tetanus prophylaxis.

In austere environments, lacerations rarely require wound closure<sup>7</sup> and sometimes may be contraindicated based on the degree of contamination and inability to reliably irrigate the wound. When closure is indicated, anesthesia will usually be needed.

Irrigation fluid type in resource-poor environments depends on local availability. Studies have shown that boiled, filtered fresh water,<sup>39</sup> or tap water is as effective as normal saline in reducing bacterial counts through irrigation—an important component of infection prevention.<sup>40,41</sup> At least 500 ml of irrigation fluid should be used at a minimum of 5 to 8 psi.<sup>39</sup> In both irrigation and debridement, the goal in austere environments is to remove any visible foreign objects and devitalized tissue prior to repair.

While suturing is easily performed by medically trained personnel and sutured laceration repair has effectively been performed in parabolic flights,<sup>13,42</sup> needle safety and body substance

isolation may present a challenge. If sutured closure is to be undertaken, a study with 50 subjects in a rural Canadian practice showed that full sterile technique versus surgically clean but non-sterile technique had no difference in healing rate or post-closure complications, including infection.<sup>43</sup>

The safest management strategy for lacerations in the wilderness is open management or closure with non-suture alternatives and appropriate prevention against infection.<sup>7</sup> Tape and Steri-Strips (3M, Minneapolis, MN) have been shown to be rapid, safe, easy, and as effective in the appropriate wound as sutures or staples.<sup>7</sup> In fact, in a prospective analysis of 147 contaminated wounds in the West Indies that were closed with Steri-Strips and without any cleaning, the sepsis rate was 1.4%, with an overall complication rate of 2.7%.<sup>44</sup> Antarctic expedition populations have also published success in using glues such as cyanoacrylates for closure of cold-induced fingertip fissures with improved finger function and faster resolution of symptoms.<sup>45</sup>

The Wilderness Medical Society recommends prophylactic antibiotics for the following indications:

- Significantly contaminated wounds requiring extensive cleaning and debridement (especially in immunosuppressed patients)
- Violation of cartilage, joint spaces, tendon, or bone
- Crush-mechanism wounds with a high potential for devitalization
- Mammalian bites

Five days of amoxicillin-clavulanate, second- or third-generation cephalosporins, fluoroquinolones, penicillinase-resistant penicillins, or tetracyclines are appropriate.<sup>39</sup>

In summary, to prevent wound infection, proper skin laceration management does not require specific irrigation fluid, but does require adequate irrigation at pressure to effectively reduce the risk of infection. With regards to wound closure, sterile technique has not been shown in austere analogs to be any more effective in reducing infection rates than non-sterile technique; non-suturable wound management is an acceptable alternative to sutures in austere environments.

### **3.4 Behavioral Emergencies**

Isolation and behavioral problems have long been reported as the largest medical issue in Antarctic expeditions.<sup>46</sup> Given that this analog is frequently used to predict exploration mission-class outcomes, it deserves significant attention. For the purposes of this discussion, behavioral emergencies are defined as suicidal or homicidal ideation, psychosis, and panic attack. Anxiety and depression are treated as a separate condition in the SMEMCL.

A case of psychosis in the Antarctic was reported in 1957 and was an impetus to extensively review U.S. Navy selection criteria for polar expeditions.<sup>47</sup> While documentation of this incident was sparse, references suggested that resources were inadequate for evacuation.<sup>48</sup>

As a result of similar psychological crises in early polar expeditions, efforts were directed toward prevention via “select out” criteria in subsequent endeavors, which drove case reports from the acute cases to chronic cases. Given the extensive efforts by the Navy and subsequent expedition

programs to select out any disqualifying conditions, the dearth of acute behavioral emergencies seems to be a reflection of the effectiveness of preventive medicine.

The concept of developing shared psychotic disorder (*folie-a-deux*) has been raised during a review of case reports, but the precise etiology of the disorder remains unclear despite documentation dating back to 1877.<sup>49</sup> However, prolonged isolation remained the principle-inciting factor.

In the event that a true behavioral emergency would occur, the Wilderness Medical Society's category 1B recommendation regarding stress reactions focused attention on the affected team member and encouraged verbalization of their emotions to an attentive caregiver who would provide feedback and empower the patient to take an active role in their own care.<sup>39</sup>

Benzodiazepines, which are usually used for anxiety and panic disorders, have been successful in austere environments.<sup>50</sup> Psychotic reactions might also be temporized with benzodiazepines. For acute psychotic events, haloperidol is safe and effective. In the event that medications are ineffective or not adequate, physical restraints can be used as adjuncts for patient and caregiver safety.

## 4. DISCUSSION

Anaphylaxis, intra-abdominal infections, skin lacerations, and behavioral emergencies are four conditions in the SMEMCL that were analyzed for treatment strategies in austere environments. Several limitations were encountered in this review. First, there is a dearth of systematic reviews on which to base clinical guidelines other than the Wilderness Medical Society's clinical guidelines, which suggest evacuation for definitive care. Next, much of the primary literature relies on small sample sizes, limiting statistical certainty from which to draw conclusions. Finally, while studies in austere environments such as Nepal or Africa exist, additional confounding factors may affect outcomes, such as socioeconomic status, chronic conditions, and other social aspects impacting the health of subjects involved, rendering these studies difficult to use for the purposes of the SMEMCL. Despite these limitations, those insights relevant to exploration-class missions are detailed below.

### 4.1 Anaphylaxis

Anaphylaxis occurs terrestrially at a lifetime prevalence of 2% to 4%, but in the context of spaceflight might increase due to immunologic effects or decrease due to good crewmember health. As discussed in the results section, allergy screening for common triggers can aid in prevention by removing concerning substances from the mission manifest. Preventive action can reduce the incidence further by ground-testing medications. Evidence from austere environments indicates that treatment can be administered safely by non-medically trained personnel. A short training session on EpiPen use should be sufficient given the infrequent and minor complications associated with its use. In addition, the mass of epinephrine is small and can be used for other medical purposes, so it would be prudent to prepare for this condition on exploration missions in order to avoid potential loss of crew life.

## 4.2. Intra-abdominal Infections

Intra-abdominal infections occurring in austere environments without significant surgical support are best treated by evacuation to a definitive care facility. In rare cases, remote surgery has been attempted but previously cited literature supports non-operative treatment with antibiotics as a temporizing measure.

Before treatment is even initiated, diagnosis may be complicated in spaceflight. For example, microgravity shifts intra-abdominal contents, which could potentially alter classic physical findings of appendicitis such as tenderness at McBurney's point. Also, acute, complicated diverticulitis would be rare in-flight, but with constipation being a known medical condition on orbit,<sup>1</sup> diverticulitis might be increasingly likely during exploration missions. Newer imaging modalities such as ultrasound could be used to mitigate difficulties with diagnoses. As discussed in the results section, early diagnosis improves the efficacy of treatment with antibiotics.

Current difficulties associated with performing surgery in microgravity support nonsurgical approaches to intra-abdominal infections. Whereas dissections and surgeries were performed on animal models during Neurolab,<sup>13</sup> human surgery during exploration missions would be complicated by mass restrictions, hardware certification, expertise, and adequate time in the training to maintain proficiency in a variety of potential surgical procedures.

If surgery is not going to be performed, then medical management will reduce the impact of an intra-abdominal infection. Non-operative management of appendicitis is already being used in austere environments with a success rate of 88% to 100%. Antibiotics should be carried in sufficient quantities to also treat a recurrence. Though non-operative management of cholecystitis may be a bridge to definitive management, cholecystectomy is currently required. Further research into non-operative management of cholecystectomy is necessary to better characterize that risk. Medical management of SBOs is possible, effective, and has a lower morbidity than the other two infections.

An important adjunct to non-operative management would be enhanced prevention to reduce the likelihood of developing an intra-abdominal infection. Prevention of intra-abdominal infections comes in two forms: screening and prophylactic surgery. Individuals with preexisting cholelithiasis and diverticular disease will be screened during astronaut selection and preflight exams. Though prophylactic surgery is rarely performed prior to entering austere environments, it might be more important before exploration missions. Long-duration spaceflight differs from many austere environments because evacuation might be impossible and, thus, might necessitate prophylactic surgery.

Prophylactic surgeries such as appendectomy or cholecystectomy increase the risk of SBO. As previously mentioned by Barabas, the risk of SBO after laparoscopic or open appendectomy is 1.4% to 1.5%. His study and similar studies found this risk to fall within a year of surgery. A 5-

year prospective study showed the mean time to post-appendectomy SBO was 1.1 years.<sup>51</sup> The rates of SBO following appendectomy are lower for a normal appendix compared to an inflamed appendix, which is 5.9%, due to exploration of the abdomen.<sup>51,52</sup> This evidence supports prophylactic appendectomy followed by a 2-year waiting period in order to reduce risk of in-flight appendicitis. Prophylactic cholecystectomy is rarely performed and not well characterized in medical literature. Further risk stratification is necessary before recommending prophylactic cholecystectomy.

### **4.3 Skin Lacerations**

Literature that has been reviewed focused on wound healing by limiting the potential for infection and wound repair techniques to enhance closure. Immunosuppression during spaceflight requires more research but might increase the risk of infection.<sup>18</sup> Since wound irrigation is the primary method of reducing infection in austere environments and spaceflight might limit irrigation capabilities, prophylactic antibiotics may be indicated. Topical and oral antibiotics taken as a prophylactic might reduce this risk even though they are not a standard of care on the ground.

Wound infection might further be reduced by utilizing non-suture wound closure. The role of tissue adhesives and Steri-Strips can be expanded in spaceflight. Tissue adhesives have successfully been applied in microgravity.<sup>18</sup> In the event of a laceration involving the vermilion border of the lip or involving critical components of the eyelids, for which plastic surgery or ophthalmology consultant services are typically requested, open management or Steri-Strips can be considered<sup>53</sup> (telemedicine guidance is another alternative for complicated repairs). Also, as described in the results section, delayed primary closure can help mitigate wound infection in the absence of adequate irrigation and is currently recommended by the Wilderness Medical Society as a potential treatment.

### **4.4 Behavioral Emergencies**

Due to the extensive psychiatric and psychological screening during astronaut selection, it is rare that a psychiatric event such as anxiety or panic disorder would surface based on genetic predisposition or preexisting psychiatric diagnosis.<sup>54</sup> The risk of psychiatric emergencies appears to be well-controlled with preventive measures and screening criteria in spaceflight. Long-duration spaceflight might trigger behavioral emergencies at a higher frequency than current mission profiles. Crew composition should also be carefully considered. For example, men may be much more likely to be violent than women,<sup>7</sup> which is important considering an exploration mission with a higher percentage of males. Standard of care disorders is followed in austere environments using benzodiazepines and haldoperidol. In spaceflight, this can be used and supplemented with supportive care and counseling from teammates or remotely. In addition, crewmembers might be trained on psychiatric disorders and offering acute support in the event of crisis.

## 5. CONCLUSIONS

The four conditions from the SMEMCL that were reviewed as a starting point for understanding treatment approaches in austere environments and research highlights are summarized below.

Anaphylaxis:

- A terrestrial treatment strategy of epinephrine, diphenhydramine, and steroid is recommended given mass, ground-based incidence, and potential mission impact of disease.
- Epinephrine can be safely administered by non-medical crewmembers with minimal training.

Intra-abdominal infection:

- Non-operative management in-flight can substitute for surgery in cases of appendicitis, diverticulitis, cholelithiasis, and bowel obstruction. However, cholecystitis is least likely to improve without surgery.
- Current literature suggests that prophylactic surgery is slightly safer than non-operative management in-flight, especially 2 years after the surgery. More research is needed to define the lifetime incidence of SBO after surgery and non-operative management of cholecystitis.

Skin lacerations:

- If copious wound irrigation is not possible in-flight, then topical and oral antibiotics should be considered as a prophylactic measure.
- The role of tissue adhesives can be expanded to include wound closure beyond the scope of ground-based lacerations.
- Delayed primary closure should be considered in complicated and contaminated wounds.

Behavioral emergencies:

- Benzodiazepines and haloperidol should continue to be supplied in medical kits for psychiatric disorders.
- Crewmember training can include acute management and assistance for psychiatric crisis.

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