Space Medicine: Impaired Wound Healing in Microgravity

Sarit Dhar, BS[1]; Dilpreet Kaeley, BS[1]; Fatima Khan, BS[1]; Madhulika Kastury, BS[1]; Catherine A. Cash, BS[1]; Amber Edson, MS, BS[1]; Richard Simman, MD, FACS, FACCWS[2,3].

1) University of Toledo, College of Medicine and Life Sciences, 3000 Arlington Ave., Toledo, Ohio.
2) Department of Surgery, Plastic Surgery, University of Toledo College of Medicine, Toledo, Ohio.
3) Jobst Vascular Institute, ProMedica Health Network, Toledo, Ohio.

THE UNIVERSITY OF TOLEDO

Introduction

As manned spaceflight missions become longer in duration and more complex in planning, the health and safety of crew members become significantly harder to predict and manage. The harsh environment of space contributes to numerous physiologic changes in the human body, in part due to the lack of gravity and exposure to radiation. These changes include the loss of bone density, muscle atrophy, cardiac dysfunction, loss of proprioception, immune dysregulation, and changes in gene expression.

In particular, the gravity environment in space, termed microgravity (uG), is responsible for much of the cellular and microscopic dysfunction of human tissue. Previous research has been shown that wound healing is impaired in a microgravity environment. This phenomenon is multifaceted and may be attributed to alterations in cell signaling, cytoskeleton, and fluid shifts due to microgravity.

There are many possible mechanisms for developing wounds in spaceflight, including trauma, radiation exposure, or medical procedures. The possibility of a crew member developing a non-healing wound increases as mission duration and complexity increase. NASA's Integrated Medical Model (IMM) considers burn wounds, skin abrasions, skin lacerations, skin rashes, and skin infections to be among the 100 most likely medical conditions to manifest during spaceflight. Therefore, it is crucial to understand the best and most practical treatment strategies for non-healing wounds before mission planning begins.

Methods

A literature review was conducted in the PubMed database limited to English language articles published between the years 1999 and 2023 using the terms: "wound healing," "microgravity," "graft," in various combinations with "spaceflight," "weightlessness," "epithelial cells," "suture," and "countermeasures." Articles describing the mechanisms for impaired wound healing and possible countermeasures were reviewed and relevant articles are discussed in the body of this paper. The references from each article were also reviewed and used for additional relevant articles. A similar search of key terms was used in Google Scholar to incorporate non-clinical information from the fields of bioengineering and space operations.

Microgravity & Wound Healing

Microgravity can cause non-healing wounds due to the dysregulation of cellular processes and inflammatory markers in each of the stages of wound healing: hemostasis, inflammation, proliferation, and remodeling.

- ***Hemostasis:*** In a study using hindlimb unloading on mice to simulate microgravity, bleeding time was found to be increased compared to the control when induced by Ristocetin or collagen indicating that the process of platelet aggregation may be impaired in space. A decrease in GPIbα surface expression and association with the cytoskeleton was noted, which may indicate impaired platelet adhesion to von Willebrand factor.
- ***Inflammation:*** Macrophages, T-cells, and neutrophils experience a significant reduction in response to wounded tissue and altered secretion of inflammatory markers, such as IL-2, IL-2R, AP-1, IL-1β, IL-1, and IL-6, in simulated microgravity conditions.
- ***Proliferation:*** Endothelial cells demonstrate delayed growth, cytoskeletal lesions, increased cell membrane permeability, cell softening, and reduced motility compared to controls. Endothelial cells also have altered secretion of growth factors, cytokines, and extracellular matrix components in microgravity conditions.
- ***Remodeling:*** Microgravity also induces dysfunction in fibroblast differentiation and migration which impair matrix remodeling capability.

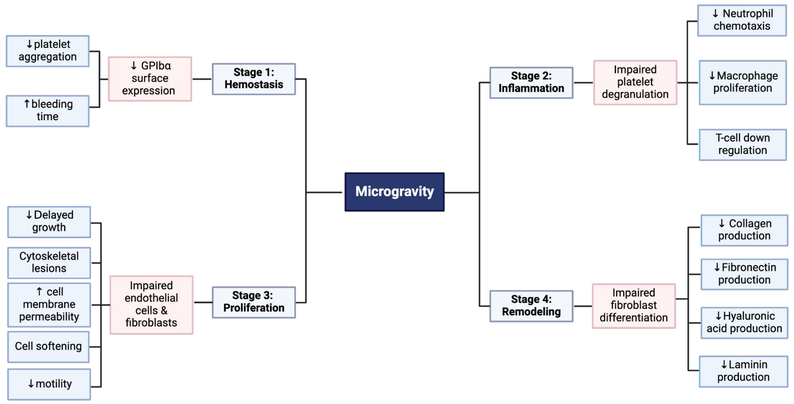

Figure 1. The impact of microgravity on the four stages of wound healing: hemostasis, proliferation, inflammation, and remodeling.

Potential Treatments

Platelet-rich plasma (PRP)

In a recent paper by Cialdai et al., a study was performed to assess the healing of sutured wounds on leeches exposed to simulated microgravity via a random positioning machine (RPM). The study demonstrated that *platelet-rich plasma (PRP)* induced a statistically significant increase in fibroblast chemotactic response and resulted in faster wound closure and prevention of altered tissue structure. However, despite this result, the short shelf-life of PRP may exclude it from being a solution to spaceflight-related wounds.

Light-emitting diodes (LED)

Another potential treatment developed by NASA is *light-emitting diodes (LED)*, which were used in animal model studies to irradiate chronic wounds. Tissue-regenerating genes such as integrin, laminin, gap-junction proteins, and kinesin proteins, were upregulated compared to untreated samples, and increased fibroblast growth was observed. By using this LED treatment, the wound healing time was decreased in crew members on a U.S. Navy submarine in a 2001 study by Whelan et al.

Conclusion

Sustaining a wound during space travel remains a significant risk, and carries with it complications for crewmember health, cost, and mission success. A full understanding of the physiologic disruption in wound healing has yet to be reached, and understanding the mechanisms and viable treatments for impaired or delayed wound healing in space is critical before long-duration missions are attempted. Each of the healing modalities typically used for wounds on Earth comes with unique pros and cons when it comes to implementation in space.

Within the next decade, treatment efficacy must be studied along with logistic planning and medical kit optimization to create standard treatment protocols for spaceflight-related wounds to ensure timely incorporation before long-duration missions. Future studies regarding these topics will be an important step in developing efficacious treatment and management of wounds in space.