Trauma Monthly 2026; 31(5): 2149-2151

10.30491/tm.2026.591691.1960

Trauma Monthly

Letter to the Editor

Bacteriophage Therapy for Trauma-Related Wound Infections: A Bacteriological Perspective on a Precision Adjunct to Antibiotics

Davood Kalantar-Neyestanaki[1,2], Ali Samareh[3], Sanaz Rastegar[1,2*]

[1] Medical Mycology and Bacteriology Research Center, Kerman University of Medical Sciences, Kerman, Iran

[2] Department of Medical Microbiology (Bacteriology and Virology), Afzalipour School of Medicine, Kerman, Iran

[3] Applied Cellular and Molecular Research Center, Kerman University of Medical Sciences, Kerman, Iran

***Corresponding Author:** Sanaz Rastegar, Ph.D., Medical Mycology and Bacteriology Research Center, Kerman University of Medical Sciences, Kerman, Iran; Email: sanazrastegarr@gmail.com; Telephone: 03431320500-678; ORCID: https://orcid.org/0000-0001-9793-0092

Article type: Letter to the Editor

Running title: Phage Therapy in Trauma-Related Infections

Keywords: Bacteriophage therapy; Trauma-related infection; Multidrug resistance; Biofilm; Bacteriology

Dear Editor,

Trauma-related wound infections remain a serious concern in acute care, orthopedic trauma, burn medicine, and reconstructive surgery. Although early debridement, source control, antibiotic therapy, and infection prevention efforts have improved outcomes, bacterial infection continues to complicate wound healing, prolong hospitalization, and contribute to sepsis and treatment failure, particularly when wounds are contaminated, polymicrobial, biofilm associated, or caused by multidrug resistant (MDR) organisms[1]. Recent estimates indicate that antimicrobial resistance (AMR) caused approximately 4.71 million deaths worldwide in 2021, with projected annual mortality reaching 8.22 million by 2050 without effective intervention. This burden is particularly relevant in orthopedic trauma, where fracture related infections may involve resistant Gram-negative pathogens, including *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa*, with carbapenem-resistant, extended-spectrum β-lactamase-producing, and MDR isolates reported in trauma center cohorts[2,3]. Future management of fracture related infection (FRI) and other trauma-related infections should therefore be microbiology driven, integrating rapid diagnostics, stewardship, source control, and pathogen specific adjuncts.

Bacteriophage therapy is re-emerging as a biologically plausible option in this context. Bacteriophages are viruses that specifically infect bacteria, and strictly lytic phages kill bacterial cells by replicating and lysing them. Their specificity is attractive for trauma related infections because it may allow targeted pathogen elimination while sparing commensal microbiota, and phages may be particularly useful against biofilm-associated bacteria implicated in delayed healing, implant infection, and recurrent FRI[4]. Phage therapy should not be presented as a replacement for antibiotics but as a precision adjunct, since bacterial burden, necrosis, impaired perfusion, foreign bodies, and biofilm architecture all limit antimicrobial efficacy in traumatic wounds; phages are therefore likely most effective combined with debridement, drainage, and rational antibiotic therapy. Phage-antibiotic combinations may produce additive or synergistic effects, and bacterial resistance to phages can in some cases restore antibiotic susceptibility, though these effects are strain-specific and require laboratory confirmation[4]. Trauma itself imposes host factors that complicate phage based treatment. Hemorrhagic shock, the systemic inflammatory response, and post-injury

Copyright © 2026 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

immunosuppression can alter bacterial clearance and phage pharmacokinetics, while impaired tissue perfusion and microvascular injury may limit phage penetration into necrotic or poorly vascularized wound beds. These disturbances argue for close coordination between resuscitation and any phage intervention, and favor local over systemic delivery when perfusion is compromised[3,5]. Case reports support phage therapy as an adjunct in trauma-related musculoskeletal infection. Nir-Paz *et al*. reported successful treatment of an FRI of the proximal tibia caused by extensively drug-resistant *A. baumannii* and MDR *K. pneumoniae* using intravenous personalized phages combined with antibiotics and surgery, with bacterial eradication and no adverse events over an 8 month follow-up[6]. Racenis *et al*. described a femoral FRI and osteomyelitis caused by MDR *P. aeruginosa* and vancomycin-resistant *Enterococcus faecium*, in which local irrigation with the BFC1 phage cocktail combined with ceftazidime-avibactam and surgery achieved clinical improvement and microbiological eradication[7]. A further trauma-relevant consideration is the host immune response to phages themselves. Both innate phagocytic clearance and adaptive antibody responses can rapidly neutralize circulating phage, and murine and clinical studies show that repeated systemic dosing can induce neutralizing antibodies associated with reduced efficacy on re-treatment. Local or intra-wound administration appears less susceptible to this effect and may be preferable when anatomically feasible[8]. For trauma-focused bacteriology laboratories, this field creates practical priorities: preserving isolates from infected wounds when MDR, recurrent infection, or biofilm-associated disease is suspected; developing phage susceptibility testing alongside conventional testing; genomically screening candidate phages for lysogeny, toxin genes, resistance genes, and transduction risk; and embedding phage programs within multidisciplinary teams of trauma surgeons, infectious disease specialists, microbiologists, and wound-care experts. Anatomical features of trauma wounds, such as poor vascularization, exposed bone, and fixation devices, may favor topical, intra-wound, or intra-articular phage formulations over systemic administration alone, with the delivery system and timing remaining central to this approach[9-11]. A practical barrier specific to acute trauma is time: personalized phage matching, susceptibility testing, and regulatory clearance typically take days to weeks, a timeline poorly suited to the urgency of early source control in FRI, so it cannot substitute for empirical antibiotics at presentation. Phage therapy also faces a narrow host range, potential resistance development, inconsistent regulatory pathways, and strict manufacturing requirements for sterility, purity, and reproducible potency, which are especially important in trauma patients who may be critically ill or at risk of bloodstream infection[9,10].

In conclusion, trauma-related wound infections and FRI demand an integrated, bacteriology-guided therapeutic strategy. Phage therapy should be considered a targeted adjunct, not a replacement for antibiotics, and should be used only alongside debridement, fracture stabilization, soft-tissue management, and culture-directed antimicrobial therapy. In the AMR era, optimal outcomes will likely depend on combining rigorous surgical source control with precision microbiological approaches.

Authors' Contributions

All authors contributed to conceptualization, interpretation of the literature, drafting, critical revision, and final approval of the manuscript.

Acknowledgment

The authors are grateful to the Medical Mycology and Bacteriology Research Center, Kerman University of Medical Sciences, Kerman, Iran, and the Applied Cellular and Molecular Research Center, Kerman University of Medical Sciences, Kerman, Iran.

Funding

No funding was received for this work

Competing Interests

The authors confirm that they have no competing interests

Consent for Publication

Not applicable

Ethical Issues

Not applicable

Declaration of Generative AI and AI-assisted Technologies

None.

References

1. Mende K, Akers KS, Tyner SD, Bennett JW, Simons MP, Blyth DM, et al. Multidrug-resistant and virulent organism's trauma infections: trauma infectious disease outcomes study initiative. *Mil Med*. 2022; 187:42-51.

2. Chen W, Zeng Y, Zheng J, Wang J, Gu W, Li M, et al. Evaluation of antimicrobial resistance governance across 193 countries to

inform the 2026 Global Action Plan update. *Nat Med*. 2026; 32:1362-73.

3. Zhang Z, Liu P, Wang W, Wang S, Li B, Li J, et al. Epidemiology and drug resistance of fracture-related infection of the long bones of the extremities: a retrospective study at the largest trauma center in Southwest China. *Front Microbiol*. 2022; 13:923735.

4. Rastegar S, Kalantar-Neyestanaki D, Mohammadpour S, Samareh A, Samare-Najaf M, Moghadam MT, et al. Potential of phage therapy for the treatment of diabetic foot infections. *Folia Microbiol (Praha)*. 2026:1-17.

5. Kelly EJ, Oliver MA, Carney BC, Shupp JW. Infection and burn injury. *European Burn Journal*. 2022; 3:165-79.

6. Nir-Paz R, Gelman D, Khouri A, Sisson BM, Fackler J, Alkalay-Oren S, et al. Successful treatment of antibiotic-resistant, poly-microbial bone infection with bacteriophages and antibiotics combination. *Clinical infectious diseases*. 2019; 69:2015-8.

7. Racenis K, Rezevska D, Madelane M, Lavrinovics E, Djebara S, Petersons A, et al. Use of phage cocktail BFC 1.10 in combination with ceftazidime-avibactam in the treatment of multidrug-resistant Pseudomonas aeruginosa femur osteomyelitis—A case report. *Front Med (Lausanne)*. 2022; 9:851310.

8. Bosco K, Fabijan AP, Iredell J, Dabrowska K, Khatami A. Immune responses to phage therapy in humans: A review. *J Infect Dis*. 2026;233: e1094-e1103.

9. Chen B, Moriarty TF, Metsemakers W-J, Chitto M. Phage therapy: a primer for orthopaedic trauma surgeons. *Injury*. 2024; 55:111847.

10. Shevchenko OV, Kharina AV, Korniienko NO, Budzanivska IH, Andriichuk OM, Pozhylov IM, et al. Phage therapy in traumatology: A review on perspectives for treating acute wounds and Post-Surgical complications. *Mikrobiol Zh*. 2024; 86:117-36.

11. Bhale B, Shirodkar S, Sawarkar S, Omri A. Phage therapy: innovations, challenges, and future directions in combating superbugs and antibiotic resistance. *Expert Rev Anti Infect Ther*. 2026; 24:213-37.