

Addressing the anthrax threat: A synthesis of clinical management and public health priorities

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To the Editor,

Anthrax, caused by the spore-forming bacterium *Bacillus anthracis*, remains a pathogen of significant global public health concern. Its historical notoriety as a biological weapon, combined with the intrinsic characteristics of environmental persistence and high lethality, requires a sustained and vigilant posture from both medical and security communities.^[1] The 2001 anthrax letter attacks in the United States served as a pivotal case study, moving the threat of bioterrorism from the realm of contingency planning to an urgent, tangible challenge. That incident revealed, with sobering clarity, how a release of limited geographical scope could nonetheless trigger a nationwide emergency, severely stress medical response systems, and mandate protracted and resource-intensive environmental remediation.^[2,3] This Letter to Editor seeks to synthesize key clinical features, current management strategies, persistent challenges, and future priorities necessary for mitigating the threat posed by this formidable agent.

The clinical presentation of human anthrax is dictated by the route of spore entry. In the context of deliberate release, inhalational exposure is of primary concern because of its associated high mortality. Inhalational anthrax follows a biphasic course. An initial prodromal phase presents nonspecific influenza-like symptoms, including fever, chills, fatigue, nonproductive cough, and mild chest discomfort.^[1,4] This phase, which may last from several hours to several days, presents a major diagnostic challenge, as it is easily mistaken for common viral respiratory infections. The subsequent fulminant phase begins abruptly and is characterized by severe dyspnea, hypoxemia, stridor, and septic shock. A pathognomonic feature is hemorrhagic mediastinitis, evident on imaging as a widened mediastinum. Progression to death may be rapid, often occurring within 24 to 36 hours

of symptom escalation, with mortality historically approaching 100 percent in the absence of prompt and appropriate intervention.^[1,4]

The formidable virulence of *B. anthracis* is plasmid-mediated. The tripartite anthrax toxin, encoded on plasmid pXO1, consists of protective antigen (PA), lethal factor (LF), and edema factor (EF). PA facilitates the cellular entry of LF, a zinc metalloprotease that disrupts key signaling pathways, and EF, a potent adenylate cyclase that induces extensive edema. A second plasmid, pXO2, directs synthesis of an antiphagocytic poly-D-glutamic acid capsule. This combination synergy of toxin-mediated cellular damage and immune evasion underpins the rapid systemic collapse observed in severe infection.^[5]

In addition to inhalational disease, two other primary clinical forms are recognized. Cutaneous anthrax, the most common naturally occurring presentation, results from spore inoculation through skin abrasions. The lesion progresses from a papule to a vesicle and then ulcerates, forming a characteristic painless eschar with a black necrotic center, often surrounded by significant edema. Gastrointestinal anthrax, which results from the ingestion of contaminated meat, manifests as severe oropharyngeal or abdominal disease, frequently progressing to sepsis and shock with high mortality.^[6,7]

Effective management of systemic anthrax rests on two interdependent pillars: prompt antimicrobial therapy and adjunctive antitoxin administration. For inhalational, gastrointestinal, or disseminated cutaneous diseases, immediate intravenous antimicrobials are imperative.^[5,8] Ciprofloxacin and doxycycline are first-line agents, with treatment recommended for a minimum of 60 days to address the risk of delayed spore germination. However, antimicrobials target only the vegetative bacilli and do not neutralize the lethal toxins already circulating. Accordingly, timely administration of an antitoxin is an essential element of care in severe cases. Agents such as human anthrax immunoglobulin or monoclonal antibodies (e.g., raxibacumab) bind to PA, preventing further cellular intoxication and significantly improving survival outcomes when combined with antimicrobials.^[5,8]

Significant challenges persist in anthrax preparedness and response. Diagnostic delay remains a major obstacle. Confirmatory testing relies on specialized laboratory methods, such as culture, polymerase chain reaction, and immunohistochemistry, which are not available at the point of care. Improved syndromic surveillance for clusters of severe influenza-like illness is therefore necessary for early outbreak detection.^[1,6]

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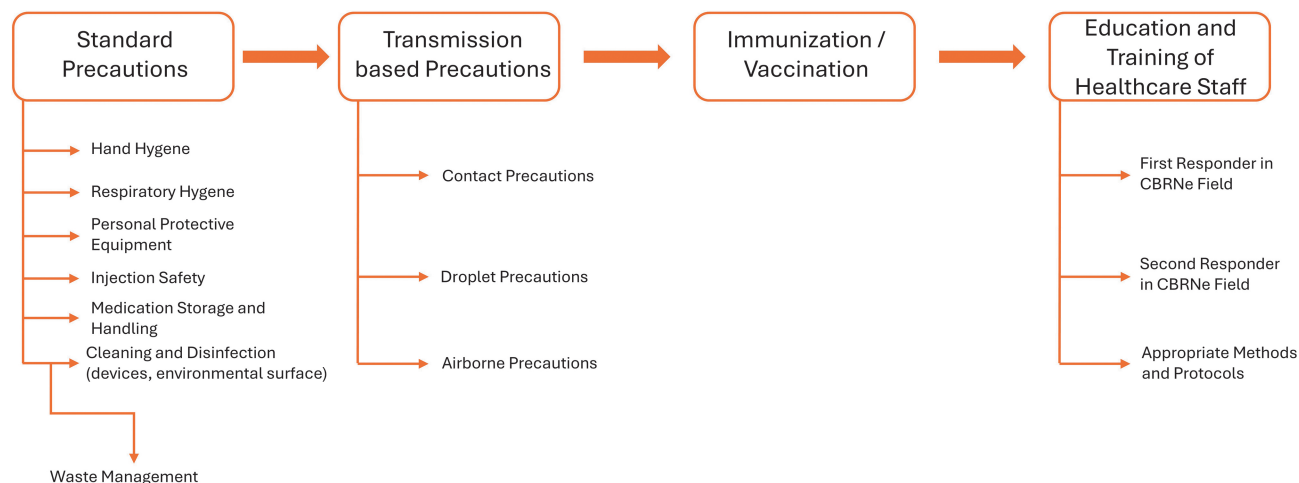


Figure 1: Flow chart for emergency management using a CBRNe approach. CBRNe: Chemical, Biological, Radiological, Nuclear, and explosives.

Given these persistent diagnostic and therapeutic challenges, anticipate preparedness requires a dual strategy: advancing next-generation countermeasures while reinforcing operational resilience. Of particular concern is the potential development or deliberate engineering of antimicrobial-resistant strains, which would undermine existing prophylaxis and treatment strategies. Research efforts should therefore prioritize novel antimicrobial classes and next-generation antitoxins and vaccines.^[1,5,8] Concurrent investment in rapid, field-deployable diagnostic platforms is essential to accelerating response times. Finally, technological advances must be coupled with an unwavering commitment to operational readiness. Regular, large-scale, multidisciplinary exercises simulating a deliberate release are indispensable for testing response plans, breaking down institutional silos, and promoting seamless coordination among public health, healthcare, and emergency response organizations during a crisis within the Chemical, Biological, Radiological, Nuclear, and explosives framework (Figure 1).^[2,3,9,10]

In conclusion, *B. anthracis* endures as a paradigm of a high-consequence biological threat. A comprehensive defense requires a dual strategy: continuous advancement of scientific countermeasures paired with sustained investment in operational preparedness and interagency collaboration. Through this integrated approach, the global health community can improve its resilience and capacity to manage the complex challenges posed by anthrax, thereby safeguarding public health security.

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Author Contributions

Gian Marco Ludovici was responsible for the conceptualization and writing of this research highlight, ensuring that the key findings were accurately summarized and effectively communicated. Paola Amelia Tassi and Samuele Maria Giorgio provided scientific suggestions for conceptualization and manuscript revision. Alba Iannotti and Colomba Russo contributed through conceptualization, creating the figure, and reviewing the manuscript, thereby enhancing the visual appeal and ensuring the accuracy

of the presented information. Andrea Malizia provided expert supervision, reviewing, and editing of this research highlight. All authors have read and approved the final manuscript.

Conflicts of Interest

None.

References

- [1] Ogunleye SC, Olorunshola MM, Fasina KA, et al. Anthrax outbreak: exploring its biological agents and public health implications. *Front Trop Dis* 2024;4:1297896. doi:10.3389/ftd.2023.1297896.
- [2] Ludovici GM, Tassi PA, Iannotti A, et al. Bioterrorism and CBRNe threats: The role of Ebola in global security. *Ethics Med Public Health* 2025;33:101138. doi:10.1016/j.jemep.2025.101138.
- [3] Ludovici GM, Ricci C, Manenti G, et al. The threat of Monkeypox virus: a review of its potential use as a biological weapon. *Eur Phys J Plus* 2025;140:827. doi:10.1140/epjp/s13360-025-06721-2.
- [4] Gutting BW, Nichols TL, Channel SR, et al. Inhalational anthrax (Ames aerosol) in naïve and vaccinated New Zealand rabbits: characterizing the spread of bacteria from lung deposition to bacteremia. *Front Cell Infect Microbiol* 2012;2:87. doi:10.3389/fcimb.2012.00087.
- [5] Liang X, Zhu J, Zhao Z, et al. The pag Gene of pXO1 Is Involved in Capsule Biosynthesis of *Bacillus anthracis* Pasteur II Strain. *Front Cell Infect Microbiol* 2017;7:203. doi:10.3389/fcimb.2017.00203.
- [6] Ashique S, Biswas A, Mohanto S, et al. Anthrax: A narrative review. *New Microbes New Infect* 2024;62:101501. doi:10.1016/j.nmni.2024.101501.
- [7] Nakanwagi M, Ario AR, Kwagonza L, et al. Outbreak of gastrointestinal anthrax following eating beef of suspicious origin: Isingiro District, Uganda, 2017. *PLoS Negl Trop Dis* 2020;14(2):e0008026. doi:10.1371/journal.pntd.0008026.
- [8] Sangwan N, Gangwal A, Jain P, et al. Anthrax: Transmission, pathogenesis, prevention and treatment. *Toxins* 2025;17(2):56. doi:10.3390/toxins17020056.
- [9] Ciparisse JF, Cenciarelli O, Mancinelli S, et al. A computational fluid dynamics simulation of anthrax diffusion in a subway station. *Int J Math Models Methods Appl Sci* 2016;10:286–291.
- [10] Malizia A, McGovern J, Sarigiannis D, et al. Integrating the exposome framework in CBRNe risk assessment: a holistic approach to chemical, biological, radiological, nuclear, and explosive threats. *Eur Phys J Plus* 2025;140: 1103. doi:10.1140/epjp/s13360-025-07030-4.

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