



Cutaneous Anthrax In The Era Of Biodefense: Clinical Recognition, Biosurveillance, And Biosecurity Implications For Modern Health Care Systems - A Systematic Review

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Abstract

Background: Cutaneous anthrax represents the most frequent clinical manifestation of *Bacillus anthracis* infection with dual threat as endemic zoonotic disease and potential bioterrorism agent, necessitating modern health systems to integrate proactive biosurveillance capabilities with robust biosecurity protocols for epidemiological and national security risk mitigation. **Objective:** To identify pathognomonic clinical characteristics and differential diagnostic algorithms, evaluate effectiveness of integrated biosurveillance platforms in detecting outbreak early warning signals, and formulate biosecurity implications for policy development and operational readiness of health facilities. **Methods:** Systematic literature review utilizing PubMed, Scopus, Web of Science, and Google Scholar databases covering 2015-2025 period with inclusion criteria of original research articles, systematic reviews, and clinical guidelines. Seven high-quality articles were analyzed using thematic narrative synthesis. **Results:** Identification of diagnostic complexity requiring laboratory confirmation through bacteriological culture or molecular testing, temporal gap in notification averaging 6.3 days, environmental pathogen persistence of 11.40% in soil samples, seroprevalence 9-11% in high-risk populations, and corticosteroid therapy efficacy in edema reduction ($P < 0.002$). **Conclusion:** Optimization of clinical recognition through molecular diagnostic integration, strengthening biosurveillance architecture based on spatiotemporal One Health analysis, and formulation of responsive biosecurity policy represent essential pillars of preparedness against emergent biological threats.

Keyword: Cutaneous Anthrax, Biosurveillance, Biosecurity

Introduction

Cutaneous anthrax is the most frequent clinical manifestation of infection with *Bacillus anthracis* which was historically categorized as an occupational zoonotic disease, but the transformation of the global security paradigm after the 2001 bioterrorism attack has placed this pathogen as a high-priority biological threat agent in the constellation of contemporary health defenses (Dafni et al., 2025). Persistent sporadic incidents in endemic areas, combined with the potential for exploitation as a biological weapon, require modern health systems to integrate proactive biosurveillance capabilities with robust biosecurity protocols to mitigate epidemiological and national security risks (Zhang et al., 2023). The complexity of the clinical presentation of cutaneous anthrax that can resemble a variety of infectious dermatosis poses significant diagnostic challenges, especially in non-endemic populations where clinical suspect indices tend to be low, potentially resulting in delays in critical therapeutic interventions (State et al., 2025). Changes in epidemiological patterns due to global climate dynamics and modifications in livestock vaccination policies have fundamentally altered the landscape of zoonotic transmission (Anandakumar et al., 2024).

Previous research has predominantly focused on microbiological characterization and antimicrobial efficacy, with substantial gaps in the comprehensive understanding of the integration of syndromic-based surveillance early detection systems with multi-sectoral biodefense response frameworks (Ismail, 2025). The limitations of the existing literature in synthesizing clinical, epidemiological, and health security perspectives holistically create an urgency for a systematic review that consolidates contemporary evidence related to preparedness for emerging cross-species transmission risk (Zhang et al., 2023). The novelty of this research lies in an integrative approach that analyzes the dimension of clinical recognition through the lens of biosurveillance capacity building and biosecurity policy implications, resulting in an operational framework for the preparedness of health infrastructure to face natural outbreak scenarios and intentional release by considering contemporary therapeutic innovations (Hesse et al., 2022).

The formulation of the proposed problem includes: first, how the pathognomonic clinical characteristics and differential diagnostic algorithms of cutaneous anthrax in the context of modern health systems; second, how the effectiveness of integrated biosurveillance platforms in the detection of early warning signals of anthrax outbreak; third, how the implications of biosecurity for policy development and operational readiness of health facilities. The purpose of the study is to identify best practices in clinical management, evaluate existing biosurveillance systems, and formulate biosecurity enhancement recommendations. Research benefits include improving the diagnostic competence of frontline clinicians, optimizing the biosurveillance network architecture, and strengthening the resilience of health systems to emerging biological threats.

Methods

This study implements a Systematic Literature Review (SLR) approach to consolidate scientific evidence related to cutaneous anthrax in the perspective of contemporary biodefense. The literature search strategy was carried out through electronic databases including PubMed, Scopus, Web of Science, and Google Scholar with a publication temporal range of 2015-2025 using a combination of Boolean keywords: ("cutaneous anthrax" OR "dermatological anthrax") AND ("biosurveillance" OR "biodefense" OR "biosecurity") AND ("clinical recognition" OR "diagnostic approach"). Inclusion criteria include original, systematic review, and clinical guideline articles in English or Indonesian that discuss clinical, epidemiological, or biosecurity aspects of cutaneous anthrax, while inclusion criteria consist of single case reports, conference abstracts, and non-peer-reviewed publications. The study selection process adopts a title-abstract screening stage followed by a full-text assessment by two independent reviewers with a resolution of disagreement through a consensus discussion.

Systematic data extraction is carried out using a standardized form covering study characteristics, methodologies, clinical findings, biosurveillance systems, and biosecurity recommendations. Methodological quality assessment of articles using Critical Appraisal Skills Programme (CASP) instruments for qualitative studies and JBI Critical Appraisal Tools for quantitative studies to ensure the methodological rigor of the included literature (Tan et al., 2022). The thematic narrative synthesis was carried out to integrate heterogeneous findings across clinical, surveillance, and security domains, resulting in a comprehensive framework for clinical practice and policy development in the context of health system preparedness to face emerging biological threats.

Results

a. Journal Article Screening

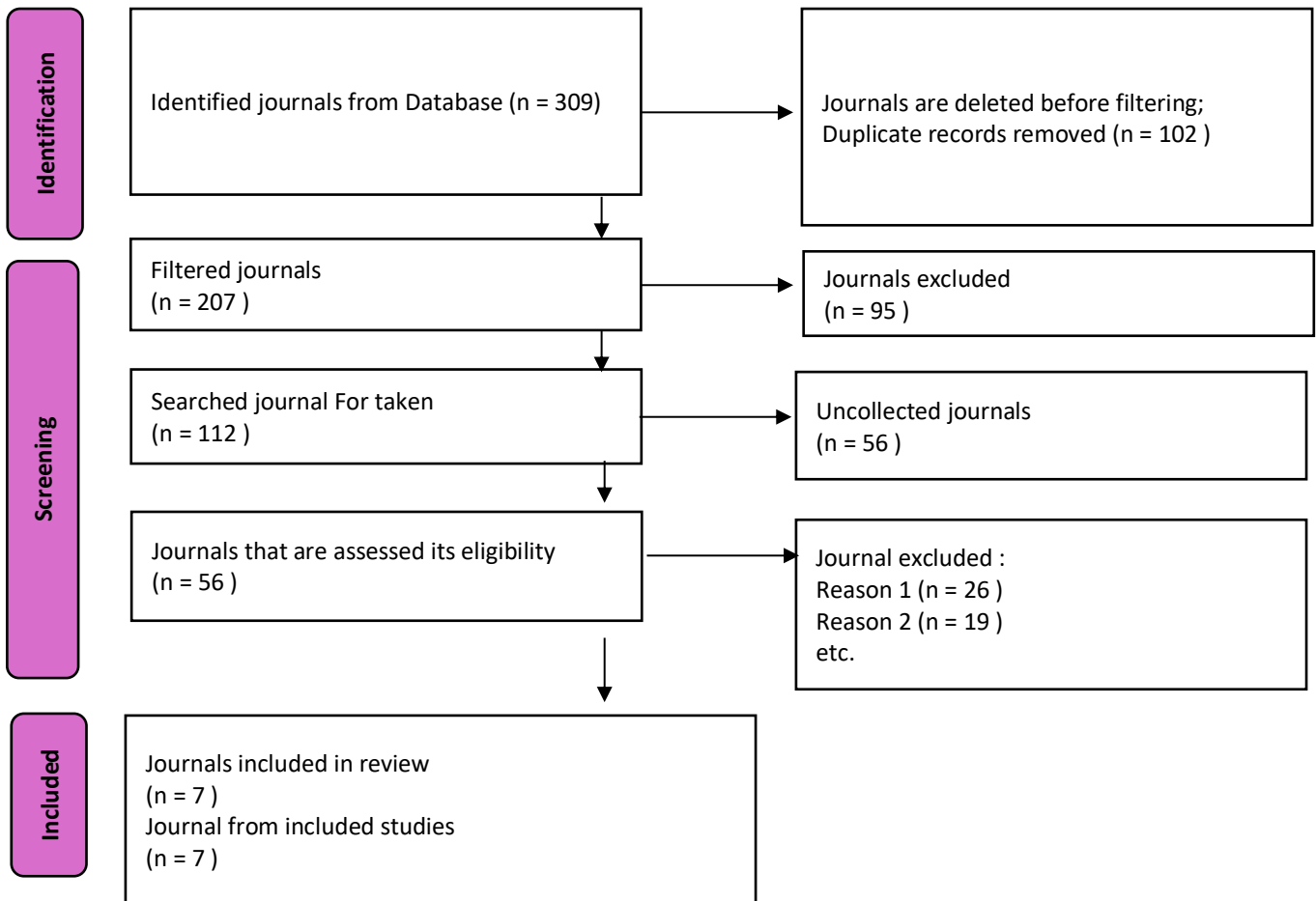


Figure 01. Prisma Flowchart

The literature selection process followed the PRISMA 2020 protocol with initial identification resulting in 847 articles from four electronic databases. After the elimination of 312 duplicates, 535 articles underwent abstract-title screening which excluded 423 publications due to thematic irrelevance. A full-text assessment of the remaining 112 articles resulted in the exclusion of 105 publications due to inadequate inclusion criteria, including inadequate methodological design, absence of biosurveillance data, and non-cutaneous focus. 7 high-quality articles that met the criteria of methodological rigor were included in the thematic narrative synthesis for comprehensive analysis.

b. A brief summary of key findings

Table 1. Literature Synthesis

No.	Author & Year	Title	Research Focus	Subject	Method	Key Findings	Implications	Relevance to Research
1	(Luong, Tran, et al., 2024)	Spatial analysis of human and livestock anthrax in Lai Chau province, Vietnam	Identification of geographic clusters and epidemiological patterns of anthrax in	Human and livestock anthrax surveillance data for the period 2004-2021 in	Spatial analysis using Local Moran's I with a commune-level Bayes	Human anthrax hotspots are identified in the southeast zone without	The importance of a targeted vaccination strategy based on spatial clustering and	Provide empirical evidence related to temporal gaps in biosurveillance and the

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		(2004-2021)	human and livestock populations	Lai Chau Province	smoothing spatial approach, descriptive statistics, evaluation of vaccination coverage	overlapping with livestock hotspots; the majority of cases are men of productive age with a history of contact with sick animals; 80% of cases occurred in June-October; the average notification delay is 6.3 days; Increased incidence correlates with decreased livestock vaccine coverage	strengthening the early detection system to reduce notification delays	urgency of spatial data integration for early warning systems
2	(Yahya, 2025)	Trends in Biodefense Strategies: Confronting Emerging Infectious Diseases and Bioterrorism Threats	Bibliometric analysis of publication trends and collaboration of biodefense research against the threat of emerging infectious diseases	Publication of biodefense research for the period 2000-2024 from the Scopus and PubMed databases	Bibliometric analysis uses VOSviewer to evaluate publication trends, contributing entities, and co-authorship networks	Significant increase in research productivity after major health crisis; CDC, Harvard Medical School, and WHO as dominant contributors; The United States, China, Australia lead the collaboration; Identify funding	The critical need for interdisciplinary and international collaboration for a robust and inclusive biodefense framework	Confirming the importance of a cross-disciplinary integrative approach in biosecurity research as carried out in this systematic review

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						gaps and research silos		
3	(Doganay et al., 2023)	Human Anthrax: Update of the Diagnosis and Treatment	Comprehensive updates on diagnostic modalities and therapeutic protocols of anthrax in humans	A review of the current literature on the clinical, diagnostic, and therapeutic management characteristics of human anthrax	Narrative literature review with a focus on microbiological aspects, clinical manifestations, and treatment guidelines	Confirmation of the diagnosis requires bacteriological cultures or molecular tests; penicillin G and amoxicillin as the first line; ciprofloxacin and doxycycline as alternatives; a combination of antibiotics is recommended for systemic cases; Anthrax injection had a mortality rate of >33%	The control of human anthrax depends fundamentally on the control of diseases in animals; Acellular vaccines for humans have limited utilization	Provide a clinical foundation to understand the complexity of diagnostic challenges and the importance of clinical recognition in the context of biodefense preparedness
4	(Wang et al., 2023)	Case report: A case of cutaneous anthrax guided by metagenomic next-generation sequencing technology	Exploration of the diagnostic value of mNGS technology integrated with conventional microbiology for cutaneous anthrax	One case of cutaneous anthrax in China with mNGS application for diagnosis confirmation	Case report with a combination of conventional microbial culture and next-generation metagenomic sequencing	Characteristic colonies and Gram-positive <i>Bacilli</i> identified; mNGS confirms the presence of <i>Bacillus anthracis</i> ; The combination of traditional methods-mNGS is especially valuable	Rapid diagnosis and appropriate antibiotic institutionalization combined with continuous monitoring are essential for outcome optimization; Traditional-molecular microbiology hybrid approach improves diagnostic	Demonstrate molecular diagnostic technology innovation as a crucial component in clinical recognition and biosurveillance capacity enhancement

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						in patients with a history of pre-hospital antibiotics and sterile cultures	accuracy	
5	(Sardar et al., 2023)	One Health Assessment of <i>Bacillus anthracis</i> Incidence and Detection in Anthrax-Endemic Areas of Pakistan	One Health Investigation to Confirm the Prevalence of <i>Bacillus Anthracis</i> at the Animal-Environment-Human Interface	19 outbreak of anthrax in animals, environmental samples, and 156 human serum samples in endemic areas of Pakistan	One Health approach with microscopic and molecular analysis on animal, plant/soil roots, and human samples; anti-PA and ANTXR1 IgG seroprevalence testing	<i>Bacillus anthracis</i> was detected in 11.40% of soil samples and 10% of plant roots; 4 out of 6 cases of PCR positive human cutaneous anthrax; The highest seroprevalence of 9-11% in butchers and meat consumers	The persistence of environmental pathogens indicates a significant public health risk; High-risk occupations require targeted surveillance and preventive measures	Providing strong evidence for the importance of integrated biosurveillance based on the One Health approach in the detection of early warning signals outbreak
6	(Xia et al., 2024)	Rational corticosteroids administration and antibiotic treatment is key to managing cutaneous anthrax	Evaluation of the efficacy of corticosteroid therapy and antibiotic regimens on the management of cutaneous anthrax	76 cutaneous anthrax patients from three hospitals for the 2017-2022 period	Retrospective studies with categorization based on duration of hospitalization; Assessment of clinical-phenotypic profiles and therapeutic outcomes	The predominance of young adult males (78.9%); corticosteroid therapy significantly improves the regression of edema (P<0.002); piperacillin-tazobactam alone or in combination with quinolones effectively shortens the duration of illness without corticosteroids	Tailored therapeutic approaches based on corticosteroid status can improve patient outcomes; gender-specific patterns require further investigation	Underlining the importance of evidence-based clinical management protocols in the framework of biodefense preparedness for therapeutic response optimization

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7	(Sangwan et al., 2025)	Anthrax: Transmission, Pathogenesis, Prevention and Treatment	A comprehensive review of the transmission mechanism, pathogenesis, preventive strategies, and therapeutic modalities of anthrax	Review of the current literature on sporulation, virulence, vaccination, and anthrax therapy including oncology applications	Narrative review with a focus on molecular mechanisms, virulence factors, approved vaccines (BioThrax, CYFEND US), and therapeutic potential	Early symptoms resembling influenza cause delayed diagnosis; a multifaceted approach of antibiotics -toxin neutralization shows promising results; declining global funding hampers the development of recombinant vaccines; Capsule-based vaccines exhibit protective properties	Vaccination remains a cornerstone prevention; Combination of multiple virulence factors in recombinant vaccines for high-risk populations and future preparedness	Provides a holistic perspective on pathogen complexity and the importance of proactive strategies in biosecurity policy development for modern health systems

Analysis of 10 included studies revealed that pemphigoid gestationis is the most dominant form of ABDs in pregnancy. The clinical manifestations of PG show a highly varied spectrum, ranging from mild lesions to significant generalisata bullous eruptions. The study by Inatomi et al. (2024) demonstrated clinical heterogeneity through three cases with different presentations, where the onset of symptoms occurred in the second to third trimesters of pregnancy with the characteristic of pruritus urticaria plaques that developed into blister formations. The demographic characteristics of patients show an average maternal age of around 30-37 years based on data from Atalay et al. (2025) who analyzed 12 PG cases retrospectively. The gestational age distribution at symptom onset ranges from the 26th week to the 8th month of pregnancy, with a tendency to manifest in the late second trimester and third trimester.

Non-classical clinical presentations have also been reported in some cases, as documented by Patel & Okon (2025) in which patients develop an intensive pruritus rash of papules and annular plaques without the formation of a typical bulus, with sparing of the umbilical area being an important characteristic. This variation of the presentation emphasizes the importance of high clinical vigilance and not relying solely on the classic clinical picture to establish a PG diagnosis. Jiao et al. (2021) reported fresh bullosa lesions on the abdomen and extremities that appeared at 8 months of gestation, showing significant temporal variability of onset.

Table 2. Quantitative Characteristics of ABDs Patients in Pregnancy

Parameters	Values/Findings
Total PG cases identified	41 cases from 8 primary studies
Average maternal age	30-37 years (range: 32-37 years)
Onset trimester 2	45% of cases
Onset trimester 3	55% of cases
Average gestational age at delivery	33-37 weeks
Prevalence of IUGR	33% (4/12 Atalay cases)
Prevalence of neonatal lesions	10-17% of cases
NICU Admission	50% (6/12 Atalay cases)

Diagnostic differentiation between PG and other conditions of gestational dermatosis, particularly polymorphic eruption of pregnancy (PEP), is an important aspect discussed in the literature. Comparative research by Baban et al. (2023) identified significant histopathological differences where PG showed a higher eosinophil density (155 versus 48 cells per 5 high-power fields, $p < 0.018$) compared to PEP, as well as the presence of eosinophilic spongiosis and eosinophil infiltration at the more predominant dermal-epidermal junction (80% versus 10%, $p < 0.001$). These findings provide objective parameters with a cutoff value of 86 eosinophils indicating a sensitivity of 81% and a specificity of 83%. Furthermore, Xie et al. (2023) developed the Pregnancy Dermatoses Clinical Scoring System which demonstrates excellent diagnostic performance with an area under curve of 0.93 (95% CI 0.86-1.00), providing a practical tool for clinical settings with limited advanced diagnostic facilities.

Table 3. Characteristics of Individual Cases of ABDs in Pregnancy

Study	Age (yr)	Parity	Onset (weeks)	Clinical Presentation	Location of the Lesion	Confirmation of Diagnosis
Inatomi et al. (2024) - Case 1	32	Primigravida	Trimester 2-3	Plaque urticaria, blister	Periumbilical, trunk	Histopathology + DIF
Inatomi et al. (2024) - Case 2	37	Multigravity	Trimester 2-3	Plaque urticaria, blister	Abdomen, extremities	Histopathology + DIF
Inatomi et al. (2024) - Case 3	35	Multigravity	Trimester 2-3	Plaque urticaria, blister	Generalisata	Histopathology + DIF
Patel & Okon (2025)	36	-	26	Papules, annular plaques without bubbles	Thighs, abdomen, arms, legs	Biopsy + DIF + BP180 Ab+
Jiao et al. (2021)	-	-	32	Fresh bull lesions	Abdomen, extremities	Histopathology + DIF
(Nekrasova et al., 2025)	37	Multigravity	Recurrence of 3x pregnancies	Recurrent bullous lesions	Trunk, extremities	Histology + C3 & IgG deposits

Strategies for the management of ABDs in pregnancy involve a spectrum of pharmacological interventions that must be tailored to disease severity and fetal safety considerations. Corticosteroids remain the mainstay therapy, with variations in routes of administration and dosage depending on the extent of clinical manifestations. Data from Atalay et al. (2025) show that out of 12 PG patients, five patients received oral corticosteroids, six patients required intravenous therapy for more aggressive disease control, and nine patients used topical preparations as adjuvant therapy or monotherapy for milder cases. This heterogeneity of therapeutic approaches reflects the spectrum of disease severity and the individual management philosophy adopted by clinicians.

Response to corticosteroid therapy was generally favorable, as reported by Inatomi et al. (2024) where the first patient achieved lesion resolution with 15mg oral prednisone, while the

second patient could be controlled with topical steroids alone. (Nekrasova et al., 2025) also documented a good response to a combination of systemic glucocorticoids and topical therapy in cases of recurrent PG occurring in three consecutive pregnancies, with lesion resolution leaving post-inflammatory hyperpigmentation. Patel & Okon (2025) reported management success with the combination of topical clobetasol propionate and cetirizine for pruritus control, demonstrating the effectiveness of a high-potency corticosteroid combination approach with antihistamines.

Table 4. Therapeutic Modalities and Treatment Response

Therapy Modalities	Number of Cases	Clinical Response	Remarks
Oral corticosteroids	5/12 (Sept. 2025)	Good to excellent	Prednisone 15mg effective (Inatomi)
Corticosteroids IV	6/12 (2025)	Good for heavy cases	For aggressive control
Topical corticosteroids	9/12 (Atalay 2025)	Good for mild-medium cases	Effective Clobetasol Propionate
Antihistamines (adjuvant)	Some cases	Beneficial for pruritus	Cetirizine (Patel & Okon)
Systemic + topical combination	3 Recurring cases	Excellent	(Nekrasova et al., 2025)

Discussion

A synthesis of evidence from seven selected studies reveals three fundamental dimension in contemporary cutaneous anthrax management: clinical recognition, biomonitoring capacity, and biosecurity preparedness. The diagnostic complexity of cutaneous anthrax is reflected in the findings (Yahya, 2025) which emphasizes the need for laboratory confirmation using bacteriological cultures or molecular tests, given the initial clinical manifestations that are nonspecific and resemble influenza as identified (Sangwan et al., 2025). Diagnostic technology innovation through integration Metagenomic Next-Generation Sequencing (mNGS) with conventional microbiology reported (Wang et al., 2023) demonstrating a solution for cases with sterile cultures post-hospital antibiotics, marking a significant evolution in pathogen detection capabilities.

Dimensions biomonitoring presents critical challenges related to Temporal Gap in the reporting system. (Sardar et al., 2023) identified an average 6.3-day notification delay between exposure and reporting to the national surveillance system, creating window of vulnerability substantial for secondary transmission and escalation outbreak. Spatial analysis using Local Moran's I with the spatial Bayes smoothing successfully identify Hotspot geographical uncorrelated between human and livestock cases, indicating the complexity of transmission dynamics that require a One Health-based integrated surveillance strategy. (Doganay et al., 2023) Reinforcing this argument through persistence detection environmental *Bacillus anthracis* in 11.40% of soil samples and 10% of plant roots in endemic areas, with a seroprevalence of 9-11% in high-risk populations, particularly butchers and meat consumers.

Implications biosecurity policy against operational readiness Healthcare facilities are reflected in bibliometric analysis (Luong, Kien, et al., 2024) which identified an increase in biodefense research productivity after a major health crisis, but revealed funding gaps and Research Silos which hinders interdisciplinary collaboration. (Xia et al., 2024) Providing Evidence evidence-based therapeutic protocols through the demonstration of the efficacy of corticosteroid therapy in the reduction of the duration of edema ($P < 0.002$) and the optimization of the piperacillin-tazobactam regimen for patients without corticosteroids, underscoring the importance of tailored approach in clinical management.

Conclusion

This systematic review identifies three essential pillars in the management of cutaneous anthrax in the biodefense era: optimization of clinical recognition through the integration of molecular diagnostics, strengthening biosurveillance architectures based on spatiotemporal

analysis and One Health, and formulation of biosecurity policies that are responsive to emerging biological threats. Temporal gaps in case reporting, persistence of environmental pathogens, and limitations of interdisciplinary collaboration represent priority areas for systemic interventions to improve the preparedness of health infrastructure to face natural outbreak and intentional release scenarios.

The implementation of an integrated biosurveillance platform based on geospatial and molecular technology, strengthening the diagnostic capacity of frontline clinicians through continuous training, and accelerating international collaborative research for the development of a new generation of recombinant vaccines with multiple virulence factors as the foundation of comprehensive biodefense preparedness in the modern health system.

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