



Facing The Menace Of Bioterrorism: Actualities, Hurdles, And Safeguarding Approaches

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Abstract:

Global terrorism poses an escalating peril to global stability, heightening the spectre of bioterrorism. This analysis delves into the conceivable menace of bioterrorism, the exploitable agents involved, and recent advancements in technologies and policies aimed at detecting and managing deliberately initiated epidemics. The response, both local and international, to infectious disease outbreaks, such as severe acute respiratory syndrome and the West African Ebola virus epidemic, laid bare significant deficiencies that could be exploited by bioterrorists instigating an epidemic intentionally. Prioritizing the development of novel vaccines and antimicrobial treatments, alongside expediting clinical trials through innovative methodologies, remains imperative. Enhanced measures are warranted to safeguard healthcare personnel operating in hazardous settings, particularly in regions lacking adequate infrastructure. Novel and refined strategies should be devised for surveillance, early detection, prompt response, efficient patient isolation, control of potentially infected individuals' movements, and effective risk communication. Prudent regulation of access to hazardous pathogens is essential, ensuring progress in countermeasure development is not hindered. It is deduced that readiness for deliberate outbreaks not only fortifies preparedness for natural epidemics but also reciprocally enhances it.

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Key Words: *Biological Weapons, Bio-Terrorism, Virus, Bacteria, Anti-Biotics.*

Introduction

The Biological Weapons Convention, established in 1975 and subject to periodic reviews, prohibits the production and deployment of biological weapons. Presently, it boasts 180 adherent nations. Regrettably, terrorist factions and renegade regimes are unlikely to adhere to international accords. Of particular concern is the potential for bioterrorism, capable of instigating disease, fatalities, and widespread panic, often surpassing the investment of resources.

Several documented instances of bioterrorism exist. In 1984, a religious sect in the USA deliberately tainted restaurant salad bars with *Salmonella typhimurium*, aiming to disrupt local elections, resulting in hundreds of cases of salmonellosis but no fatalities. The anthrax letters incident in 2001 in the USA caused 11 cases of inhalation anthrax, resulting in five deaths, and additional cases of cutaneous disease. While evidence strongly suggests a civilian employee of the US military as the perpetrator, a clear motive remains elusive. Thousands received prophylactic treatment, and contaminated structures underwent costly decontamination. In 1993, a Japanese cult launched an anthrax spore attack without physical casualties, yet post-traumatic stress syndromes

were later identified in victims. The culprits had plans to employ other agents such as Q fever bacteria, botulinum toxin, and Ebola viruses but were apprehended before executing further assaults.

This review examines the menace of bioterrorism, potential instigators, and foundational preparedness strategies. It scrutinizes the distinctive attributes of biological agents suitable for bioterrorism, advancements in disease prevention and treatment, and persisting shortcomings in managing and containing potential bioterrorist crises. Throughout, the principle remains that resources developed for bioterrorism readiness can also be instrumental in combating naturally occurring epidemics.

Key Messages:

1. Enhancing readiness for deliberate outbreaks bolsters responsiveness to naturally occurring epidemics.
2. Sustaining high-level leadership with clear responsibility and authority is crucial.
3. Healthcare providers must remain vigilant regarding potential bioterrorism agents and acknowledge the presence of unknown pathogens.
4. Emergency room and community physicians should receive regular updates on clinical presentations of diseases caused by potential bioterrorist agents and emerging infectious diseases.
5. Improvements in personal protective equipment should prioritize user-friendliness.
6. Augmented surge capacity, particularly in peripheral regions, is imperative for swiftly managing sudden, substantial increases in patients with serious, contagious diseases.
7. Expanding the capabilities of general and reference laboratories is necessary to advance the development of faster, more reliable diagnostic tests.
8. Development of new and enhanced vaccines (both pre-exposure and post-exposure) and treatment protocols is essential.
9. Heightened clinical and environmental surveillance is imperative.
10. Maintenance of syndromic surveillance systems enables the registration of suspicious or confirmed cases reported by physicians, facilitating improved risk communication programs and outbreak monitoring.
11. Adequate national and international stockpiles of vaccines and medications must be maintained.
12. International cooperation should include joint exercises involving multiple nations and continuous enhancement of information exchange on potential bioterrorism threats and their management to fortify preparedness for both natural and bioterrorist outbreaks.

The spectre of bioterrorism and its potential perpetrators have become prominent concerns, especially following the dissolution of the former Soviet Union. There was apprehension that the loss of control over their biological weapons program might grant access to terrorist factions, alongside their scientific acumen. Furthermore, recent advancements in microbial genetics have amplified worries about the misuse of emerging technologies. Due to numerous uncertainties, accurately gauging the risks and menaces posed by bioterrorism remains exceptionally challenging.

The primary culprits could encompass disgruntled individuals, terrorist cells, or renegade nations known for harbouring affiliations with international terrorism. While lone attackers are unlikely to inflict mass casualties, organized terrorist groups could wield considerable menace if they acquire access to sophisticated biological armaments, materials, or scientific knowledge. Despite the implementation of regulations and safeguards to secure hazardous pathogens in research laboratories across most nations, the effectiveness and breadth of these measures vary considerably. Rogue nations possess the requisite capabilities for conducting bioterrorist activities, yet they may be deterred by the prospect of facing a unified global reprisal.

Information gleaned from legitimate research, which could potentially be harnessed for bioterrorism, falls under the category of dual-use. Consequently, regulatory oversight of legitimate research on infectious diseases has intensified. The perpetual risk of an "insider threat," typically involving a solitary individual, underscores the importance of ensuring that new regulations genuinely bolster security while minimizing adverse impacts on legitimate research endeavors. The indirect costs of regulatory measures imposed on infectious disease research, such as missed opportunities for international collaboration, pathogen exchange, and sharing of innovative agents, often go unrecognized. Fostering a culture of safety and security within research laboratories is imperative to mitigate risks effectively while promoting scientific progress.

Preparation for Bioterrorism

Given the nature of a bioterrorist attack as a scenario with low probability but high impact, maintaining effective and continuous readiness is pivotal for both deterring and managing such an event. Although a bioterrorist assault shares commonalities with naturally occurring public health crises stemming from

infectious diseases, there are notable distinctions. Deliberate intent to cause harm necessitates heightened security considerations. The resultant outbreak may diverge significantly from naturally occurring epidemics, often manifesting as a point source outbreak affecting numerous individuals simultaneously. The infectious agent employed is likely to be atypical, possibly genetically modified to resist existing medications and vaccines, and engineered to enhance its transmission or virulence. Consequently, early clinical manifestations following exposure to a bioterrorist agent may deviate from the norm, complicating both diagnosis and treatment and potentially fuelling public panic.

Despite parallels with naturally occurring infectious disease outbreaks, preparedness for bioterrorist attacks presents a more intricate challenge. In many aspects, a bioterrorist incident resembles a mass casualty event, necessitating reinforcement of specialized infrastructure to manage critically ill patients within a limited timeframe. Novel preventive and therapeutic strategies for uncommon diseases are imperative to ensure prompt accessibility when required, alongside clearly defined protocols for handling and studying hazardous pathogens. When determining the allocation of resources toward bioterrorism preparedness, the potential impact on funding for other significant health and security concerns must be carefully weighed. Notably, readiness for bioterrorism inherently enhances the capacity to detect and control various infectious diseases, particularly emerging and re-emerging ones. Thus, investments diverted towards bioterrorism readiness serve a dual purpose. For instance, funding directed towards developing vaccine technologies for potential bioterrorist threats is highly likely to yield advancements in vaccine development for prevalent infectious agents such as Zika virus, dengue virus, or Middle East respiratory syndrome (MERS) coronavirus.

Despite substantial resource allocation to address the challenges of a bioterrorist attack, significant gaps persist in preparedness for epidemics caused by highly pathogenic organisms, as evidenced by responses to outbreaks like the severe acute respiratory syndrome (SARS) coronavirus, 2009 H1N1 influenza virus, and Ebola virus in 2014's West African epidemic. These episodes underscore deficiencies that could facilitate the widespread transmission of highly contagious infectious diseases before containment efforts are effectively executed.

Panel 1: Insights from the West African Ebola Virus Epidemic

Deficiencies in Global Preparedness:

- The World Health Organization (WHO) took too long to declare a public health emergency of international concern.
- Coordinated international assistance was delayed in implementation.
- Challenges in logistics hindered the delivery of support for epidemic response.
- WHO's regional and country-level capacities were found lacking.
- Absence of global strategies to address high-risk pathogen outbreaks in underdeveloped urban areas.
- Evaluation of potential vaccines and treatments was delayed.

Weaknesses in Local Preparedness:

- Inconsistent implementation of border controls heightened the risk of disease spread.
- Quarantine measures were not uniformly enforced.

Shortcomings in National Healthcare Infrastructure:

- Shortage of specialized equipment and skilled personnel for diagnostic tests.
- Early cases were mistaken for endemic diseases, delaying the recognition of Ebola.
- Confirmation delays in Ebola diagnosis increased quarantine risks.
- Insufficient hospital beds and staff to handle high-risk patient volumes.
- Lack of training, resources, and skills for home-based patient care led to continued transmission risks.
- Limited training on personal protective equipment, exacerbated by discomfort in hot climates.
- Research infrastructure inadequacies delayed clinical intervention evaluations.

Failures in Accounting for Local Customs and Traditions:

- Traditional burial practices increased transmission risks.
- Patient and corpse transportation exacerbated disease spread.
- Challenges in ensuring safe burials for a large number of deceased.
- Resistance to interventions from at-risk local populations sometimes posed security risks for responders.

Inadequate Understanding of Ebola Virus Disease:

- Survivors can transmit the virus sexually months after recovery.
- Post-Ebola syndrome observed among survivors.

Biological Agents with Bioterrorism Potential

During the Cold War era, identification of potential biological weapons focused on certain characteristics: their pathogenicity towards humans, animals, or plants; capacity to induce disability or fatality; stability and infectivity in aerosolized small particles; and ease of rapid production and weaponization. Additional attributes have since been incorporated, such as the feasibility of medical prevention or treatment and the risk posed to the perpetrator.

The US Centres for Disease Control and Prevention (CDC) delineated bacteria, viruses, and toxins with potential weaponization capabilities. In 2002, they classified these into three groups—A, B, and C—based on dissemination ease, severity of illness, and lethality. Biological agents are classified as infectious and contagious, infectious but typically non-contagious, or toxins if they lack infectivity. Category A agents were deemed the most significant threat to public and national security. The recent categorization of Tier 1 select agents and toxins closely resembles the Category A classification.

Panel 2:

Potential Bioterrorist Agents Identified by the US Centres for Disease Control and Prevention and Their Associated Conditions.

Bacteria:

- *Bacillus anthracis* (causes anthrax)
- *Clostridium botulinum* (responsible for botulism)
- Various species of *Brucella* (causing brucellosis)
- *Burkholderia mallei* (causes glanders)
- *Burkholderia pseudomallei* (linked to melioidosis)
- *Coxiella burnetii* (associated with Q fever)
- *Escherichia coli* O157:H7 (results in haemolytic uraemic syndrome)
- *Francisella tularensis* (causes tularaemia)
- Various species of *Salmonella* (causing salmonellosis)
- *Salmonella typhi* (leads to typhoid fever)
- Various species of *Shigella* (resulting in shigellosis)
- *Vibrio cholerae* (associated with cholera)
- *Yersinia pestis* (responsible for plague)

Viruses:

- Arenaviruses (linked to Junin and Lassa fever)
- Ebola virus (causes Ebola virus haemorrhagic fever)
- Lassa virus (associated with Lassa fever)
- Marburg virus (causes Marburg virus haemorrhagic fever)
- Variola major (causes Smallpox)

Toxins:

- Botulinum toxin (causes botulism)
- Ricin toxin derived from *Ricinus communis*

Table 1

Bacteria	Characteristics	Associated condition	Likelihood of transmission
<i>Bacillus anthracis</i>	Gram-positive, spore-forming, rod-shaped bacillus	Anthrax	None
<i>Francisella tularensis</i>	Gram-negative, spore-forming, aerobic coccobacillus	Tularaemia	Moderate
<i>Burkholderia mallei</i> and <i>Burkholderia pseudomallei</i>	Gram-negative, rod-shaped, aerobic bacteria	Melioidosis	Moderate

Viruses	Characteristics	Associated condition	Likelihood of transmission
Ebola virus	Family Filoviridae, negative -sense RNA virus	Ebola virus haemorrhagic fever	High
Marburg virus	Family Filoviridae, negative -sense RNA virus	Marburg virus haemorrhagic fever	High
Variola major and Variola minor	Family Poxviridae, DNA virus	Smallpox	Very high
Foot and mouth disease virus	Family Picornaviridae, positive-sense RNA virus	Foot and mouth disease	High

Other agents, including naturally occurring pathogens, are associated with diseases classified as intermediate risk to public health (e.g., brucellosis, glanders, Q fever). These diseases are moderately easy to spread and encompass emerging and re-emerging infectious diseases. However, genetic alterations could enhance their virulence, manifest atypical clinical symptoms, boost resistance to treatments and vaccines, and alter their transmission dynamics or host specificity. Synthetic biology tools enable genetic modifications, exemplifying dual-use research potential. For instance, in 2005, researchers reconstructed the 1918 Spanish influenza pandemic virus, and nearly two decades ago, the poliovirus was synthesized. Introduction of an immunomodulatory gene into the mousepox virus genome in 2001 rendered the mousepox vaccine ineffective, a technique that could potentially be applied to the smallpox virus. The recent synthesis of the extinct horsepox virus serves as a stark reminder that reconstructing the smallpox virus is feasible, prompting reevaluation of regulations aimed at preventing misuse of widely available and inexpensive tools. This scenario also prompts consideration of whether research findings should sometimes be censored or withheld from publication if the potential for harm is deemed too high.

Diagnosis of Diseases Caused by Bioterrorist Agents

The urgency surrounding rapid diagnostics amplifies during bioterrorist incidents, driven by both health and security imperatives. Significant advancements in diagnostic capabilities have occurred since the 2001 anthrax attacks, particularly in sequencing technologies. Enhanced speed and reduced costs in sequencing, facilitated by highly sensitive PCR-based systems and modern sample preparation techniques, have made sequencing technologies more accessible, portable, and multiplexed. With the advent of field-deployable patient-side diagnostics and cloud-based networks linking sequencing outputs, healthcare providers globally can expedite decision-making for individual care or outbreak detection. Notable developments include a rapid, cartridge-based assay for Francisella tularensis and a microsphere-based system capable of detecting antibodies and antigens for Ebola virus and Lassa virus infections.

While diagnostic ELISA tests for anthrax antibodies are available, the GeneXpert system integrates sample processing and PCR amplification, yielding results in approximately 90 minutes. Additionally, a point-of-care method employing antibody immuno column for analytical processes (ABICAP) immune-filtration has been developed for rapid and sensitive detection of smallpox virus, providing results in about 45 minutes. Diagnostic electron microscopy remains a viable method for identifying smallpox and other viral agents. During the Ebola outbreak in Sierra Leone, rapid sequencing facilitated linking sporadic cases with transmission chains. Advanced proteomics and multiplexed suspension arrays offer promise for simultaneous immunodetection of anthrax, plague, and tularaemia from blood cultures. Next-generation sequencing coupled with informatics tools enable virus identification in samples containing human or other nucleic acids. Enhanced networking and collaboration among laboratories further bolster the response to intentional outbreaks.

Infectious Disease Surveillance and Early Detection

Robust global surveillance of infectious diseases is indispensable for controlling both intentional and naturally occurring epidemics. Surveillance data not only track outbreak progress but also inform risk communication efforts. Syndromic surveillance, involving ongoing collection of health-related data to monitor symptom and sign patterns indicative of an outbreak, has been introduced to expedite information gathering. However,

reliance solely on syndromic surveillance can lead to desensitization and paralysis of the system due to frequent reports of non-specific illnesses. Therefore, early detection largely relies on vigilant, prepared clinicians. Regular updates on clinical signs and symptoms associated with common bioterrorist agents are essential for emergency room and community physicians. Syndromic surveillance systems prove most beneficial after physicians report suspicious or confirmed cases, enabling focused analysis against background disease rates to detect changes and glean disease dynamics insights. Legislative measures may be required to gain access to medical records for more in-depth analysis.

The internet offers alternative surveillance avenues for infectious diseases. Pro-Med, established by the user community, has proven effective in connecting clinicians and scientists worldwide, serving as an early warning system for outbreaks such as SARS and MERS. Social media has also been explored for epidemic monitoring, as evidenced during the 2010 cholera epidemic in Haiti, where it facilitated epidemiological pattern estimations.

International collaboration plays a pivotal role in infectious disease surveillance and response. WHO's International Health Regulations, updated in 2005 to address bioterrorism threats, mandate immediate reporting of serious health risks by member countries. Entities like the Global Outbreak Alert and Response Network and the European Union's BICHAT program foster cooperation in preparedness and response to biological and chemical attacks. Additionally, the World Organisation for Animal Health has protocols to address bioterrorism attacks on food-producing animal populations. Informal global collaborations foster trust among knowledgeable scientists and clinicians, serving as early warning mechanisms for both natural and intentional outbreaks. The One Health initiative advocates collaboration between health professionals, critical not only for bioterrorism preparedness but also for managing emerging infectious diseases and combatting global antimicrobial resistance.

Treatment of Patients

Managing patients infected during bioterrorism incidents poses significant challenges. Precautions and treatment protocols for various bioterrorist agents are outlined. While supportive care remains fundamental, advancements in treatment for specific diseases have been notable. Treatment for inhalation anthrax, for instance, has improved with advancements in critical care and antimicrobial therapy. Pleural effusions are routinely drained, and more options for antimicrobial therapy are available. Treatment duration for anthrax exposure or diagnosis typically spans 60 days alongside anthrax vaccination. For bacterial infections other than anthrax, shorter antibiotic courses are usually sufficient. Tularaemia is typically treated with ciprofloxacin or doxycycline. In the case of smallpox, antivirals like cidofovir have demonstrated efficacy in preventing mortality, suggesting their potential utility in smallpox outbreak preparedness. Ribavirin may offer some efficacy in post-exposure prophylaxis for viral haemorrhagic fevers, while GS-5734 has shown promise in treating Ebola virus infection.

Precautions and treatment regimens for patients affected by selected agents are delineated in Panel 4. For smallpox, standard contact and airborne precautions are recommended alongside supportive therapy and antibiotics for secondary infections. Cidofovir and tecovirimat, approved under the Animal Rule, show efficacy against orthopoxviruses, including smallpox. Pneumonic plague treatment involves antibiotics such as ciprofloxacin, levofloxacin, and doxycycline, while tularaemia can be treated with ciprofloxacin, levofloxacin, or doxycycline. Ribavirin is approved for Lassa fever treatment and can be effective against other haemorrhagic fevers. Inhalation anthrax management entails supportive therapy and antibiotics like ciprofloxacin, doxycycline, and ampicillin. Botulism treatment involves supportive care and passive immunisation with equine antitoxin, neutralising botulinum toxin serotypes.

Isolating patients and quarantining

Isolating patients and quarantining contacts pose significant challenges during sudden outbreaks of contagious diseases, as seen in previous epidemics such as MERS coronavirus, SARS, Ebola virus disease, and avian influenza. Specialized hospital units with adequate isolation facilities, including negative pressure air filtration, are essential. In instances where facilities are insufficient, implementing strict barrier nursing protocols becomes imperative. In the event of widespread outbreaks, makeshift isolation facilities may need to be set up in public spaces, particularly in regions with limited infrastructure. Alternatively, providing treatment to patients in their homes might be necessary, albeit with proper precautions due to the infectious nature of the deceased. While modifying burial procedures might be inevitable, cultural and religious practices should be respected.

Quarantining individuals potentially exposed to the infectious agent presents its own set of challenges, as evidenced during the SARS and west African Ebola virus epidemics. Quarantined populations include both exposed and unexposed individuals, heightening the risk of disease transmission. During the Ebola virus outbreak, suspect cases were held until cleared, which often took several days pending PCR results. Nationally, limiting population movement can be contentious, potentially disrupting commercial activities. School closures are effective in promoting social distancing and curbing transmission. The efficacy of public mask usage during outbreaks remains uncertain, with variability influenced by factors such as facial shape, correct application, and duration of use.

Moving to the protection of health-care workers during infectious disease outbreaks, a notable proportion of cases and fatalities occurred among this group during SARS and Ebola virus epidemics. Specific guidelines tailored to each pathogen are available for health-care personnel, public health workers, and emergency responders regarding mask usage and personal protective equipment. The establishment of the National Ebola Virus Training and Education Center in the USA underscores efforts to train health-care workers and support hospitals in managing patients infected with high-hazard viruses. Laboratory workers handling dangerous pathogens must undergo rigorous training and adhere to strict safety protocols, as these pathogens are subject to distinct regulations compared to routine public health pathogens.

Effective communication of risks is crucial during intentional outbreaks of epidemics as it helps to mitigate uncertainty and build public trust in authorities. Providing clear and accessible information to the public enhances confidence and encourages compliance with recommended countermeasures. Despite advances in diagnostic and treatment capabilities, skepticism regarding the necessity and safety of interventions such as the anthrax vaccine persists, underscoring the importance of transparent and timely communication.

Effective risk communication should occur at all stages of an outbreak, from suspicion to confirmation and throughout the event and its aftermath. Trusted spokespersons, well-informed and credible, play a vital role in disseminating accurate information. However, unexpected events and misinformation, especially with the proliferation of social media, can challenge communication efforts. Flexibility in policy and proactive measures to address emerging issues are essential components of effective risk communication strategies.

Environmental surveillance for biological agents is critical and requires further development, particularly in fast screening and detection technologies. While stockpiling of medical resources is common practice, constant re-evaluation and adaptation of policies are necessary to address evolving threats. The response to previous epidemics, whether intentional or natural, underscores the importance of preparedness and collaboration on a global scale.

Anticipating future threats, including bioterrorism, necessitates a rational approach integrating intelligence data and predictive models. Bioterrorism risks should be addressed alongside other infectious disease threats, emphasizing the need for ongoing vigilance and preparedness. Collaboration at the international level is crucial, not only to deter bioterrorism but also to strengthen responses to naturally occurring epidemics. Adequate funding for biodefense is essential to ensure robust preparedness and response capabilities.

Conclusion

Effective communication, robust surveillance, and collaborative preparedness efforts are key to addressing the complex challenges posed by intentional outbreaks. By investing in these measures, countries can enhance their resilience not only to bioterrorism but also to naturally occurring epidemics, safeguarding public health on a global scale.

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