

Preventing the Use of Biological Weapons: Improving Response Should Prevention Fail

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This article presents an overview of the nature and scope of the challenges posed by biological weapons, and offers ways by which the infectious diseases professional community might address the challenges of biological weapons and bioterrorism.

Biological Weapons Cause Epidemics

Biological weapons are devices intended to deliberately disseminate disease-producing organisms or toxins in food, water, by insect vector, or as an aerosol. As would be the case following exposure to any infectious disease, those infected would experience an incubation period of variable duration, depending on the pathogen, the size, and route of the inoculum, and the immune response of the affected persons. The incubation period could be days to weeks. If sufficient numbers of people were infected by the dispersal of a biological weapon, or if the agent were contagious and person-to-person transmission outran disease control measures, the result could be large-scale, possibly catastrophic epidemics. It is this outcome—the prospect of a pestilence intentionally unleashed on large civilian populations—that most concerns physicians, public health experts, and political leaders.

Public health, medical, military, and law enforcement experts have met in a number of settings in efforts to identify the most threatening of the biological weapons, specifically those weapons that merit priority concern in the development of public health and medical preparedness measures [1–4]. The criteria for this determination have included feasibility of aerosol dissemination (thought by many to be the most likely means of exposing large populations), high case-fatality rates, the potential for secondary spread, and the availability of protective vaccines or antimicrobial agents. A limited number of agents are consistently recognized as being of greatest concern: *Variola major*, *Bacillus anthracis*, *Yersinia pestis*, Botulinum toxin (produced by *Clostridium botulinum*), *Francisella tularensis*, and a number of the causative agents of the syndrome termed viral hemorrhagic fever. Recommendations for the medical and public health management of these weapons are being published elsewhere in a series of consensus papers [1, 2].

The scope and impact of an epidemic caused by a biological weapon would depend on the characteristics of the pathogen or toxin, the design of the weapon or delivery system, the environment in which the weapon was used, and the speed and effectiveness of the medical and public health response. Fortunately, the few attempts to use biological weapons in this century have produced limited numbers of casualties [5]. These efforts, however, were not supported by the technological resources of nation-states [6]. There is little dispute that biological weapons have the capacity to initiate epidemics on a scale and with a degree of lethality unparalleled in modern history [7–9]. Although it is impossible to predict the probability that a nation-state, a state-sponsored terrorist, or an autonomous group might use a highly destructive biological weapon, there is little disagreement among experts that such an event is both feasible and becoming more likely [10–13].

There are few modern analogs that provide insight into the potential ramifications of a major epidemic caused by one of the more serious biological weapons. In the United States, the single event that might most closely resemble the aftermath of a biological weapon would be the influenza pandemic of 1918–1919. That epidemic caused widespread societal disruption and placed enormous burdens on both the health care system and the civil infrastructure. Yet even in this comparison, crucial distinctions exist. Pandemic influenza resulted in estimated case-fatality rates ranging from 1.9% [14] to 5% [15]; the case-fatality rate for smallpox would approximate 30% [1], and for untreated anthrax, it would exceed 80% [2].

The experience following the importation of 1 case of smallpox into Yugoslavia in 1972 suggests the events that might accompany a modern epidemic. A pilgrim returning from Iraq developed a mild illness with a nondescript rash and fever. Two weeks later, 11 persons who had been in close contact with him developed similar symptoms. None of the 11 knew one another, and no physician recognized smallpox in the initial case patient or in the subsequent 11 cases. (The last case of smallpox in Yugoslavia had occurred in 1927.) One of the 11 developed hemorrhagic smallpox, a uniformly fatal, highly contagious form of the disease. He alone infected 38 persons, including physicians and nurses. Ultimately, the outbreak was recognized 4 weeks after the initial case became ill. Although childhood

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population-wide smallpox vaccination was in place in Yugoslavia, the discovery of a growing epidemic of smallpox led to the mandatory vaccination of the entire nation's population of 20 million persons. In addition, some 10,000 contacts of patients were quarantined in hotels guarded by the military. All surrounding countries closed their borders to travel and commerce from Yugoslavia. The outbreak ended about 8 weeks after the first case patient became ill. There were a total of 175 smallpox cases and 35 deaths [16]. Smallpox experts considered this a small outbreak.

Biological Weapons Are an Increasing Concern

The technology associated with the manufacture of biological weapons is relatively inexpensive, and because it is similar to that used in vaccine production facilities, it is easy to obtain [17]. The microbial agents needed for most biological weapons are widely available [18]. It is difficult to gauge the extent of biological weapons development in other nations since production facilities require little space and are not easy to identify [19]. The acquisition and dissemination of even the most highly restricted organism, *Variola major*, is not an implausible scenario [13].

In 1970, the United States abandoned its offensive bioweapons program by presidential executive order. There were several reasons for this decision, including the determination that biological weapons were not essential for national security [20]. The 1972 Biological Weapons and Toxin Convention (BWTC) calls for banning the development, possession, or use of biological weapons. It has been signed by 162 states [21], including most of the 17 states suspected of having offensive biological weapons in a recent report [22]. Seven of the 17 are named sponsors of international terrorism [23]. States are not the only entities to pursue the development of biological weapons. Individuals and groups, both internationally and within the United States, have also done so [6].

Three events in particular have fueled recent concern about biological terrorism. First, investigations following the 1995 release of sarin nerve gas by the Aum Shinrikyo religious cult in the Tokyo subway system revealed that cult members made at least 9 failed attempts to use biological weapons in central Tokyo with the intent to kill tens of thousands [24]. Second, the vast extent and sophistication of the biological weapons program of the former Soviet Union has become increasingly evident over the past decade coincident with revelations provided by defectors from its program [9]. There is growing concern that biological weapon designs or materials from this program might find their way to other nations or terrorist groups [25]. Finally, the series of revelations following the Gulf War regarding the true capacity and scope of Iraq's biological weapons program has been alarming. In addition to creating many tons of pathogens and toxins, including *B. anthracis* and *C.*

botulinum toxin, Iraq also admitted that it had loaded bombs and missiles with biological agents [19].

What the Infectious Diseases Community Can Do to Support Prevention Efforts

The ID community has important contributions to make in crafting strategies to forestall the development or use of biological weapons. Prevention strategies of particular salience include raising awareness among researchers and practitioners about the risk, involving researchers from universities and industry in efforts to strengthen the BWTC, creating mechanisms to consider appropriate scientific response to research with potential bioweapons application, and supporting programs that seek to employ former bioweaponeers in peaceful pursuits.

Each state party to the BWTC undertakes "never in any circumstance to develop, produce, stockpile or otherwise acquire or retain microbial or other biological agents, or toxins ... of types and in quantities that have no justification for prophylactic, protective or other peaceful purposes [21]. Although the 1972 BWTC may have served as a partial barrier to biological weapons proliferation [21], it has been unsuccessful in preventing a number of countries from undertaking substantial programs of research and development [22]. Efforts to strengthen the treaty are now being debated [26]. It is not yet evident whether these efforts will be supported with the necessary political will, whether these efforts will make the BWTC a more useful tool in combating biological weapons proliferation [27], or how treaty verification and enforcement procedures might impact biological research in industry or in universities [27, 28]. The ID community is vitally concerned about the likelihood and price of success of such treaty mechanisms and should participate in the development of modifications, revisions, or enhancements on the basis of a careful assessment of the threat and actions likely to prevent biological weapon proliferation.

The ID community is a logical home for new initiatives for international scientific collaboration. Efforts that seek to establish communication with and create structures that offer practical support for scientists who once researched and developed biological weapons but are now being asked to change course should be encouraged.

Preparation to Respond to Biological Weapon Use

Existing prevention strategies are insufficient to guarantee that biological weapons will not be used. Furthermore, it is clear that biological weapons are proliferating. Supporting a broad awareness of the perils of biological weapons will itself advance understanding of useful response measures. The ID community could take a number of additional actions that would strengthen the nation's capacity to respond to the use of a biological weapons. ID expertise will be critical to early recognition of the diseases that would follow biological weap-

ons use, to recommend the most rapid diagnostic procedures, to assist in the development of medical treatment strategies, to support the creation of hospital response policies, and to undertake research into new diagnostic and therapeutic interventions.

Awareness and education. ID professionals are called on every day to diagnose and treat patients with fever, pneumonia, rash, and flulike symptoms; therefore, it is the ID professional who would be among the clinicians most likely to recognize the diseases caused by biological weapons. Professional educational and training curricula should be enhanced so that ID professionals are better capable of recognizing the diseases that would follow use of a biological weapon such as anthrax, plague, or smallpox. The perils of delayed recognition of one of these diseases, both for the patient and for the involved community, would be grave. Fostering strong working relationships between clinically based ID professionals (especially hospital epidemiologists) and health department-based ID professionals is an important step toward improving the capacity to both detect and respond to bioterrorist attacks.

Laboratory diagnosis. Should the recognition of an unusual disease or pattern of illnesses prompt consideration of possible biological weapon use, members of the ID community will be called on to advise upon the most rapid procedures for diagnostic confirmation of disease. In anticipation of this, ID experts should become familiar with the processes by which either the hospital laboratory or the local or state health department, in consultation with the Centers for Disease Control and Prevention (CDC) as necessary, will perform diagnostic studies to implicate or exclude biological weapons use. A process that establishes criteria and training measures for laboratory diagnosis of these diseases is being undertaken jointly by the Association of Public Health Laboratories and the CDC.

Systems for distributing therapeutics. Should a biological weapon use be confirmed, treatment and intervention strategies for the ill and for the exposed but not yet ill will be critical. Depending on the disease, antibiotics, and/or vaccines or other therapies, as well as quarantine, could be lifesaving. Public health agencies have begun to explore systems for emergency distribution and treatment of antibiotics and vaccines, systems that would also be useful should emergency interventions be needed for naturally occurring epidemics, such as pandemic influenza. The ID community should play an important role in the shaping of such efforts.

Hospital response. Hospitals will bear the brunt of caring for the sick and dying should a biological weapon be used. Yet few hospitals are prepared to cope with even a handful of cases of a highly contagious, life-threatening disease, and few hospitals are prepared to manage even a modest surge in the numbers of seriously ill patients. Hospital leaders should examine current policies in relation to this threat and develop new policies as appropriate. Infection control practices are but one critical component of such planning efforts. Numerous other

issues are of compelling importance, such as hospital roles and authorities, prevention of disease transmission amongst staff, personnel requirements, security needs, communication both within and outside the hospital, and media interactions. ID expertise is of clear relevance to many of these issues.

Scientific research. The ID community already does research that seeks new strategies for diagnosis, prevention, or treatment for infectious disease. Commensurate with this, the ID community might elect to encourage and reward basic science research efforts that seek to produce novel diagnostic technologies, preventive, or therapeutic interventions for the diseases caused by biological weapons. At the same time, ID professionals can be compelling advocates for directing increased funding or attention toward critical needs, such as substantially augmenting the smallpox vaccine reserve and the development of a second generation anthrax vaccine.

Conclusions

It is hoped that this *CID* special section will serve to enhance expertise among the ID community regarding the medical and public health implications of biological weapons and provide a forum for review and scientific dialogue supporting prevention of biological weapons proliferation. As Robert Jay Lifton wrote of nuclear weapons in *Indefensible Weapons*, "In many cases, there appears to be an extraordinary impact made upon people simply by new information.... New information makes contact with amorphous fears.... The menace one has known, but kept hidden comes into the open. And there is a beginning sense that one might, just possibly, be able to do something about it" [29].

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