

Bioterrorism

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Abstract

Although biological agents have been used in warfare for centuries, several events in the past decade have raised concerns that they could be used for terrorism. Revelations about the sophisticated biological-weapons programs of the former Soviet Union and Iraq have heightened concern that countries with offensive-research programs, including those that sponsor international terrorism, might assist in the proliferation of agents, culturing capability, and dissemination techniques, and might benefit in these undertakings from the availability of skilled laboratory technicians. Release of sarin nerve agent in the Tokyo subway system in 1995 by the Aum Shinrikyo cult demonstrated that in the future terrorists might select unconventional weapons. Certain properties of biological pathogens may make them the ideal terrorist weapon, including 1) ease of procurement, 2) simplicity of production in large quantities at minimal expense, 3) ease of dissemination with low technology, and 4) potential to overwhelm the medical system with large numbers of casualties. Dissemination of a biological agent would be silent, and the incubation period allows a perpetrator to escape to great distances from the area of release before the first ill persons seek medical care. Countermeasures include intelligence gathering, physical protection, and detection systems. Medical countermeasures include laboratory diagnostics, vaccines, and medications for prophylaxis and treatment. Public health, medical, and environmental health personnel need to have a heightened awareness, through education, about the threat from biological agents.

The intentional use of biological pathogens to kill or incapacitate one's enemies has occurred sporadically for centuries. One of the earliest documented cases occurred at the Crimean port city of Kaffa (now Feodosia, Ukraine) in 1346. Besieging Tatar armies were stricken with bubonic plague and decided to turn this unfortunate incident to their advantage by catapulting plague-ridden corpses into the city (1). Genoese defenders within the city walls subsequently contracted plague and fled to Italy, thus carrying the disease to Europe. The resulting epidemics culminated in what we now know as the Black Death, which wiped out nearly one-third of the European population in the Middle Ages.

Until recently, concern over biological weapons focused mainly on their use by an adversary on the battlefield. Several events, however, have heightened concerns that these agents could be employed by terrorists. As many as 18 countries currently are suspected of having biological-weapons research and development programs (2). Of the seven countries listed by the State Department as sponsors of international terrorism, at least five are known or suspected to have bioweapons programs (3). Most notably, before the Gulf war, intelligence sources suspected that the Iraqis had a biological weapons program. In 1995, the Iraqis admitted to having weaponized anthrax, botulinum toxin, and aflatoxin (4).

Revelations by defectors from the biological weapons program of the former Soviet Union revealed the massive extent of that program, including the industrial capacity to produce tons of biological agents, such as anthrax and smallpox, each year (5). The Soviets used the signing of the Biological Weapons Convention in 1972 as a launching point for accelerating their program. Moreover, they also saw the global eradication of smallpox and the subsequent discontinuation of vaccination against the disease as an opportunity to exploit smallpox as a weapon. Since the breakup of the Soviet Union, there has been concern that many of the scientists put out of work by the deteriorating economies of former Soviet states could take their expertise to a country developing a biological warfare program (3).

A wake-up call came with the 1995 sarin nerve agent attack in the Tokyo subway system by the terrorist organization Aum Shinrikyo. This event demonstrated that terrorist organizations had acquired the ability to use unconventional weapons. It was later revealed that the cult had used sarin once previously in Matsumoto, Japan, in 1994, and had made several attempts to release the biological agents anthrax and botulinum toxin (6).

Given that a terrorist organization could choose to use conventional, chemical, or nuclear weapons, why might it resort to a bioagent? There are several reasons, which, when considered as a whole, might point to biological weapons as the ultimate terrorist weapons. First, the agents themselves are relatively easy to procure. Organisms such as *Clostridium botulinum*, the agent that produces botulinum toxin, and hence botulism, is ubiquitous in soil. Other organisms, such as *Bacillus anthracis*, the causative agent of anthrax, and *Yersinia pestis*, the causative agent of plague, could be collected from areas around the globe where the diseases are endemic—either from the soil (anthrax) or from diseased animals (anthrax and plague). Moreover, numerous legitimate laboratory supply houses around the world sell many agents that might be adapted for use as weapons. A terrorist conceivably could obtain pathogens by illegitimate means from these supply houses or from research laboratories. Second, a 1969 United Nations expert panel concluded that the relative cost to produce mass casualties over 1 square kilometer was \$600 for a chemical weapon, \$800 for a nuclear weapon, \$2,000 for a conventional weapon, and only \$1 for a biological weapon (7). Furthermore, to produce biological weapons, one might employ the same fermentation technology that is commonly used in the production of legitimate products such as antibiotics, vaccines, wine, and beer. This circumstance makes biological-weapons production relatively easy to conceal and makes compliance with existing weapons conventions difficult to verify. A 1970 study by the World Health Organization (WHO) demonstrated that many of the biological pathogens can have great downwind spread and high morbidity and mortality (Table 1) (8). To disseminate such agents as aerosols, a terrorist could fairly easily modify common spray devices, such as those used in the agricultural industry, to produce particles in the proper size for infecting humans (9). An important feature distinguishing bioweapons from other weapons is the incubation period characteristic of each biological agent. This period ranges from hours to weeks, but is generally on the order of days. A perpetrator could thus release an agent and be out of the country by the time the effects are recognized.

There are three general routes by which a bioweapon may produce infection: percutaneous, oral, and inhalation. Unlike with chemical agents, which are dermally active, intact skin provides an impermeable barrier to most biological weapons, with the exception of T2 mycotoxins. Therefore, to infect someone, a microorganism must enter through a break in the skin. This is what happened in 1978, when Bulgarian exile and BBC announcer Georgi Markov was assassinated by the Bulgarian secret service (supplied by the KGB) in London. A spring-loaded device was placed inside an umbrella, which injected a tiny metal pellet into Markov's leg. The pellet was through-bored, filled with ricin, and sealed with wax. The ricin, a toxin

derived from the common castor bean, then leaked out of the pellet as the wax melted at body temperature (10).

A second route of infection involves oral intake of contaminated food or water. This route was demonstrated in 1984 when the Rajneeshee cult infected local salad bars in Dalles, Oregon, with *Salmonella typhimurium* in an attempt to influence the outcome of local elections. At least 751 cases of salmonellosis resulted (11). Today, our society is perhaps more vulnerable to such foodborne contamination because more of our food sources are centralized. If an agent is used to successfully contaminate food at a central production or processing facility, persons across the country could be affected. Fortunately, it would be rather difficult to contaminate a large water reservoir successfully with a biological weapon for several reasons. First, the dilution effect of a large reservoir would require that extremely large quantities of agent be used, which would be beyond the scope of a less-sophisticated terrorist and would make detection of the perpetrator at the time of attempted contamination easier. Second, common disinfection with chlorination and filtering would render many—although not all—agents ineffective.

The third possible route of exposure is through inhalation. This route has the greatest potential to cause mass casualties. For exposure to occur through inhalation, inhaled particles must circumvent the respiratory muco-ciliary apparatus. Particles in the range of 1 to 5 micrometers (μm) are best able to do this. Particles greater than 5 to 10 μm would be captured and expelled by the muco-ciliary apparatus, and particles of less than 1 μm would likely be inhaled and subsequently exhaled.

One might ask whether biological weapons should concern us at all, as there are few known cases of their use against large populations. While there is some truth to this argument, numerous smaller-scale "biocrimes" attest to the fascination of criminal elements with biological weapons (12). Unfortunately, use, threat of use, interest in use, interest in acquisition, and actual acquisition have all increased notably during the decade of the 1990s. Several factors likely account for this, including the widespread knowledge provided in lay publications and on the Internet, and the attention that this issue has garnered in the media. Although most cases of use have involved small-scale biocrimes, the ability clearly exists to acquire and produce these agents. We must not ignore individuals or groups who might try to use them on a larger scale.

Hundreds of agents can cause disease in humans. For most of these agents, whose potential for large-scale infection or intoxication is limited, local care providers and health departments can deal adequately with the consequences of a small-scale natural, accidental, or intentional release. Working groups from the Johns Hopkins Center for Civilian Biodefense and the Centers for Disease Control and Prevention (CDC) recently convened to consider diseases that might cause a maximum credible event (defined as an event with the potential to cause large loss of life, panic, and overwhelming of health care resources) and for which specific and intense planning are needed to handle the consequences of a release on a large population. Such agents include smallpox, anthrax, plague, tularemia, botulinum toxin, and viral hemorrhagic fevers (13–15).

A number of defensive measures have been taken to prevent a maximum credible event from occurring. Recent laws passed by Congress impose criminal penalties for the possession, manufacture, or use of biological weapons and give law enforcement agencies the right to seize potential agents or delivery devices (16). New regulations governing hazardous biological agents and their legitimate transfer went into effect in 1997. Intelligence agencies and law enforcement personnel are developing sophisticated systems to monitor potential terrorists and to learn what they might use, and when they might use it.

In the case of an unannounced biological attack, the first sign of the attack would likely be ill individuals seeking care. Surveillance systems are being developed that will identify an event rapidly, thus allowing medical countermeasures to be instituted in a timely fashion. Depending on when information or identification of a bioterrorist incident occurs, health care providers and their public health counterparts could institute measures ranging from prophylaxis to treatment. There are only two licensed vaccines against high-threat agents: the anthrax and smallpox vaccines (17). Pre-exposure vaccination against anthrax in an unannounced bioterrorism incident would be unlikely, but because of concerns that some spores may lie dormant in the lungs for extended periods after exposure, the treating physician might use the vaccine as part of a postexposure prophylaxis regimen, along with antibiotics, for those not yet clinically ill (17,18). The vaccine against smallpox could be used to limit the propagation of an outbreak (19). The current supply of both anthrax and smallpox vaccines, however, is limited.

Many bacterial diseases have licensed treatments, although one must be somewhat concerned that an organization with the sophistication to deploy an agent effectively might also be capable of developing antibiotic-resistant strains. For viral agents, treatment is more problematic, since no effective antivirals are licensed for treatment of bioterrorism threat agents. In the case of smallpox, if an attack were to occur today, the best prevention would be immediate vaccination and isolation of those exposed, although research into effective antivirals is ongoing. Ribavirin has been shown to increase survival rates in patients with Lassa fever and has shown promise in the treatment of other viral hemorrhagic fevers (20,21).

Physical protection affords an additional countermeasure. The gas masks provided by the military are effective against both chemical and biological agents. A HEPA-filtered mask would be expected to be effective in a biological weapon attack if one has no other means of protection.

Unlike chemical agents, most biological agents can be effectively removed from human skin with soap and water. Therefore, there is no need, except perhaps in the case of highly contaminated individuals, to use bleach or other decontaminating agents. Also, by the time the incubation period has passed and the victims become ill, they may have changed clothes and bathed, making decontamination of little utility. Biological agents are nonvolatile and relatively difficult to re-aerosolize, so even without specific decontamination, secondary exposure would be unlikely. This is in contrast to the circumstances associated with chemical agents, in which victims generally present immediately after an attack and may still have volatile agent on their bodies or clothes, putting the care provider and hospital environment at risk of contamination and secondary exposure.

With biological agents, detection is more difficult than with chemical agents. Various organizations are currently developing technologies to improve the speed and accuracy of methods for detecting and diagnosing biological agents.

Several different response teams are being fielded or planned. Some of these are civilian, under the auspices of the National Disaster Medical System (the Metropolitan Medical Response System, the National Medical Response Team, and the Disaster Medical Assistance Team); the Centers for Disease Control and Prevention and various public health departments also are building teams to analyze and track epidemics. The military has several response teams (the Marine Corps' Chemical Biological Incident Response Force, the U.S. Army's Chemical-Biological Rapid Response Team, the National Guard Weapons of Mass Destruction-Civil Support Teams, and the Joint Task Force for Civil Support). In the case of a large-scale event, it is planned that civilian personnel would have the lead role in mitigating the consequences, with the military providing support when requested.

Finally, it is important for health care providers to become more aware of the threat of bioterrorism and how they will manage should a release occur. Education is one of the

cornerstones of our defense. Through forums such as NEHA's annual symposium, the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) annual satellite broadcast on the medical defense against biological weapons, and other military and nonmilitary educational efforts, more health care providers will, it is hoped, maintain a heightened awareness and an appropriate level of concern.

Table 1
Estimated Possible Primary Effects of Limited (Single-Bomber) Biological Warfare Attack on Unprotected Civilian Population Groups*

Agent	Downwind Reach (km)	Killed	Killed/Incapacitated
Venezuelan equine encephalitis	1	400	35,000
Tickborne encephalitis	1	9,500	35,000
Influenza	1	100	35,000
Epidemic typhus	5	19,000	85,000
Rocky Mountain spotted fever	5	11,500	85,000
Brucellosis	10	500	100,000
Plague	10	55,000	100,000
Q fever	>20	150	125,000
Tularemia	>20	30,000	125,000
Anthrax	>>20	95,000	125,000

*Approximately 50 kilograms of dried powder containing 6×10^{15} organisms are assumed to have been aerosolized to form a band 2 kilometers (km) long at right angles to the wind direction under type F meteorological conditions (stable atmospheric conditions at approximately midnight in the United Kingdom). Population groups are defined as urban populations of approximately 500,000 in developing countries.

(Reprinted with permission from the World Health Organization [8].)

Editor's Note: The opinions expressed in this article are those of the authors and do not necessarily reflect the positions of the U.S. Department of Defense, the Army, or the U.S. Army Medical Research and Materiel Command.

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References

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1. Derbes, V.J. (1966), "DeMussis and the Great Plague of 1348, a Forgotten Episode of Bacteriological Warfare," *Journal of the American Medical Association*, 196(1):59-62.
2. Siegrist, D.W. (1999), "The Threat of Biological Attack: Why Concern Now?" *Emerging Infectious Diseases*, 5(4):505-508.
3. Office of the Secretary of Defense (1997), *Proliferation: Threat and Response*, Washington, D.C.: Government Printing Office.
4. Zilinskas, R.A. (1997), "Iraq's Biological Weapons: The Past as Future?" *Journal of the American Medical Association*, 278(5):418-424.
5. Alibek, K. and S. Handelman (1999), *Biohazard*, New York: Random House.
6. Olson, K.B. (1999), "Aum Shinrikyo: Once and Future Threat?" *Emerging Infectious Diseases*, 5(4):513-516.
7. *NATO Handbook on the Medical Aspects of NBC Defensive Operations: AmedP-6(B)* (1996), Washington, D.C.: Departments of the Army, Navy, and Air Force.
8. World Health Organization Group of Consultants (1970), *Health Aspects of Chemical and Biological Weapons*, Geneva, Switzerland: World Health Organization.
9. *The Biological & Chemical Warfare Threat* (1999), Washington D.C.: U.S. Government Printing Office.
10. Compton, J.F. (1988), *Military Chemical and Biological Agents—Chemical and Toxicological Properties*, Caldwell, N.J.: The Telford Press.
11. Torok, T.J., K.A. Birkness, L.R. Foster, J.M. Horan, J.R. Livengood, S. Mauvais, M.R. Skeels, R. Sokolow, R.V. Tauxe, and R.P. Wise (1997), "A Large Community Outbreak of Salmonellosis Caused by Intentional Contamination of Restaurant Salad Bars," *Journal of the American Medical Association*, 278(5):389-395.
12. Carus, W.S. (1998, revised 1999), "Bioterrorism and Biocrimes: The Illicit Use of Biological Agents in the 20th Century," Working paper, Washington, D.C.: Center for Counterproliferation Research, National Defense University.
13. Henderson, D.A. (1999), "The Looming Threat of Bioterrorism," *Science*, 283(5406):1279-1282.
14. Khan, A.S., D.A. Ashford, R.B. Craven, S.D. Deitchman, R.P. Gaynes, E.K. Gray, S.L. Groseclose, E.W. Gunter, P.K. Halverson, J. Hughart, A.B. Johnson, A.M. Levitt, S.A. Morse, C.J. Peters, P. Quinlisk, M.J. Sage, R.A. Spiegel, D.L. Swerdlow, and A.L. Wilson (2000), "Biological and Chemical Terrorism: Strategic Plan for Preparedness and Response. Recommendations of the CDC Strategic Planning Workgroup," *Morbidity and Mortality Weekly Report*, 49(RR04):1-14.

15. Kortepeter, M.G., and G.W. Parker (1999), "Potential Biological Weapons Threats," *Emerging Infectious Diseases*, 5(4):523-527.
16. Ferguson, J.R. (1997), "Biological Weapons and the Law," *Journal of the American Medical Association*, 278(5):357-360.
17. Cieslak, T.J., G.W. Christopher, R.C. Culpepper, E.M. Eitzen, M.G. Kortepeter, J.A. Pavlin, and J.R. Rowe (2000), "Immunization Against Potential Biological Warfare Agents," *Clinical Infectious Diseases*, 30(June):843-850.
18. Inglesby, T.V., M.S. Ascher, J.G. Bartlett, E. Eitzen, A.M. Friedlander, J. Hauer, D.A. Henderson, J. McDade, M.T. Osterholm, T. O'Toole, G. Parker, T.M. Perl, P.K. Russell, and K. Tonat (1999), "Anthrax as a Biological Weapon: Medical and Public Health Management," *Journal of the American Medical Association*, 281(18):1735-1745.
19. Henderson, D.A., M.S. Ascher, J.G. Bartlett, E. Eitzen, J. Hauer, T.V. Inglesby, P.B. Jahrling, M. Layton, J. McDade, M.T. Osterholm, T. O'Toole, G. Parker, T.M. Perl, P.K. Russell, and K. Tonat (1999), "Smallpox as a Biological Weapon: Medical and Public Health Management," *Journal of the American Medical Association*, 281(22):2127-2137.
20. Franz, D.R., W.R. Byrne, G.W. Christopher, E.M. Eitzen, A.M. Friedlander, D.L. Hoover, P.B. Jahrling, D.J. McClain, and J.A. Pavlin (1997), "Clinical Recognition and Management of Patients Exposed to Biological Warfare Agents," *Journal of the American Medical Association*, 278(5):399-411.
21. Centers for Disease Control and Prevention (1988), "Management of Patients with Suspected Viral Hemorrhagic Fever," *Morbidity and Mortality Weekly Report*, 37(S-3):1-16.