Preparedness for Biological Terrorism in the United States: Project BioShield and Beyond

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The terrorist attacks of September 11, 2001, demonstrated that the United States is no longer isolated from a dangerous world or protected by its geography. Oceans and borders can be readily crossed, making the United States as vulnerable as other nations to acts of terrorism. International unrest and terrorism have become all too familiar to Americans. Although the predominant weapons of international terrorism continue to be improvised explosive devices, as evidenced by the bombings in London in July 2005 and Madrid in March 2004, acts of biological terrorism are a potential threat that could have serious immediate and long-term consequences. The intentional release of such infectious agents as Bacillus anthracis (anthrax), Clostridium botulinum toxin, Variola major (smallpox), Yersinia pestis (plague), or Filoviridae viruses (Ebola hemorrhagic fevers) could cause mass casualties, resulting in significant morbidity and mortality, societal disruption, and long-term human and economic hardship. The strain that such events would place on the medical infrastructure—from hospital beds and antidote supplies to emergency departments (EDs), family practice offices, and medical clinics—would probably be unprecedented, especially given the fact that an attack with biological weapons would in all likelihood not be announced in advance.

Although more than 150 nations have signed the 1975 Biological and Toxin Weapons Convention (BTWC), which bans the development, production, stockpiling, acquisition, and retention of biological weapons, many countries are believed to be violating the terms of this agreement. Some estimates list as many as 60 nations with biological weapons capabilities. Stockpiles of various biological agents are believed to be in the possession of several nations and terrorist organizations that would have motives to harm Americans and to undermine the policies of the United States. For example, experts in weapons proliferation suspect that China, Iran, Libya, North Korea, and Syria are among the nations that have stockpiles of biological weapons, as well as other types of weapons of mass destruction (WMD).

Furthermore, the former Soviet Union’s biological weapons program, especially in the areas of smallpox and plague research, was known to be highly advanced. Inadequate security after the fall of the Soviet Union left its biological weapons research materials minimally guarded. Much of these biological agents are now unaccounted for, apparently having been lost or stolen. Many international observers have expressed fears that some of this unaccounted-for material may have fallen into the hands of Al Qaeda or other global terrorist organizations.

The threat that these nations and terrorist groups pose is not merely hypothetical. Aum Shinrikyo, a Japanese doomsday cult with significant financial and political resources, has used nerve agents and other lethal substances against a variety of targets. The most deadly of these attacks happened in March 1995, when the group released sarin gas, a potent nerve agent, into the Tokyo subway system, killing 12 and wounding thousands of others. Aum Shinrikyo has also experimented—apparently so far without success—with biological agents, including B anthracis and C botulinum toxin. Al Qaeda and other militant Islamic organizations have often expressed interest in a wide range of WMD, including biological agents. Al Qaeda has even maintained instructional sites on the Internet that feature highly detailed information for creating homemade explosives and rudimentary, but nevertheless effective, biological weapons.

Concerns about the purposeful release of infectious agents add to growing worries about the readiness of the United States and other nations to confront emerging, naturally occurring threats. For example, severe acute respiratory syndrome and the H5N1 strain of avian influenza have presented imposing challenges for public health authorities in recent years.

In the aftermath of the September 11 attacks, tremendous efforts have been expended to enhance US preparedness against biological agents and other WMD. Proper preparedness suggests the ability to respond to a threat and prevent injury.
or unnecessary loss of life. Achieving this ability requires the translation of national policy initiatives into the implementation of local programs.18

One preparedness effort that connects national policy with local implementation has been the enhancement of the Strategic National Stockpile (SNS), a large repository of antibiotics, vaccines, and other medical response materials.19 The SNS was originally established by Congress in 1999 as the National Pharmaceutical Stockpile. The stockpile became known as the SNS in 2003 after the US Department of Homeland Security (DHS) and the US Department of Health and Human Services (HHS) jointly assumed management.19 (Previously, the stockpile had been managed by the HHS and the Centers for Disease Control and Prevention [CDC]). In the event of a biological terrorist attack or other public health emergency, plans call for HHS officials to distribute medicines and supplies from the SNS to any state in need within 12 hours. Each state has its own plans to distribute the SNS materials as quickly as possible.19

Provisions of Project BioShield

New medications and vaccines developed under Project BioShield are to be added to the SNS. Project BioShield, signed into law by President George W. Bush on July 21, 2004, is the most prominent of various legislative acts and programs addressing biological terrorism preparedness (Figure 1).20 It establishes a mandatory and protected source of funds within the annual budget for countermeasures—ranging from vaccines to biodosimetry to surveillance—related to biological weapons and other WMD. Budgetary appropriations for fiscal year 2004 included almost $6 billion over 10 years for DHS and other government agencies to develop and make available next-generation medications and vaccines to protect against biological, chemical, radiological, and nuclear weapons.21

Among such next-generation countermeasures would be new vaccines to protect victims of biological attack against smallpox and anthrax and a new antitoxin for botulinum toxin.21

In May 2005, the National Institute of Allergy and Infectious Diseases (NIAID), the main federal institute supporting biological defense research, awarded ten grants and two contracts under Project BioShield to fund development of new therapeutics and vaccines against several biological agents.22 These grants, which were the first made by NIAID using authorities provided by Project BioShield, totaled approximately $27 million.22 The largest contract awarded under Project BioShield to date has been $878 million, to VaxGen Inc of Brisbane, Calif, for the development of a next-generation recombinant anthrax vaccine.23

Provisions have been made in Project BioShield to address the need for a safer, more effective smallpox vaccine. The United States ended routine vaccinations for smallpox in 1972 after the disease had been eradicated in the country as a natural threat.24 Since then, only military personnel and other high-risk groups have received smallpox vaccinations, which contain a lyophilized preparation of live *Vaccinia virus*. Growing concerns over biological terrorism have prompted calls to renew the smallpox vaccination program for the general public. Although there is generally a low risk for high-consequence adverse reactions from the *Vaccinia* vaccination, healthcare providers must carefully screen potential recipients to identify those individuals who are at risk for serious adverse outcomes, such as cardiac toxicity.

In March 2005, positive interim data were reported from a phase 1/phase 2 US clinical trial of a live attenuated smallpox vaccine called LC16m8, which has been licensed in Japan since 1980. The researchers reported that in 100% of the vaccinated individuals (n=66), a pock formed at the site of injection—a traditional measure of a smallpox vaccine’s effectiveness in producing an immune response.25 In addition, the vaccine was well tolerated, with no signs of cardiac toxicity.25 Other smallpox vaccines are in various stages of development.26

Challenges Remain Despite Project BioShield

Despite the actions taken under Project BioShield, the need persists to increase our capabilities against a wide variety of potential biological weapons.27,28 It is important to continue to develop newer, safer, and more effective medical countermeasures, because licensed therapies and vaccines are unavailable or inadequate for many biological agents. Unfortunately there are significant barriers in the process of developing medical interventions against biological weapons. Obstacles to pharmaceutical and vaccine development include inadequate funding for research, insufficient protections against corporate liability, and constraints related to safety considerations.5,29–31 Typically, the drug-development process in the United States is largely initiated by the National Institutes of Health, which supports basic research through funding scientists. Although the development of a new medication usually takes several years between the time that research begins to the time that the medication is marketed, developing medical interventions against potential biological weapons is especially intense in terms of time, labor, and finances.5,30,32,33

The development of countermeasures against biological weapons introduces an additional challenge beyond those encountered with general pharmaceutical development, in which the US Food and Drug Administration (FDA) requires clinical studies of human safety and efficacy. In a typical clinical trial, patients are provided a new medicine while suffering from the disease or infection under investigation. However, it would be ethically unacceptable to conduct human testing against biological weapons.34 Clearly, the need for expedited development of critical countermeasures must be balanced against the need to ensure that these essential interventions are safe as well as effective.

Although it has been more than a year since President Bush signed Project BioShield into law, few large pharmaceutical companies have placed bids for contracts under the
## Current Biological Terrorism Countermeasures

### Legislative Acts
- Project BioShield (2004)  
- Public Health Security and Bioterrorism Preparedness and Response Act of 2002  
- Price-Anderson Amendments to Atomic Energy Act of 1954  
  (Reauthorization bill: S 865)  

### Related Programs
- Strategic National Stockpile (2003)  
- Top Officials (TOPOFF) Program (2000)  

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**Figure 1.** Project BioShield is one of several legislative acts and government programs that have been enacted in the United States as countermeasures to address the threat of biological terrorism.

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**Figure 2.** Several pieces of legislation under consideration by the 109th Congress are designed to address shortcomings in US biological terrorism preparedness. On the international stage, there are efforts to develop a verification protocol for the Biological and Toxin Weapons Convention.

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## Countermeasures Under Consideration

### Legislative Acts
- Project BioShield II Act of 2005 (S 975)  
- Homeland Security Grant Enhancement Act of 2005 (S 21)  
- Amendments to Public Health Service Act (including S 265, S 969, HR 1570)  

### Related Program
- Verification Protocol for Biological and Toxin Weapons Convention (1975)  

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## Training of Medical Personnel and Government Officials

The development of new pharmaceuticals is not the only consideration that is important to improving the nation’s preparedness for biological terrorism. Another area of concern involves adequate training of medical personnel and other professionals involved in preparedness efforts.\(^\text{18,37}\) This issue was partially addressed by the Public Health Security and Bioterrorism Preparedness and Response Act of 2002, often called simply the Bioterrorism Act, which was signed into law by President Bush in June 2002.\(^\text{38}\) This act focuses on a number of problems related to biological terrorism, including providing funding to train and educate public health professionals on quickly recognizing and identifying biological terrorism. The act also includes measures to allow the HHS and other federal agencies to enhance surveillance of the use of biological agents, and it addresses concerns about terrorist attacks on food and water supplies.\(^\text{38,39}\)

Role-playing exercises to test the ability of the federal, state, and local governments to respond to mass-casualty incidents of biological terrorism have revealed a number of vulnerabilities in preparedness. Dark Winter, which took place in June 2001, was an exercise developed and produced by the Center for Strategic and International Studies, Johns Hopkins Center for Civilian Biodefense Studies, and ANSER (Analytic Services) Institute for Homeland Security.\(^\text{40}\) In the mock dis-
aster, former senior government officials played the roles of US president, director of the Central Intelligence Agency, secretary of HHS, and other leaders as a way of testing the government’s communication procedures and other processes that would be crucial to making decisions about responses to a smallpox attack. Dark Winter suggested that the United States does not have adequate supplies, effective organizational systems, or the communication networks necessary to deal with such an attack. The exercise also revealed that the public health system and hospitals would be rapidly overwhelmed by the enormous increase in patient demand.

The Department of Homeland Security’s Top Officials (TOPOFF) Program is a two-year cycle of seminars, planning events, and exercises designed to improve US capacity to prevent, prepare for, respond to, and recover from terrorist attacks, including those involving biological weapons. The exercises involve officials from all levels of government, fire and police personnel, and local public health and public communications personnel. The first TOPOFF exercise, in May 2000, revealed communication problems, inadequate coordination among response leadership, flaws in command structure and decision making, and inadequate disease containment and use of protective equipment within healthcare facilities.

Some of the problems noted in these training exercises were highlighted in August and September 2005 by a real-world event—Hurricane Katrina, which caused much loss of life and devastation to infrastructure after making landfall along the Gulf Coast on August 29. Federal, state, and local officials came under heavy criticism as it became clear that personnel, and local public health and public communications personnel. The first TOPOFF exercise, in May 2000, revealed communication problems, inadequate coordination among response leadership, flaws in command structure and decision making, and inadequate disease containment and use of protective equipment within healthcare facilities.

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Proposed Legislation and Other Countermeasures

Several pieces of legislation under consideration by the 109th Congress are designed to address continued shortcomings in biological terrorism preparedness (Figure 2). The Project BioShield II Act of 2005 (S 975) would provide inducements for private enterprise to increase research in medical countermeasures to identify, contain, and treat WMD-related illnesses and injuries, including those associated with biological weapons attacks. Among these inducements are federal tax incentives and patent and liability protections. The liability protections would add extra legal protections for developers of antiterrorism countermeasures, making it easier for them to receive indemnification.

The Homeland Security Grant Enhancement Act of 2005 (S 21) provides for improved coordination and streamlining of the federal grant-making process by bringing the current State Homeland Security Grant Program, Law Enforcement Terrorism Prevention Program, and Urban Area Security Initiative together into a single program. The act would also increase the amount of grant money distributed to larger and/or more densely populated regions, while preserving a minimum amount of funding for each state. The bill authorizes approximately $3 billion for grants in fiscal years 2006 and 2007. Some of these funds would be targeted to improve levels of competence of emergency personnel and planning.

A number of biological terrorism-related amendments to the Public Health Service Act are under consideration by the 109th Congress. Among these amendments are the following:

- The amendment in bill S 265 would apply more stringent requirements on state emergency medical services to promote the collection and categorization of trauma data in a consistent and standardized manner.
- The amendment in HR 1570 would extend indefinitely appropriations to revitalize the CDC, including the improvement of CDC capabilities related to biological terrorism preparedness and the construction of new CDC facilities.
- The amendment in S 969 includes various provisions to strengthen, expand, and coordinate preparations for a potential influenza pandemic. Three such pandemics occurred during the 20th century, resulting in many millions of deaths worldwide. Tools developed in response to influenza outbreaks would also be useful in response to biological terrorism attacks—and vice versa. Among the provisions in S 969 are the procurement of antivirals and vaccines needed during a pandemic and the expansion of influenza research.
- The amendment in HR 1570 would extend indefinitely appropriations to revitalize the CDC, including the improvement of CDC capabilities related to biological terrorism preparedness and the construction of new CDC facilities.

International efforts underway in 2005 to enhance security against biological terrorism include continuing calls to develop a verification protocol for the BTWC. Such a protocol would, for the first time, provide the BTWC with mechanisms for verification and monitoring of compliance.

Comment

Some groups outside of the federal government view federal involvement in emergency preparedness as a potential threat to personal liberty and a misuse of resources. For example, the American Civil Liberties Union opposes forced cooperation, vaccination, quarantine, and commandeering of services and equipment, as these emergency measures make individual civil rights subservient to societal needs.

Concerns have also been expressed that expedited new medical interventions, as supported by Project BioShield, may lower the bar on FDA standards and protocols. Of course, similar concerns are also frequently mentioned with regard to medications not related to biological terrorism, as evidenced by the medical and legal controversies surrounding rofecoxib...
In light of such concerns, it is important to keep in mind that the approval of any new countermeasures for inclusion in the SNS would require the usual process of FDA guidance, including complete data on human safety. Mark B. McClellan, MD, PhD, former commissioner of the FDA, stresses that a primary responsibility of the FDA is the expeditious development and licensing of products to counter exposure to biological terrorism agents, and he expressed confidence in 2003 that the implementation of Project BioShield would safely and effectively advance this process.

One problematic aspect of Project BioShield that has a direct effect on medical providers involves record keeping. Under the act, the secretary of HHS requires parties who manufacture, distribute, prescribe, or administer medical products during emergencies to keep records on the safety and effectiveness of these products as used in emergencies. However, the HHS does not provide precise parameters for these record-keeping requirements. Furthermore, some record-keeping requirements of Project BioShield, the Health Insurance Portability and Accountability Act, and the private sector record-keeping requirements of Project BioShield, the Health Insurance Portability and Accountability Act, and the private sector may appear to conflict with one another, making it difficult for physicians to comply with all mandates.

Other problematic factors are adding to the biological terrorism readiness challenges faced by healthcare providers in the United States. At a time when healthcare resources are limited, the capacity needed to address the surge in patient demand expected from a terrorist incident is all but nonexistent at most hospitals. Thus, enhancing the readiness of healthcare providers will require providing them with the resources they need, including vaccines, antidotes, equipment, and other countermeasures. Current federal laws are proving inadequate in addressing these needs.

Training and education—beginning in professional schools and continuing throughout professional life—are crucial to ensuring that physicians and other healthcare providers adequately prepare for, recognize, and respond to incidents of biological terrorism. To that end, the United States must greatly improve the education of its medical providers. This can be done best at the grassroots level, but in a fundamentally different way than is currently done.

For example, a primary care physician today is likely to find that he or she lacks many of the tools needed for proper preparedness, because preparedness skills are not currently emphasized in primary care training. There have been many efforts to prepare so-called “first receivers,” or “first responders,” including seminars for personnel on state boards of medicine, and there has also been limited training in response procedures for some healthcare providers. However, thorough training in biological weapons preparedness should extend to all private practice clinicians and other healthcare personnel in the “front lines” of preparedness.

Physician training to provide care in the aftermath of a disaster—whether that disaster is a natural event, such as a hurricane, or an intentional event, such as an act of biological terrorism—has tended to focus on emergency physicians. Yet, considering who would be responsible for the immediate response to an attack involving biological weapons, it would seem prudent to emphasize community primary care clinicians—both internists and family practice physicians. Once a biological terrorism event occurs, patients will not report only to the local EDs; they will also phone and make appointments to see their local physicians. Given this scenario, the importance of providing training to even the nonmedical personnel in a physician’s office, such as the office receptionist, is also evident. A well-trained receptionist would be able to alert the clinician to a potential victim of biological terrorism and assist with basic preventive measures, such as advising the patient to report to the back door of the clinic instead of allowing the patient to sit in a crowded waiting room.

Beyond the challenge of training practicing physicians, it is vitally important to train the next generation of clinicians. Although some medical schools have made education in biological terrorism and toxicology new components of the curriculum, other schools continue to offer only quick awareness courses, which are often taught by faculty not experienced in this high-stakes arena.

Compounding the challenge is the lack of recognized standards for training in WMD—even though the American College of Emergency Physicians, in collaboration with other professional societies, has developed comprehensive guidelines for such training. Other standards-based educational materials include the Basic Disaster Life Support course, developed by the National Disaster Life Support Education Consortium, and the Advanced HAZMAT (Hazardous Materials) Life Support course, developed by the University of Arizona in collaboration with local, state, and federal emergency response agencies. Such courses are crucial elements in the training of students, residents, and attending physicians, but, unfortunately, they have not been widely utilized.

Medical students and primary care physicians need to know the “who, what, when, where, how, and why” of all aspects of biological terrorism preparedness. That is why we suggest adding another requirement to the continuing medical education criteria of osteopathic physicians. The osteopathic medical profession already has the forums in place through local, regional, and national conferences, as well as a cadre of osteopathic physicians from military and medical toxicology specialties, to accomplish this training. We present the following ideas as suggested replacements for some of the customary, often-repeated, annual lectures that are presented at these conferences.

Education on biological terrorism in lectures and workshops should be directed at primary care, ED, and public health physicians. This education should include basic information specific to the responsibilities of the physician, such as who to call when a patient presents with symptoms of suspected exposure to agents of biological terrorism. Should
physicians call 911? The local or state health department? Should the physician send his or her patient to the local ED even though it is likely already overwhelmed in such an event?

Physicians must have clear response avenues at their disposal, with specific contact names of individuals who are available not only during business hours, but after business hours as well. Clarification of the local chain of command system is essential knowledge. However, information without practice is only half of preparedness. Primary care physicians need to assume active roles in their community preparedness efforts, including participating in preparedness exercises, and they should become more familiar with the preparedness efforts of their local emergency medical services. The onset of a catastrophe is not the time to get acquainted with other professionals in the preparedness hierarchy.

Physicians should be afforded the opportunity to attend regularly scheduled continuing medical education courses that focus on such issues as antidote availability, providing care with limited resources, and practical aspects of triage that are counterintuitive to the normal response to injured patients. These crisis medicine courses should include material similar to that taught in courses on Advanced HAZMAT Life Support, Advanced Disaster Life Support, and wilderness medicine. Although ER physicians are trained in these types of responses, primary care physicians are not. Knowing how to treat many victims with few resources is an important challenge for physicians; human and material resources may not be sufficient for mass casualties, but effective training will likely lessen the impact of catastrophic events.

Lectures and workshops should also be used to provide physicians with an up-to-date awareness of the biological weapons suspected to be in the arsenals of hostile states and terrorist organizations. These programs need to be regularly offered and include topics covering such agents as Bacillus anthracis, Clostridium botulinum toxin, Filoviridae viruses, V. major, and Y. pestis. Physicians need to be trained in early recognition of symptoms caused by these biological agents so that measures to control the spread of infection can be rapidly implemented.

Finally, physicians would greatly benefit from regular health policy alerts to keep them abreast of the state and national legislation related to biological terrorism preparedness, such as the legislation previously discussed.

In addition to addressing the needs of their own continuing education, physicians should be attuned to the information needs of their patients and communities. Several medical and government organizations, such as the CDC, produce easily understandable information sheets that can be downloaded from Web sites, printed out, and made available in waiting rooms. It is also essential to better inform the American public about ongoing government preparedness efforts, including the strengths and limitations of such legislation as Project BioShield.

Conclusions
It is a major challenge to prepare for an unknown event against undisclosed threats. Some public health officials might argue, especially in the aftermath of the devastation caused by Hurricane Katrina, that investments in biological terrorism detract from other important threats, such as natural disasters. But preparedness is not a zero-sum game. Enhanced preparedness for mass casualties not only provides protection against terrorist attacks, it also enables us to better protect our communities against a wide range of industrial accidents, natural disasters, and emerging infectious diseases.

Facilitating interest within the private sector and academia to create critical countermeasures to the threat of biological terrorism rests upon how effectively regulatory, financial, safety, and ethical issues are addressed, and upon how well collaborations among private, public, and regulatory entities can be established. The development of effective countermeasures requires a significant investment in research, which is time-consuming and cost-intensive. The financial costs associated with developing new medical interventions go well beyond the start-up investment and include potential product liability, testing, manufacturing, inventory, and storage.

Project BioShield was designed to encourage interest in and development of countermeasures to enhance domestic preparedness. The collaboration between government, private industry, and healthcare providers—an alliance that Project BioShield was conceived to support—is vitally necessary to sustain preparedness efforts.

The use of funds for biological terrorism preparedness has the potential to enhance attention to other public health issues, such as influenza, human immunodeficiency virus, tuberculosis, and food- and water-borne illnesses. The development of newer and safer vaccines and antimicrobials against potentially weaponized biological agents will also aid against naturally occurring global illnesses.

Project BioShield is one important component of a highly complex domestic preparedness effort. Other important components include the SNS, regional pharmacological stockpiles, local medical response teams, greater funding for hospital preparedness, enhanced and ongoing professional training, improved public education, and increased collaboration across all professional cultures within a community. Investment in the development of new vaccines and improved treatments for illnesses resulting from biological weapons and other WMD are vital for public health and preparedness.

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