Bioterrorism

New Health and Defense Strategies

By Diane Tseng

Today, the threat of a bioterrorist attack is more real than ever before. Christopher Chyba, Co-director of the Center for International Security and Cooperation at Stanford University, offers an expert's perspective on our current state of preparedness as well as a possible strategy for the future. The anthrax attacks of autumn 2001 clearly remind us of biological terrorism's considerable threat to public health and of our nation's lack of a comprehensive strategy to face it. So, what is the current status of our national preparedness? And, what measures need to be taken in order to deter, defend against, and respond to bioterrorism?

The Nature of Biological Weapons

Biological weapons are especially difficult to regulate. Airborne bacteria and viruses are both invisible and odorless, traveling undetected amidst their target population. Upon infection with a biological agent, an individual's initial symptoms are often mild and resembling the flu. Such elusive symptoms hinder clinical recognition, and thus result in aberrant diagnoses. In addition, tracing the course of a biological warfare agent is incredibly tricky. Currently, there is limited means of sharing information among local, state, and federal health departments and between the public health sector and law enforcement agencies. It is difficult to distinguish deliberate attacks from natural outbreaks, as evidenced by the 1999 appearance of West Nile virus in New York.. Soon after the outbreak an Iraqi defector claimed that Saddam Hussein planned to use the virus as a biological weapon; that claim was later proven to be a hoax. Indeed, the insidious nature of biological agents and the current organization of our public health departments make it difficult to identify and regulate bioterrorism. The incubation period of the biological agent, which is unique to bioterrorism, inevitably causes delays in this process.

What are the potential sources of bio-warfare agents? There are existing collections of "dual-use" exports—materials that serve both civilian and military purposes—that contain professional-grade bioterrorist agents. In addition, nonprofessional-grade agents are available through naturally occurring disease outbreaks (such as Ebola and West Nile Virus) or as part of legitimate scientific research (including anthrax and smallpox). Weaponizing these diseases and engineering the biological strain into powder or aerosol form enable their widespread dispersal and serve as a serious threat to public health. More threatening still is the possibility of increasing the potency of these infectious agents through genetic modifications, making them resistant to vaccines or antimicrobial drugs.

Defense Strategy: Sensitivity and Connectivity

Due to the difficulty in regulating biological weapons, Christopher Chyba suggests that our strategy for biological security needs to focus on heightened defense. Chyba states, "The criteria we apply to any countermeasure can't be, 'Will it solve the problem?' It is whether the countermeasure will make it harder to conduct an attack." Although Chyba still encourages prevention and nonproliferation (ending the acquisition of biological weapons by additional countries), he claims that biological security will have to rely more strongly on consequence management. In terms of the appropriate approach to consequence management, Chyba states, "It's natural among scientists and technologists to think in terms of high tech solutions. But I think we also need to remember that a lot of what can be done in the near future isn't very high tech. What do we need to do? We need to improve disease surveillance in response. And what that comes down to is improving the sensitivity and connectivity of the public health system." This strategy must iinclude both low-tech *sensitivity* and high-tech *connectivity* methods of dealing with bioterrorism.

Professor Christopher Chyba, Co-director of the Center for International Security and Cooperation

Sensitivity involves the recognition

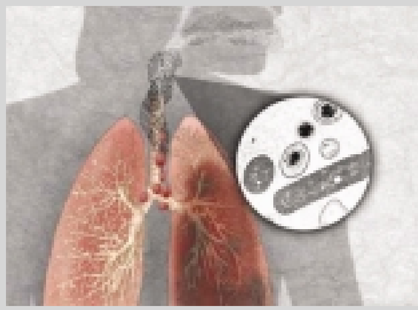
of threatening organisms. Improving sensitivity would certainly require additional training of medical personnel to identify suspicious symptoms and signs, to follow the appropriate protocol for response, and to report the case to the right people. Such bioterrorism preparedness training for medical personnel is being implemented in many institutions across the country. One of the most comprehensive response models was developed here at Stanford Hospital by the Bioterrorism and Emergency Preparedness Planning Task Force. This model seeks to improve sensitivity in order to accomplish two main objectives: (1) to ensure the health and proper treatment of patients; (2) to limit the potential exposure of hospital staff and facilities. The latter purpose is no less important. If medical personnel become contaminated while treating a patient, the whole department or facility may need to be shut down; this would lower our capability to respond to a sustained bioterrorist attack. One way to prevent this outcome is through increased sensitivity and the ability to recognize the threatening agents effectively.

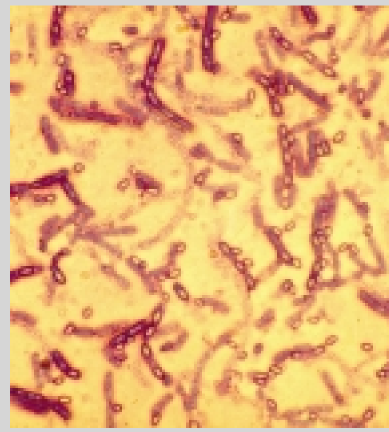
Connectivity, on the other hand, involves the sharing and reporting of the threat among various levels of organization. To improve connectivity, the medical personnel should have access to new communications technology, such as a database in which physicians enter the symptoms of their patients, view relevant statistics, and receive continuously updated geographical and temporal characteristics of symptom distribution. This could aid in distinguishing an isolated case from a national epidemic.

In the Los Alamos laboratory in New Mexico, the Rapid Syndrome Validation Project (RSVP) is currently developing such a database to facilitate rapid communications between epidemiologists and medical personnel. Development of sensitivity and connectivity undoubtedly requires efforts on both institutional and national levels, both of which are currently under way.

Anthrax Explained

Bacillus anthracis spreads mainly through the air as airborne spores, commonly entering its host via inhalation. Once inside the lungs it quickly invades the bloodstream and spreads throughout the entire body. The bacterium can also enter the blood stream through cuts in the skin and by ingestion of improperly cooked meats. Within a week following infection, the individual often experiences fever, malaise, cough, and terminal shock. For cases of inhalational anthrax, fatality rates for victims can be as high as 75 percent after symptoms occur. Anthrax is propagated by the production of dormant spores following death of the host, enabling it to spread to new hosts.





Courtesy WHO

Anthrax has many molecular components that make it extremely deadly. On the outer coat is a polymer capsule that disables the host's immune system and prevents the bacteria from being digested by the macrophages, cells that engulf foreign bodies such as bacterium. This means the bacteria cannot be stopped by the natural immune system and hosts must rely on antibiotic intervention. Without medical treatment the fatality rate is 90-100%. This high fatality is due the lethal toxin secreted by the anthrax bacterium. In fact, the toxin alone, without the bacterium, can prove deadly to hosts.

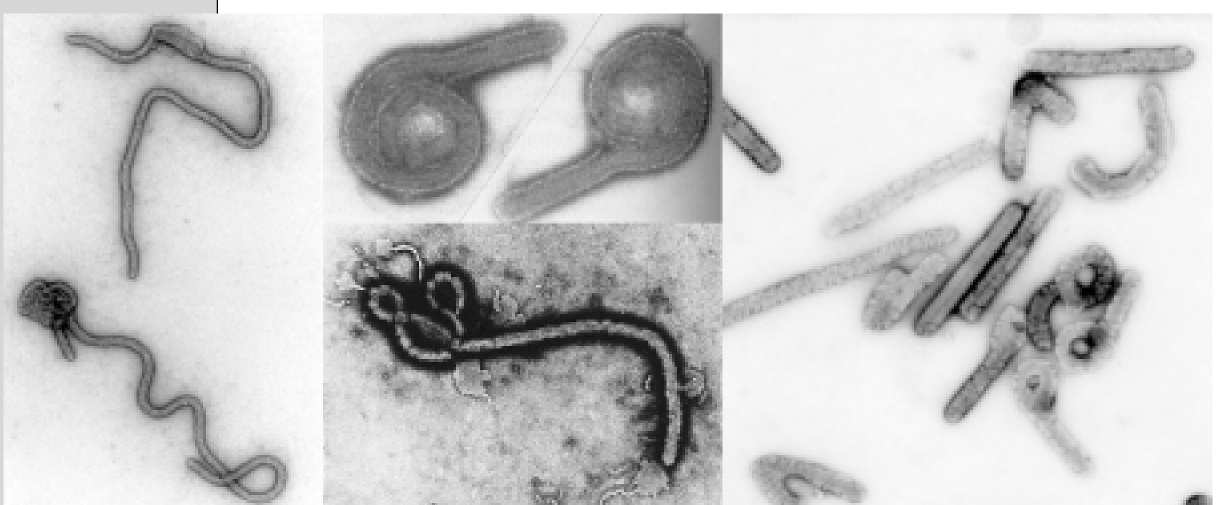
The three components of the anthrax toxin include protective antigen, edema factor, and lethal factor. The protective antigen delivers the other two components into the cell's cytosolic interior where the edema causes cellular swelling and the lethal factor destroys important enzymes. The toxin aids the bacteria in extensive replication, ultimately killing the host. Research geared at neutralization of the anthrax toxin will greatly diminish the bacterium's threat.

Courtesy Sandia National Laboratories

Ebola Explained

Unlike the aerial transmission of anthrax and smallpox, Ebola is spread through bodily fluids such as blood and semen. One rare strain has been known to spread through the air, although it affects only monkeys. Mild symptoms of infection, including fever, backache, and headache, appear within the first few days and severely escalate at the close of a week as tissues and organs begin to liquefy. Approximately 70-100% of infected individuals die within two weeks from organ system failure, massive vomiting of blood, and, in the disease's final stage, the expulsion of blood through body orifices, such as the nose and ears. Severity of the disease depends on the strain of the virus.

Little is known regarding the molecular nature of Ebola. The void in knowledge is partially due to its relatively recent 1976 discovery in Zaire. Depending on the strain, the virus resembles either a swirling noodle or a round ball. It attacks all cell types, making no distinctions between them. Often times the host immune system is simply overwhelmed by the proliferating virus as it spreads throughout the body, resulting in complete cellular breakdown and tissue liquefaction. A protein on the surface of the virus attacks the cells lining the blood vessels, causing deterioration of the vessel walls.



Under the microscope: Ebola virus

Domestic Defense

Our federal government is taking steps to implement this strategy domestically. In 1999, the Center for Disease Control developed the Laboratory Response Network for Bioterrorism, which outlines steps for strengthening public health and health care capacity to protect the United States against dangers of bioterrorism. Funding is also being channeled in the right direction. A 2002 emergency supplemental appropriations bill allocated 1 to 2 billion dollars in new spending for biological defense. On June 12, 2002, President Bush signed the Public Health Security and Bioterrorism Act, which will enhance our ability to prevent and detect bioterrorist attacks by improving port inspections, protecting the food supply, tracking biological materials, and improving response capabilities of our health care system.

When domestically allocating resources for scientific research, should efforts be focused more on preparation for a rare but potentially catastrophic event or on research for combating infectious disease killing people everyday? Experts do not have an easy answer. As much as the latter sounds like a more practical concern, we can no longer ignore the possibility of a fatal bioterrorist attack. Perhaps, the two interests are not necessarily mutually exclusive. Furthering research to protect against bioterrorism can potentially lead to developments for fighting popular diseases.

International Defense

Despite improvements in domestic preparedness, Chyba is actually much more concerned about disease surveillance internationally. The demographics of our society make it futile for the U.S. to only deal with this crisis domestically, especially considering the versatility of air travel, the difficulty of regulating national borders, and the infectious nature of diseases like smallpox. Chyba comments, "Because of the incubation times that the diseases have, there is an unavoidable, inescapable international aspect to the problem. An African issue or a smallpox outbreak in a European nation will threaten the United States, putting aside moral issues."

International efforts for development and cooperation must occur for both humanitarian and self-interest reasons. Improving another nation's biodefense response capabilities not only protects the citizens of that nation, but it also protects the health of U.S. citizens. Less wealthy countries do not have the personnel training or the infrastructure necessary to recognize and adequately respond to a biological attack. The personnel training abroad should be similar to the efforts being made domestically to allow identification of patients exposed to a biological agent and knowledge of how to exactly respond. The public health developments that will occur in poor countries should improve basic infrastructure and not have to be expensive high-tech endeavors. Christopher Chyba suggests building centers in various regions around the world where biological samples are analyzed and identified, and standards are set to secure the safe storage and transport of biological stocks that could be used for weapons. The current developments for responding to bioterrorism abroad are either insufficient or completely nonexistent. In facing the threat of bioterrorism, international cooperation must take place for efforts to be successful.

International Developments: The Past and The Present

Historically, international declarations have been made to reduce and control biological weapons. In 1925, after World War I, one of the most important international agreements concerning bioterrorism was drawn: the Geneva Protocol reaffirmed pre-war principles prohibiting the use (but not possession, development, or research) of biological and chemical weapons in warfare. The U.S., however, rejected the Geneva Protocol for fear of compromising its biodefense capabilities in the face of the protocol's challenges with verification and compliance.

On April 10, 1972, the Biological and Toxin Weapons Convention (BWC) also established a legal basis for bioterrorism by banning the production, development, and stockpiling of biological agents for purposes that were not prophylactic, protective, and peaceful. Recently, in July 2001, the Bush Administration rejected the BWC's draft compliance protocol because they felt that it did not strike a balance between the risk and benefits of compliance. The Bush Administration reiterates that they are fighting against proliferation of biological weapons, but that the BWC's approach will not work.

The Geneva Protocol and the BWC's draft compliance protocol represent a historical international commitment to combating bioterrorism. The U.S.'s role in the face of both of these international efforts poses a challenge for current multilateral initiatives for dealing with bioterrorism. However, the U.S. must fight bioterrorism on the international level. The public as well as policy makers must realize that international public health initiatives also directly benefit U.S. citizens. We must demonstrate our commitment to support nations financially and through direct aid in conjunction with local efforts abroad.

Smallpox Explained

Smallpox is caused by the variola virus and is dispersed through the air. Only very small amounts are necessary for infection, making it highly contagious and easily distributed through aerosol cans. Once the virus spreads to the host, it incubates in one to two weeks. This lengthy period allows the virus to spread to large masses of people before any symptoms appear. After incubation, hosts experience common maladies, such as fever, headache, backache, and vomiting.

Distinguishing traits of smallpox infections, present soon after these generic symptoms, include flat, red, pus-filled lesions. As such, smallpox greatly resembles chickenpox. However, smallpox lesions disseminate across the entire body while chickenpox tend to form crops along isolated regions of the body. Smallpox lesions can intensify in some cases, completely covering the skin. This often proves fatal as it causes both external and internal bleeding. Smallpox is lethal in 30% of cases, taking approximately 10-28 days to overcome its victim. Those who combat the infection are left with life-long scars that disfigure their face and body.

According to recent research, smallpox may behave molecularly in much the same way as the HIV virus. This possible explanation is based on the 1999 discovery by postdoctoral researcher Alshad Lalani and Professor Grant McFadden at University of California San Francisco that a relative of smallpox virus, the myxoma poxvirus, uses the same route of entry as HIV to invade its host. Thus, smallpox may attach to the chemokine receptors on the surface of helper T immune cells, which are stimulated by antigen to provide signals that promote further immune responses. The CCR5 and CXCR4 chemokine receptors are possible docking sites involved in the attack of helper T cells. Diseases attacking the immune system itself are very difficult to treat. Researchers are trying a new approach to studying smallpox by mapping the genome of the variola virus, hoping it will provide more insight into the virus's mechanism. The genome project has currently mapped 66% percent of its sequence with high accuracy.

Bioterrorism: The Present and the Future

Currently, many experts believe that our nation is not yet ready to deal with bioterrorism, a very real threat to national and international public health and security. Dealing with biological terrorism is very difficult due to the insidious nature of infectious disease and the difficulty of initially distinguishing between an isolated case and an epidemic. Efforts of medical personnel training and communication among public health personnel, epidemiologists, and law enforcement agencies must continue domestically. The imminent need to improve international capabilities of responding to bioterrorist attacks should prompt us to dramatically increase efforts abroad to train medical personnel and develop necessary infrastructure. The policy makers and the public should consider bioterrorism as a real threat to national and international security. Perhaps in the future, we will have to learn to live with the fear of a bioterrorist attack. While there is no way to control the limits of human cruelty, we should try to minimize the impact of bioterrorism if it were to occur and be prepared to manage its consequences to the best of our ability.

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Treatment and Prevention of Anthrax, Smallpox, and Ebola

The current treatment of anthrax focuses on halting the toxin from adversely affecting the host cells. Drugs such as soluble anthrax toxin receptor (sATR) can act as decoy hosts with special protein receptors that trick the toxin into attaching itself to the wrong host. The best treatment is close medical monitoring in conjunction with antibiotic therapy. Early detection of isolated cases as well as preventing the spread could be effective in curbing potential massive outbreaks. Vaccines offer a strong defense against such outbreaks. The currently available vaccine causes the immune system to produce antibodies against the bacterium through introduction of a weakened form of anthrax. The drawback of the vaccine is that it must be combined with antibiotics and taken over the course of several years, making national immunization nearly impossible.

The treatment for smallpox is simply intense medical care. The lack of an effective curative drug stems from the assumed eradication of the disease in the late 1970's through the use of vaccine. The smallpox vaccine uses the cowpox virus, a molecularly similar virus to smallpox that is capable of affecting only cows and rodents. A single vaccine dose was effective for 10 years and used to be given to children once in their lifetime. Following the "eradication", smallpox vaccinations were stopped to prevent complications that occasionally resulted from the immunizations. With a thirty year lapse in vaccinations, the US population is very vulnerable to a smallpox outbreak should the virus be reintroduced.

The current supply of vaccines could vaccinate only a small percent of the population. Unfortunately, even if enough were available to all, the vaccine cannot be given to people with a weak immune system such as those afflicted with autoimmune disease or those who have undergone cancer radiation treatment. The government is responding to these obstacles with research geared at both treatment and better vaccines along with massive production of the current vaccine.

The Ebola virus dwarfs both anthrax and smallpox with its lack of prevention and treatment. There are no vaccines or treatments available, making it the most difficult to deal with. However its quick kill of the host enables early identification and isolation, quelling the potential for a massive outbreak.

Anthrax, smallpox, ebola and treatment sidebars by Ben Wang.