Chapter 18
Case Study – United States of America

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Abstract The United States (US) considers the intentional use of a biological agent a serious national security threat. Over the last decade, federal, state, and local governments in the US have made concerted efforts to enhance preparedness within the public health, medical, and emergency response systems to address this threat. These activities span a wide range of areas from the enactment of new legal authorities and legislative changes to significant financial investments to enhance multiple detection and response system capabilities and the adoption of a national command and control structure for response. Many of these investments, although prompted by the concern for bioterrorism, have served to strengthen public health, medical, and emergency response systems overall and have proven invaluable in responses to other large-scale emergencies, such as the 2009 H1N1 influenza pandemic.

18.1 Public Health Infectious Disease Threats

Infectious diseases still account for a significant portion of public health activities in the United States, whether it is monitoring for and responding to foodborne related outbreaks, addressing increases in nosocomial or antibiotic resistant infections, or tackling new and emerging world-wide infectious threats such as Severe Acute Respiratory Syndrome (SARS) or pandemic influenza. Indeed, infectious diseases still account for two of the ten leading causes of death in the United States [5].

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The intentional use of a biological agent is also something that the United States considers a serious threat and the federal, state, and local governments in the US have made concerted efforts to enhance preparedness and capabilities within the public health, medical, and emergency response systems to address this threat. In 2001, this concern became a reality for the US when several letters containing anthrax spores were sent through the postal system to individuals and organizations [14]. This resulted in 22 cases of anthrax (11 inhalational and 11 cutaneous) with five deaths. Although this event may not have been the type of "mass-casualty" situation most bioterrorism preparedness planning activities were targeting, it still resulted in significant response efforts and cost; over 10,000 individuals were offered antibiotic prophylaxis because of possible exposures, over one million clinical and environmental specimens were tested, and hundreds of millions of dollars were spent on decontamination of the buildings where the letters were processed or opened [12, 22].

Although many infectious agents are capable of causing human illness, some are much more capable of causing significant morbidity and mortality if successfully used as a bioterrorism agent. In 2000, the Centers for Disease Control and Prevention (CDC) developed a process to prioritize biological threat agents based on evaluation of the following threat agent characteristics: (1) public health impact from ability to cause illness or death, (2) ability to be produced and delivered in a way that could expose a large number of people, (3) existing public perceptions of a biological agent that could contribute to heightened fear and panic, and (4) requires significant special preparedness efforts in order to diagnose, treat, or prevent illness [20]. Based on these characteristics, biological threat agents were prioritized into three different tiers. Category A (highest threat tier) included *Bacillus anthracis* (anthrax), Variola virus (smallpox), *Yersinia pestis* (plague), *Francisella tularensis* (tularemia), Clostridium botulinum toxin (botulism), and the Filo and Arenaviruses (e.g., Ebola and Marburg virus) that cause viral hemorrhagic fevers. Category B and C were lower threat tiers and included agents such as *Burkholderia mallei* and *B. pseudomallei*, *Rickettsia prowasekii* (Category B), and emerging threats such as Nipah virus (Category C). Following the release of Homeland Security Presidential Directive 10 (HSPD-10) in April 2004, the US Department of Homeland Security (DHS) became responsible for issuing biannual assessments of biological threats in order to guide the prioritization of ongoing investments in research, development, planning, and preparedness [23].

18.2 Preparedness for Public Health Emergencies

The United States has made significant investments in terrorism preparedness and response coordination over the last two decades that includes the implementation of new policies, legislation, and legal authorities in addition to significant funding investments. In 1995, Presidential Directive 39 added a terrorism annex to the Federal Response plan and defined responsibilities of federal agencies in responding to

terrorism [25]. The Homeland Security Act of 2002 established the Department of Homeland Security (DHS), a new cabinet level office whose primary mission is to prevent or reduce vulnerability of the United States to terrorism at home; coordinate homeland security responsibilities between the federal government and state, local and private entities; and minimize damage resulting from attacks and assist in the recovery. In 2003, Homeland Security Presidential Directive 5 (HSPD-5) established a nationwide system to coordinate responses to emergencies between local, state, and federal governments and responding organizations and to administer this all hazards National Response Plan through a National Incident Management System (NIMS) that provides for unified command and better multi-agency coordination [24]. Other Presidential Directives and legislation enacted in the US since the World Trade Center and anthrax letter events in 2001 have provided stronger legal frameworks and public health capacity to prevent, prepare, and respond to intentional acts of biological terrorism. The 2002 Public Health Security and Bioterrorism Preparedness Response Act (PHSBPRA) established new requirements for possession, use, and transfer of selected biological agents and toxins (Select Agent List) that could pose threats to human, animal, and plant health and safety as well as established other authorizations and appropriations necessary to carry out essential public health and medical preparedness and response activities [19]. This act authorized more than 1.5 billion US dollars in grants to state and local governments and healthcare facilities to improve planning, training, detection, and response capacity as well as funding to expand the federal Strategic National Stockpile of medications and vaccines and upgrade food inspection capacity and CDC facilities that deal with public health threats. The Project Bioshield Act (July 2004) and Pandemic and All-Hazards Preparedness Act (December 2006) also specifically provided for new authorities and funding to address significant gaps that existed for the development, acquisition, and utilization of medical countermeasures (e.g. antimicrobials, vaccines, chemical antidotes) for chemical, biological, radiological, and nuclear (CBRN) threats.

In 2002, the CDC asked the Center for Law and Public Health at Georgetown and Johns Hopkins Universities to draft a model state public health law (the Model State Emergency Health Powers Act or Model Act) for state and local jurisdictions to use in addressing either bioterrorism or naturally occurring disease outbreaks [9]. The Model Act (available at http://www.publichealthlaw.net/MSEHPA/MSEHPA.pdf) outlines five major public health functions to be allowed by law including preparedness, surveillance, management of property, protection of persons, and communication. In addition to ensuring sufficient authority to collect disease surveillance data, conduct contact tracing, and provide preventive measures to those at risk, public health laws must enable local health officials to implement quarantine measures, if needed, to control a contagious disease outbreak with epidemic potential that could lead to severe morbidity or mortality (e.g. smallpox). This authority should be linked with specific, scientifically appropriate criteria that would be met before quarantine could be implemented. In addition, public health laws should provide for due process measures to protect those affected. Ideally, quarantine strategies would be determined and operational procedures would be in place prior to an emergency.

Ongoing broad-based investments to improve response planning and coordination, surveillance, training, information systems, and communications have been made that serve to improve public health capacity for all threats and hazards. Starting in 1999, the US Government began providing funding to 62 state, local, and territorial health departments to build stronger capacity for surveillance and epidemiology, laboratory diagnostic capacity, communications, countermeasure distribution, and emergency response planning, exercise, and evaluation. The initial investment into these public health system upgrades started at 40 million US dollars per year with a primary focus on addressing bioterrorism threats. Following the events of 2001, funding to support enhancements in the national public health infrastructure increased to approximately 1.5 billion per year. The current state of progress towards specific preparedness goals identified for CDC funded preparedness and response activities in the 62 state, local, and US insular areas is provided in the "2010 Report – Public Health Preparedness: Strengthening the Nation's Emergency Response State by State" which can be found online at http://emergency.cdc.gov/publications/2010phprep/.

Additionally, more targeted investments have been made that address surveillance, detection, and illness prevention or treatment needs for specific high priority threats. Examples of these targeted initiatives include the Laboratory Response Network (LRN), the Strategic National Stockpile (SNS), and an environmental monitoring system called BioWatch. In 1999, the CDC and other partners formed the Laboratory Response Network (LRN) [3]. The LRN is a network of approximately 170 national and international public health, veterinary, agriculture, food, military, and environmental laboratories that have increased diagnostic capability for the rapid identification of multiple biological and chemical threat agents in multiple sample types. Participation in the network is voluntary and these pre-existing laboratories work under a single operational plan and adhere to policies on safety, security, and bio-containment. LRN members agree to perform testing using LRN procedures and are provided training, equipment, rapid detection assays and reagents, protocols, and secured communication and data reporting systems to increase testing and laboratory response capabilities in a standardized and coordinated fashion. There are three types of laboratory designation within the LRN: national, reference, and sentinel. National labs have unique capabilities and resources that allow them to handle highly infectious agents and perform strain-level identification and other agent characterization testing. Reference laboratories are mostly based at state and large city health departments and have the capability to perform rapid confirmatory testing for certain agents and toxins while sentinel laboratories (primarily hospital and commercial clinical laboratories) can perform routine clinical testing on patient specimens with additional training and protocols for notification and rapid referral of isolates in the event that they are unable to rule-out a biothreat agent. In addition to the central role the LRN played in detecting and responding to the 2001 anthrax letter event, the commitment to infrastructure support and standardized platform testing capacity within the LRN has also proven extremely beneficial in assisting with more rapid and broader deployment of tests developed in response to other emerging public health threats such as the 2003 Severe Acute

Respiratory Syndrome (SARS) and the 2009 H1N1 avian influenza pandemic. LRN laboratories are also trained on chain-of-custody requirements and protocols which allow them to serve as a local testing resource for law enforcement linked samples where there is a concern for biological threat agents. Approximately 90% of the US population lives within 100 miles of an LRN laboratory, which provides for more rapid access to confirmatory diagnostic testing to evaluate potential illness from or exposures to threat agents.

The SNS (formerly the National Pharmaceutical Stockpile) program began in 1999 to acquire and store a stockpile of medications, vaccines, and other medical supplies whose rapid availability is vitally important for response to a large-scale event involving certain biological, chemical, or radiological agents [4]. Without a pre-purchased and stored stockpile, most of these medications and vaccines would not be readily available through other sources in appropriate amounts or in a timeframe that would allow for the prevention or effective treatment of illness. Partnerships with storage and transportation companies have been created that provide strategically located storage facilities, allowing rapid delivery of SNS materiel to any location in the US or its territories within 12 h of the federal decision to deploy. Certain medical countermeasures may be eligible for the shelf-life extension program managed by the Food and Drug Administration and the Department of Defense, which allows for expiration date extension based on potency and other test results. In addition, agreements with pharmaceutical companies and medication distribution partners have allowed for rotation of certain medications back into the commercial supply chain for use prior to their expiration in order to help mitigate replacement costs. Although the SNS was originally developed as a medical countermeasure response resource for intentional biological, chemical, and radiological emergencies, it has been deployed and used multiple times to support the medical needs of other public health emergencies, including Hurricanes Katrina and Rita, the recent H1N1 influenza pandemic, the 2001 World Trade Center and the anthrax letter attacks.

The successful distribution of the SNS is dependent on the capacity of state and local jurisdictions to rapidly dispense these countermeasures to the public. Planning for the timely provision of antibiotics and/or vaccines to large populations requires the involvement of public health, emergency management, and the local medical community. Mass prophylaxis plans need to consider the specific challenges of potentially vulnerable populations, such as children, pregnant women, and those who are isolated and without resources and social supports, such as the homeless and homebound. Contingency plans for setting up community-based Points of Dispensing (PODs) for mass prophylaxis have been developed by most state and local jurisdictions, with a focus on ensuring sufficient staffing resources, equipment and space requirements, and expediting patient flow. The capacity of health officials to rapidly vaccinate the community was recently tested in the United States during the 2009 H1N1 pandemic and demonstrated the need for flexibility and coordination in distribution of vaccine, including school-based programs, community health centers, pharmacies, and large health department sponsored vaccination clinics.

Multiple initiatives have been supported to further strengthen public health disease surveillance and reporting that include an emphasis on traditional disease

reporting as well as the utilization of non-traditional data that may provide an earlier indication of community health events or more likely assist with situational awareness assessments during an identified event [8]. Traditional public health surveillance for illness associated with potential bioterrorism agents relies on enhancing the medical and laboratory communities' familiarity with these agents, with the goal of improved reporting of suspected or confirmed illnesses, as well as reporting of unusual disease manifestations or illness clusters. Most local and state health codes require that physicians, hospitals, and laboratories report a defined list of notifiable infectious diseases. State public health agencies have added CDC Category A and B agents to their reportable disease lists. These lists are available at http://www.cste.org/dnn/Programs andActivities/PublicHealthInformatics/PHIStateReportableWebsites/tabid/1 36/Default.aspx. In addition, recognizing the need to detect newly emergent diseases that are not yet listed on the health code, most states also require reporting of any unusual disease clusters or manifestations. Early recognition of a bioterrorism-associated event depends in large part on astute clinicians and laboratorians recognizing one of the index cases based on a suspicious clinical, radiologic, or laboratory presentation (e.g. a febrile illness associated with chest discomfort and a widened mediastinum on chest radiograph in an otherwise healthy adult suggests inhalation anthrax). Isolated cases presenting at separate hospitals will not be recognized as a potential outbreak unless they are reported promptly to the local health department, where the population-based aberrations in disease trends are more likely to be noticed. Previous examples of astute clinicians recognizing and reporting unusual disease clusters or manifestations that led to the detection of a more widespread outbreak include an outbreak of hantavirus in the southwestern US [7], Legionnaires' disease associated with the whirlpool on a cruise ship [13], an outbreak of *Cyclospora* associated with contaminated raspberries imported from Guatemala [11], and the initial outbreak of West Nile virus in New York City in 1999 [18]. Similarly, the initial detection of anthrax in 2001 was due to a physician who recognized that large gram-positive rods in a patient's cerebrospinal fluid could be *B. anthracis* [1]. By reporting this suspected case of meningeal anthrax, rapid confirmation was facilitated in a state public health LRN reference laboratory. Weeks later, a suspected case of inhalation anthrax was recognized and promptly reported to and confirmed by public health authorities in New York City [17].

With the continued emergence of new zoonotic disease threats, including those related to bioterrorism, local, state, and federal public health agencies have taken steps to improve communication between human and animal health communities. Notifiable disease requirements have been expanded to include reporting by animal health specialists of suspected or confirmed illness in an animal that might be caused by a potential biothreat agent.

Because many medical providers and laboratorians in the United States have limited experience with most potential bioterrorist agents, early diagnosis may be delayed. Therefore, the first indication that a large-scale bioterrorist attack has taken place might be an increase in nonspecific symptoms at the community level. Surveillance for these increases in nonspecific syndromes (e.g. respiratory, gastrointestinal, or neurologic) constitutes the cornerstone of syndromic surveillance used for emergency response purposes.

Many health jurisdictions have begun collecting and monitoring other types of health-related information such as symptom complexes presented during emergency room visits (e.g. lower respiratory tract illness, gastrointestinal illness, rash with fever), healthcare utilization information (e.g. emergency room visits, 911 calls), or other data that may be affected by a community-wide health event (e.g. school absenteeism, flu or diarrhea over-the-counter medication sales) [10, 15].

Though the approaches and cost for implementing syndromic surveillance vary, the tools and concepts for syndromic surveillance are adaptable and have been successfully implemented in both developed and developing countries to address routine surveillance, outbreak monitoring, and health security needs [6]. While initially conceived for early detection for bioterrorism, these systems also can be used to monitor natural infectious disease outbreaks and trends in noninfectious events of public health importance. Information from syndromic systems has proven to be useful for detecting, monitoring, and characterizing seasonal outbreaks of influenza, winter gastroenteritis (e.g. norovirus and rotavirus) and asthma. Furthermore, syndromic systems were utilized extensively in the US during the novel H1N1 influenza pandemic of 2009, along with other methods, to estimate the scale of community-wide influenza transmission.

An additional concept to specifically improve early detection of an intentional biological agent release is the use of environmental monitoring systems. If an agent can be detected quickly following an aerosol release, response timelines can be significantly improved, allowing for more time to intervene and potentially prevent illness in a significant portion of the exposed population. In 2003, the United States implemented BioWatch, an environmental monitoring system that consists of a network of samplers that collect air on a continuing cycle [21]. Filters from the monitors are removed on a frequent basis and screened in a laboratory for the presence of several biological threat agents. BioWatch is currently operational in multiple US cities. Environmental monitoring in this fashion requires a significant financial commitment and is a complex system to operate as experience with this type of system was limited prior to its implementation. Natural environmental presence of the target organisms and/or very closely related organisms and the size of the area to be monitored present ongoing challenges for establishing system sensitivities and specificities that appropriately balance the potential value of early detection of a bioterrorism attack with the risk of inappropriately responding to a positive test that is caused by naturally occurring organisms in the environment. A separate system of detectors has also been deployed that monitors the US mail system, the method of "dissemination" used in the 2001 anthrax letter attacks. The US Postal BioHazard Detection System (BDS) has been operational since 2004 [16]. Unlike traditional disease and syndromic surveillance systems for human and animal health which monitor for both intentional and naturally occurring disease, these environmental systems are single purpose with the primary focus being early warning of bioterrorism.

One of the more effective preparedness planning tools are tabletop and field exercises, with involvement of representatives from key local, state, and federal agencies, as well as representatives from the local medical and laboratory communities.

These exercises provide the opportunity to test assumptions in existing plans, and work out issues related to decision-making authority and respective roles and responsibilities among the various disciplines that would be involved in responding to a bioterrorist attack or other local emergency. Post exercise debriefings should be conducted to highlight gaps in preparedness that can then be addressed through follow-up planning meetings and revision of written plans, if indicated, and re-evaluated with repeat exercises.

18.3 Response to Public Health Emergencies

Depending upon the size and scope, responses to public health emergencies may involve resources and responsibilities that span multiple agencies at the local (city or county), state, and federal government levels. Emergency events begin at the community level (single or multiple communities) and local personnel and resources (medical, public health, emergency services, police, fire, etc.) provide the initial response. If local resources are overwhelmed or authorities require special assistance or resources that are not locally available, assistance from the state or federal level can be requested. This may be done through a direct assistance request to an agency or agencies (e.g. a request to CDC to assist with a food outbreak investigation or test samples) or through the formal declaration of an emergency that activates state and federal emergency support functions (e.g. declaration of state of emergency that activates the Federal Emergency Management Agency (FEMA) and other federal assistance as needed through the National Response Framework (NRF) and the associated Emergency Support Functions (ESF)). Emergency responses and their coordination in the US primarily involve civilian agencies and authorities, with the military providing support as needed.

Central to the ability to successfully coordinate a response to a large-scale emergency is the ability to integrate information flow, resources, and personnel into an organizational structure that is similar across all responding agencies, whether the emergency is primarily public health in nature or due to some other cause. This Incident Management System or Incident Command System (ICS) structure, has been used for many years by traditional first responder agencies such as fire and law enforcement and was formally identified as the national emergency response structure in 2003 [24]. ICS has also been adopted and used to a much greater extent by federal, state, and local public health agencies responding to public health emergencies. CDC utilized the ICS to coordinate its response to public health emergencies such as the 2009 H1N1 pandemic and multi-state foodborne outbreaks but has also benefited from better integration of its response activities into larger-scale, multi-hazard emergency responses such as Hurricane Katrina and the recent Haiti earthquake.

The US Department of Health and Human Services (DHHS) has the lead for coordinating the federal public health and medical services support functions outlined in ESF 8 (http://www.fema.gov/pdf/emergency/nrf/nrf-esf-08.pdf).

These support functions include response activities in the following areas: (1) assessment of public health/medical needs, (2) health surveillance, (3) medical care personnel, (4) health/medical/veterinary equipment and supplies, (5) patient evacuation, (6) patient care, (7) safety and security of drugs, biologics, and medical devices, (8) blood and blood products, (9) food safety and security, (10) agriculture safety and security, (11) all-hazard public health and medical consultation, technical assistance, and support, (12) behavioral health care, (13) public health and medical information, (14) vector control, (15) potable water/wastewater and solid waste disposal, (16) mass fatality management, victim identification, and decontaminating remains, and (17) veterinary medical support. Several agencies exist within DHHS that help carry out these activities, including CDC, the Food and Drug Administration (FDA), the National Institutes for Health (NIH), and the Substance Abuse and Mental Health Services Administration (SAMHSA) among others. In addition, DHHS manages the National Disaster Medical System (NDMS) which includes disaster medical, surgical, and mortuary response teams as well as veterinary response teams. In addition to providing medical response to a disaster area, NDMS also coordinates patient movement into hospital care in unaffected areas for definitive medical care with the support of the Department of Defense (DoD). In addition to DoD, multiple other agencies and departments provide support to DHHS for ESF8 functions, including the Department of Agriculture (DoA), DHS, FEMA, the Department of Transportation (DoT), the Department of Veterans Affairs (VA), the American Red Cross (ARC), and others.

Once a bioterrorist event is recognized and then confirmed by laboratory testing, there will be a need for large-scale mobilization of surveillance and epidemiologic investigations. The focus of these investigations will be (1) tracking the number of cases to define the scope of the incident and (2) performing epidemiologic investigations to determine the common source(s) and site(s) of exposure. This information will be most critical in the event of a covert bioterrorist event to determine where and when the attack occurred, and who else may have been potentially exposed (either at the event or due to downwind distribution of the aerosol) and thus require prophylaxis. As active surveillance would need to be initiated rapidly once a bioterrorist event is recognized, many local and state health departments have developed materials and plans to facilitate the ability to rapidly implement an investigation, including template surveillance instruments and protocols for urgently mobilizing and deploying active surveillance surge teams to hospitals in the affected area.

Response to public health emergencies that result from an intentional biothreat agent, such as the 2001 US anthrax letter attacks, have an added investigational and coordination complexity due to the necessary law enforcement component of the event [2]. If an event is known to be secondary to an intentional act, local law enforcement officials and the Federal Bureau of Investigation (FBI) have a greater leadership role in coordinating the investigation and communication, however, public health and other responding entities are still responsible for carrying out their usual surveillance and emergency response activities. In this scenario, activities such as interviewing victims to determine the common site and/or sources of exposure,

specimen or sample collection and testing, and public messaging would be coordinated with the FBI or other law enforcement officials in order to preserve evidence and investigative information that may be essential for attribution and conviction of the perpetrators. Some activities such as sample collection or victim interviews may even need to be planned and conducted jointly by public health and law enforcement officials. Although law enforcement has the responsibility for conducting the criminal investigation, their primary mission is also the preservation of life and health and investigative activities are targeted towards accomplishing that goal in addition to obtaining the evidence needed to identify and convict those responsible. Many local, state, and federal public health and law enforcement authorities in the US have recognized the investigation and communication coordination that would be required in a bioterrorism or other intentional chemical, radiological, or toxin induced event that affects the health of individuals or communities and have established working relationships for preparedness as well as formalized agreements for information sharing and joint investigative activities in this type of event. A model for a Memorandum of Understanding (MOU) that can be used to create formalized working agreements between public health and law enforcement officials was developed by a working group convened by the CDC and the US Department of Justice. This model MOU has been distributed to state and local authorities and a copy can be requested through the CDC Public Health Law Practice website at http://www2a.cdc.gov/phlp/mounote.asp.

18.4 Summary

The United States considers bioterrorism a serious threat to its national security and has made concerted efforts over the last decade to bolster public health and other response capacity capabilities. Many of these efforts, though initially begun to address the needs for bioterrorism preparedness, have proven beneficial for public health in responding to other emergencies, including those due to naturally occurring disease threats such as pandemic influenza. Specifically, efforts that focused on improving: (1) laboratory diagnostic capacity, (2) surveillance data sources, analysis, and reporting, (3) risk communication (4) emergency response planning and training, and (5) overall response coordination have proven extremely beneficial for supporting public health responses to all types of health threats. In most state and local health departments in the US, bioterrorism surveillance and response capacity is fully integrated into the general infectious disease and all hazards emergency response infrastructure. The same staff that surveil for and respond to both routine and emergency infectious disease outbreaks would be called upon to respond to a bioterrorism attack. This dual-use capacity is more efficient and ensures that front line public health staff maintain and exercise the skills required to detect and respond to disease threats, regardless of whether intentional or natural. The 2009 H1N1 pandemic provided one of the best training opportunities for what might be encountered in the event of a large scale bioterrorist outbreak, including the need to implement

enhanced surveillance to provide greater real time situational awareness, with the initial reliance on the public health laboratory system for reference testing, and the implementation of a large scale vaccination campaign. Although bioterrorism is not accorded the same level of concern everywhere, investments that help build or support stronger public health and medical systems provide the foundation for responding to all health threats and are essential, should an unthinkable event such as a large-scale bioterrorism attack occur.

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