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CHAPTER 7

Case Studies

What's true of all the evils in the world is true of plague as well. It helps men to rise above themselves.

Albert Camus, The Plague (1947)

Objectives

The study of this chapter will enable you to:

- 1. Analyze biological events, natural, accidental, and intentional, with an eye toward understanding the challenges of detection and subsequent containment and mitigation efforts.
- 2. Discuss the significance of the six case studies presented in this chapter.
- 3. Identify opportunities and challenges in detecting an emerging disease.
- **4.** Compare the differences in disease transmission from natural, accidental, and intentional biological events.
- 5. Compare the economic and societal impact from natural, accidental, and intentional biological events.

INTRODUCTION

The six case studies presented within this chapter should be viewed as drawing attention to weaknesses in a system of detection first, followed perhaps by issues in containment and mitigation as a result. In looking at these events from a system perspective, we should be aware that the point at which a system fails is often a weakness due to failure in other parts of the system. A *system* is defined as "a dynamic order of parts and processes standing in mutual interaction with each other" (von Bertallanfy, 1968). Therefore it is necessary for all professionals reading this text to examine all of the parts and processes, especially the interactions among the parts.

The manner in which the case studies are presented in this chapter runs the risk of being categorized as anecdotal and, as such, dismissed by some purists. It is not practical for us to completely recreate or chronicle the accounts for the case studies presented here, and more elaborate and definitive references are easily retrieved from open sources. As such, references and websites are provided at the end of the chapter to allow additional, in-depth exploration of the described events. Early detection of biologic events requires an innate ability to make sense of seemingly subtle and random events, often lacking scientific explanation. The practice of medicine is an example of the need to combine science, experience, and instinct in the development of a plan of action. Rarely do patients themselves progress in clinical presentation and disease etiology as the pages in a textbook might suggest. In 1973, Sacks wrote that

We need, in addition to conventional medicine, a medicine of a far profounder sort, based on the profoundest understanding of the organism and of the life. Empirical science is the key to one form of knowledge, the generalized knowledge that gives us power over nature; the key to wisdom however, is the knowledge of particulars.

We anticipate that the reader will filter and interpret this material within the context of his or her chosen vocation. Applying some of these lessons may allow future generations, regardless of their particular vocational path, to detect early on the emergence of a biologic event and conceivably achieve improved outcomes. Herd health and wellbeing may take precedence over individual rights and outcomes. No doubt this is a hard pill for some to swallow. However, improved outcomes portend a decrease in morbidity and mortality, minimization of social or economic impact, or perhaps even decreased international interest.

ANTHRAX, SVERDLOVSK, SOVIET UNION, 1979: ACCIDENTAL RELEASE OF WEAPONIZED MATERIAL

In April 1979 an unusual epidemic of anthrax occurred in Sverdlovsk, a city of 1.4 million people 140 km east of Moscow in the former Soviet Union (Meselson et al., 1994). Shortly after the cases emerged, Soviet officials explained that the source of the outbreak was related to the ingestion of contaminated meat. According to their report, contaminated animals and meat from an anthrax epizootic south of Sverdlovsk caused 96 cases of human anthrax (Meselson, 1988). Of these cases, 17 were cutaneous anthrax and 79 were gastrointestinal anthrax. Of the 96 cases, 64 of the gastrointestinal anthrax cases were fatal. At the time, there was great debate among officials from other nations as they tried to determine if the outbreak may have actually been due to covert Soviet bioweapons production.

The following report comes from a recently declassified Defense Intelligence Agency's *Intelligence Information Report* dated March 21, 1980:

A fourth source reports in late April 1979, the population was awakened by a large explosion that was attributed to a jet aircraft. Four days later, seven or eight persons from the military installation were admitted to hospital number 20 in the suburbs where the military installation is located. Their symptoms were high fever (104°), blue ears and lips, choking, and difficulty breathing. They died within 6–7 h, and autopsies revealed severe pulmonary edema plus symptoms of a serious

toxemia. About 6 days after the illness first appeared, the source and other doctors from various hospitals were called together by the district epidemiologist. The number of fatalities had risen sharply, and the source estimated deaths by this time at 40. The epidemiologist announced the outbreak of an anthrax epidemic and gave a lecture on the disease. He claimed the epidemic was caused by an illegally slaughtered cow suffering from anthrax in a town about 10 km northeast of Sverdlovsk. He said the beef had been sold in the suburb where the fatalities were occurring. This explanation was not accepted by the doctors in attendance because the fatalities were caused by pulmonary anthrax as opposed to gastric or skin anthrax, which would be more likely if anthrax-contaminated beef were eaten or handled.

As more reports emerged, US intelligence reviewed satellite imagery and signal intercepts from the spring of 1979 and found corroborative signs of a serious accident. This included roadblocks and decontamination trucks around what was then known as Compound 19, a military installation in Sverdlovsk. In addition, officials learned that the Soviet defense minister had visited the city shortly after the incident. The anthrax explanation also seemed plausible given the long-standing history of Soviet efforts to mass produce *Bacillus anthracis* into a biological weapon (Wampler and Blanton, 2001).

US intelligence agency officials believed that the incident had to be due to inhalation of spores that were released from a secret bioweapons plant in the city. Victims presented with severe respiratory distress and died within a few days of the onset of symptoms. This belief came from epidemiological data showing that most victims lived or worked in a narrow zone extending from the bioproduction facility to the southern city limit. Furthermore, livestock downwind from the point of release died of anthrax along the same zone's extended axis. The zone paralleled the northerly wind that prevailed shortly before the outbreak (Meselson et al., 1994). Other scientists harbored doubts about the official US accusation, noting that an accidental release of anthrax spores could have been in connection with a defensive biological warfare research program, which was allowed under the 1972 convention. It was later concluded that the escape of an aerosol of anthrax pathogen at the military facility caused the outbreak.

The reports of a possible anthrax outbreak in Sverdlovsk, linked to an incident at a suspected Soviet biological warfare facility, served to further deepen already worsening US-Soviet relations, which were heading back toward a new Cold War in the wake of the Soviet invasion of Afghanistan. In the 1980s during the Reagan administration, Sverdlovsk would become one of the major points in the US indictment of the Soviet Union to build the case that the Soviets were violating the ban on the use of biological weapons imposed by the 1972 Biological Warfare Convention, which both the United States and the Soviet Union had signed. Despite the proof that Western scientists had, the Soviets (see Fig. 7.1) refused to discuss the incident and maintained their position that they did not have a program in bioweapons



Figure 7.1 This symbol of Soviet victory bears two stars, the hammer and the sickle. *Courtesy of the Centers for Disease Control and Prevention*.

development and production. In fact, the strain of anthrax produced in Military Compound 19 near Sverdlovsk was believed by experts to be the most powerful in the Soviet arsenal ("Anthrax 836").

Critical Thinking

Could there be legitimate national security reasons for not disclosing the source of such an outbreak? If there are reasons, what are the potential ramifications for recognition, containment, and mitigation of the danger from the organism?

The final breakthrough did not come until after the Soviet Union had ceased to exist, at the end of 1991, and Boris Yeltsin came to power as the new head of the Russian government. Yeltsin had a personal connection to the Sverdlovsk issue because he had been Communist Party chief in the region at the time of the anthrax outbreak, and he believed the KGB and military had lied to him about the true explanation. At a summit meeting with President George H. W. Bush in February 1992, Yeltsin told Bush that he agreed with US accusations regarding Soviet violation of the 1972 Biological Weapons Convention and that the Sverdlovsk incident was the result of an accident at a Soviet biological warfare installation, and he promised to clean up this problem. In a May 27 interview Yeltsin publicly revealed what he had told Bush in private:

We have now circumscribed the time of common exposure to anthrax. The number of red dots we can plot on our spot map places nearly all of the victims within a narrow plume that stretches southeast from Compound 19 to the neighborhood past the ceramics factory... we have clarified the relation of the timing of animal and human deaths and believe the exposure for both was

nearly simultaneous. All the data—from interviews, documents, lists, autopsies, and wind reports—now fit, like pieces of a puzzle. What we know proves a lethal plume of anthrax came from Compound 19.

Wampler and Blanton (2001)

The Sverdlovsk incident represents one of the leading examples of how an unknowing population can be affected by the release of formulated biological agents. It seems pretty clear at this point that the release was accidental. However, questions remain unanswered as to exactly how much *B. anthracis* was released, how far down range did it travel, and how many people were affected by the release.

SALMONELLOSIS AND THE RAJNEESH, THE DALLES, OREGON, UNITED STATES, 1984: INTENTIONAL FOODBORNE OUTBREAK

On September 9, 1984, a man was admitted to the county's only hospital complaining of intense stomach cramps, nausea, and high fever. Two friends were also ill. All three had eaten at a local restaurant earlier that day. In the following week, 13 employees and dozens of customers of the restaurant became violently ill. Many called and threatened to sue.

Within 48 h after the first patient presented to medical professionals, a pathologist at Mid-Columbia Medical Center had determined the cause was food poisoning from *Salmonella* bacteria. However, it was a full week before the first complaint of this foodborne outbreak was reported to the county health department. By September 21, reports of new cases had subsided; the state laboratory had identified the strain of *Salmonella* used. That is when the second wave struck. Two days later every bed in the local hospital was filled with *Salmonella* victims. Almost one-third of the town's restaurants were implicated (10 in all). This was enough to basically shut down the economy of The Dalles; many of these restaurants would close forever.

On September 25 the local health department called in assistance from the Centers for Disease Control (CDC). By the time the first CDC officers began to arrive, the county health department had already confirmed 60 cases of *Salmonella enterica* serotype *Typhimurium* from the outbreak. They had also found the main epidemiologic connection: most of the sick people had eaten from salad bars. By the time the CDC arrived in force the county health department had already done the main work involved in stopping the outbreak.

Key Activities in The Dalles Outbreak

- The local public health office began immediately tracking patients through passive surveillance. Three-day food histories were completed for each patient. These interviews quickly showed that most of the ill people had eaten at a salad bar at one of the affected restaurants. Restaurants were asked to close their salad bars; all 38 restaurants in the county immediately complied.
- Colleagues were interviewing and inspecting restaurants in the county. However, they found nothing that would indicate how 10 restaurants had created a single outbreak using the exact same pathogen.

- They found that the 10 affected restaurants used several distinct suppliers, and no supplier served more than 4 restaurants. In addition, the epidemiologic investigation found that various foods were risk factors at various times. The first wave of illness centered on items such as potato salad; the second wave on blue cheese dressing. No major violations were found in the distributors or suppliers.
- Samples were taken from both water systems that served the area restaurants, from the restaurants themselves and at the municipal level. These samples were negative for any form of bacteria, and all had acceptable color and chlorine levels.

Despite the suspicions of the community and the lack of any other explanation, an epidemiologic investigation failed to demonstrate that the outbreak was deliberately caused. The state did not want to be considered backward or insensitive to the Rajneeshees, and the investigation may have been influenced by such political pressure and would hold to a theory of multiple coincidental cross-contaminations throughout the county.

Critical Thinking

The Rajneeshees incident occurred in 1984. However, had this event occurred after the 2001 anthrax attacks, do you think investigators would be so quick to discount an intentional attack? Many years have passed since the 2001 attacks; do you think our vigilance has a shelf life?

In all, 751 cases of salmonellosis were confirmed from more than 1000 patients; approximately 12% of the community became ill. Although the illness struck simultaneously in 10 restaurants dispersed throughout the county, the state health department's epidemiologic investigation concluded that the outbreak was caused by unsanitary hand-washing practices at the restaurants involved. An initial criminal investigation agreed with the health department's conclusion. One year later a representative of the Bhagwan Shree Rajneesh sect, which had a ranch in the county, announced that members of that sect had poisoned local salad bars with *Salmonella* bacteria in a test run for a plan to influence local election results in the sect's favor (Fig. 7.2). A subsequent criminal investigation found that the sect had ordered the exact strain of *Salmonella* used by mail from a licensed commercial laboratory company.

When the CDC analyzed the data, things looked much different. Employees generally had symptoms at the same time as customers, and the strain of *Salmonella* encountered was not at all the same as any other area cases in recent years. The outbreak occurred in two distinct waves that flew in the face of a single-exposure event. In this case the initial state health report denied local law enforcement the probable cause they needed to open an investigation.

Even in the face of strong evidence suggesting a deliberate attack, investigators initially discounted this theory, giving several reasons why they reached this conclusion.

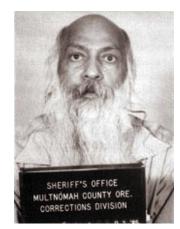


Figure 7.2 Bhagwan Shree Rajneesh, the leader of the Rajneeshie cult whose followers perpetrated the largest act of bioterrorism in the United States in Oregon in 1984. *Courtesy of the Oregon Department of Corrections.*

Among the reasons were these: there was no apparent motive, no one claimed responsibility, and nothing like this had ever occurred before. These points reinforce the need to maintain a high index of suspicion and follow epidemiological clues to reach a plausible explanation of any unusual outbreak. Early involvement of law enforcement personnel may enable investigators to remain subjective in their determination and cognizance of evidentiary matters should a reasonable index of suspicion be warranted.

Had investigators used more aggressive surveillance techniques to gather more information (ie, surveying doctor's offices for symptomatic persons), they may have received additional information for the investigation and might have produced enough evidence to change the investigator's position on whether the outbreak was accidental or intentional. Accounts from community members support the position that numerous patients did not report to the medical community and chose to stay home and treat themselves (personal communication, J. Glarum).

PNEUMONIC PLAGUE, SURAT, INDIA, 1994: NATURAL OUTBREAK

The population of Surat, in the western state of Gujarat, boomed shortly after World War II. Surat's population grew from 237,000 to approximately 1.5 million residents. The city divided into two parts, the "old city," or city center, remained the most heavily populated area, accounting for 77% of the total population. The newer settled, outer portions of the city were characterized by their universal lack of planning. Incorporating a mix of industry and lower class residences, these areas were largely devoid of proper sewage facilities and only 60% of total daily garbage produced was regularly collected (Shah, 1997). Less than half of the city had access to treated drinking water. The unhygienic conditions and

poor working conditions within Surat were commonly identified by public health officials as the causes for regular epidemic outbreaks within the city of malaria, gastroenteritis, pneumonia, and diarrhea.

In September 1993 an earthquake occurred, which killed an estimated 20,000 people, and because of the poverty of the area, many of the dead were not properly buried. Floods in August 1994 created an unbelievable mix of human waste, refuse, and human and animal remains left behind. These events, in addition to the poor refuse disposal and sewer services, created an abundant food supply for rats and other vermin. Some reports point to a possible precursor event, which involved the die-off of rats in Mamala village to such an extent that they were "falling off rafters, dead, in great numbers" (John, 1994). By mid-September, despite the available epidemiological clues, 10% of the village population was ill with bubonic plague.

The Indian government initially appeared unable or unwilling to mitigate the spread of the disease created by a series of events in and outside of the country. Poor crisis communication regarding the outbreak caused the population to take measures to keep themselves safe in the areas affected and chose to leave, potentially carrying disease with them to unaffected areas. Contact tracing was not initially accomplished, once more leading to spread of disease. Once the disease became obvious and there was little being done by the government to contain it, panic ensued and more people fled, carrying the disease. It has been estimated that 25% of the 1.5 million people fled the area.

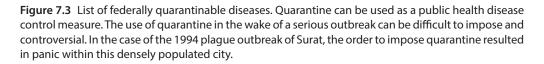
A **cordon sanitaire** (a French term that translates to "sanitary cord." It is used to denote an extreme use of quarantine in which public health authorities implement large-scale quarantine measures to contain the spread of disease. In this case, a small section of the city would have been under quarantine order. As one might imagine, this would be difficult to implement and enforce) may have proven useful in plague containment; however, it would have affected India's diamond-cutting and silk-production center in the area of the slums. Sealing off this area from the rest of the city would have prevented workers getting to the factory, cutting off their income, as well as slowing production (see Fig. 7.3). In addition, the encroachment of the holiday season with the associated visitors and large conferences with international guests drawing thousands of international tourists were planned, and tourism is one of India's major financial businesses. This is a similar situation to China's dilemma on dealing with the outbreak of severe acute respiratory syndrome.

Several countries put restrictions on travelers from India, with Moscow imposing a 6-day quarantine for all visitors from India and banning all travel to the country. Estimates for business losses for the city of Surat alone were over \$260 million. It has been estimated that India lost more than \$1 billion in export earnings and 40–60% of its anticipated tourism (Steinberg, 1995). Several million people lost income when they were unable to work, locally or internationally; many more millions suffered panic, fear,

Federal isolation and quarantine are authorized for these communicable diseases:

- Cholera
- Diphtheria
- Infectious tuberculosis
- Plague
- Smallpox
- Yellow fever
- Viral hemorrhagic fevers
- Severe acute respiratory syndromes
- Flu that can cause a pandemic

Federal isolation and quarantine are authorized by Executive Order of the President. The President can revise this list by Executive Order.



or dislocation. Thousands of squatters had their dwellings inspected and condemned. As a nation, India found its modernity, its efficiency, its health administration, and its local governance called into question. Locally, agricultural exporters saw their share prices tumble as some foreign countries not only refused Indian exports but closed their borders. The United Arab Emirates was reported to have cut off postal links with India out of fear that the plague would spread via mail.

Given the economic upheaval, it is interesting to note that approximately 900 people fell ill, with the total death toll only 56. This is the point: fear and panic due to poor risk communication and appropriate containment measures caused the bigger problems for the financial markets and economy than the actual disease. Control of this disease outbreak would have had to include selective quarantine, contact tracing, treatment, and prophylaxis as well as elimination of potential vectors and animal hosts.

In hindsight, investigators identified a 35-year-old man on September 12 as the first case. He had been admitted to a hospital 4 days earlier with respiratory symptoms and fever (Shah, 1997). Over the next week or so, through September 20, approximately 15

individuals were admitted to various hospitals, mostly to be diagnosed with and treated for malaria. Not until September 21 did the presumption of plague surface. Public health authorities were alerted, word began to spread through the medical community, and the one hospital was designated for new suspected plague admissions. Shops began closing in the most heavily affected region of the city, medical practitioners began to leave the city, and local pharmacies sold out of available tetracycline. Hospital admissions continued to grow and public health authorities were barely able to locate sufficient antibiotics to treat the ill and their care providers. Within 3 weeks the case-fatality rate had dropped from 80% to below 10%. Until adequate government supplies of tetracycline begin to arrive, approximately 30% of Surat's population fled, businesses closed, and public facilities (schools, swimming pools) shut down. By the end of September, adequate supplies, plans, and personnel had the epidemic under control (Shah, 1997).

Modern public health and medicine are capable of intervening effectively in outbreaks of bacterial diseases, such as plague, through combinations of medical screening, immunization, antibiotic treatment, and supportive care. Even in the absence of effective medical intervention, proper behavior, such as contact avoidance, can profoundly alter the disease progression cycle. If any measure is overlooked or botched in its implementation, it is easy to see how containment can be slow or nonexistent.

AMERITHRAX, UNITED STATES, 2001: INTENTIONAL RELEASE OF A FORMULATED AGENT

In late September 2001 an avid outdoorsman whose pastimes were gardening and fishing left for a short vacation in North Carolina. His job as a photo editor required that most of his work time was spent reviewing photographs submitted by mail or over the Internet, so no doubt he looked forward to this trip. Soon after arriving in North Carolina, the first symptoms of illness developed; these included muscle aches, nausea, and fever. The symptoms waxed and waned for the duration of the three-day trip.

The day after he returned home he was taken to the hospital for medical evaluation at the emergency department of a Florida medical center after he awoke from sleep with fever, emesis, and confusion. Because he was disoriented at the time of his presentation at the hospital, he was unable to provide further relevant information. Treatment with intravenous cefotaxime and vancomycin was initiated for presumed bacterial meningitis while the patient awaited a lumbar puncture (Malecki et al., 2001).

On physical examination he was found to be lethargic and disoriented. His temperature was 39°C (102.5°F), blood pressure was 150/80 mmHg, pulse was 110, and respirations were 18. No respiratory distress was noted; his arterial hemoglobin saturation, as indicated by pulse oximetry while he was breathing ambient air, was 97%. Examination of the ear, nose, and throat detected no discharge or signs of inflammation. Chest examination revealed rhonchi without rales (Bush et al., 2001).

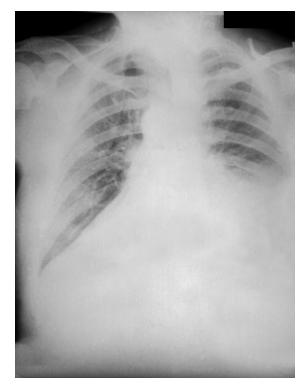


Figure 7.4 Typical chest X-ray from a case patient with inhalation anthrax. This aspect shows a widened mediastinum (lower separation seen on film between lobes of the lungs) and pleural effusion (opaque area below right). *Courtesy of the Centers for Disease Control and Prevention*.

The initial chest radiograph was interpreted as showing basilar infiltrates and a widened mediastinum (see Fig. 7.4). The results of a computed tomography scan of the head were normal. A spinal tap was performed under fluoroscopic guidance within hours after presentation at the hospital and yielded cloudy cerebrospinal fluid.

The patient was admitted to the hospital with a diagnosis of meningitis. After a single dose of cefotaxime (a broad-spectrum cephalosporin) he was started on multiple antibiotics. A short time later he had generalized seizures and was intubated for airway protection. The next day a new array of antibiotics was initiated, replacing those previously prescribed. He remained febrile and became unresponsive to deep stimuli. His condition progressively deteriorated, with hypotension and worsening kidney function. The patient died on October 5. Autopsy findings included hemorrhagic inflammation of lymph nodes in the chest as well as disseminated *B. anthracis* in multiple organs (Bush et al., 2001).

Gram staining of cerebrospinal fluid revealed many polymorphonuclear white cells and many large gram-positive bacilli, both singly and in chains. On the basis of the cerebrospinal fluid appearance, a diagnosis of anthrax was considered, and high-dose intravenous penicillin G was added to the antibiotic regimen. Within 6 h after plating on sheep blood agar the cultures of cerebrospinal fluid yielded colonies of gram-positive bacilli.

The clinical laboratory of the medical center presumptively identified the organism as *B. anthracis* within 18 h after plating; this identification was confirmed by the Florida Department of Health laboratory on the following day. It was evident that making a diagnosis of anthrax would have serious ramifications. Although the case was reported to local public health authorities when anthrax was first suspected, final laboratory confirmation of the diagnosis was awaited before a public announcement was made.

Extensive environmental samples from the patient's home and travel destinations were negative for anthrax. Moreover, the finding of *B. anthracis* in regional and local postal centers that served the work site implicates one or more mailed letters or packages as the probable source of exposure (see Fig. 7.5). Coworkers report that the patient had closely examined a suspicious letter containing powder on September 19, approximately 8 days before the onset of illness. This index case highlights the importance of physicians'

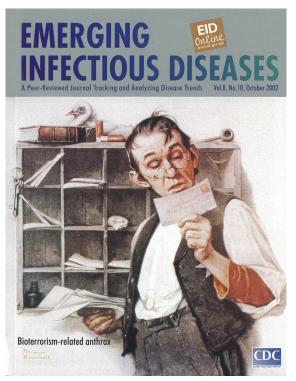


Figure 7.5 Cover of the October 2002 Centers for Disease Control publication *Emerging Infectious Diseases*. It portrays the national sentiment at the time that something as seemingly benign as getting a letter in the mail is potentially life threatening. *Courtesy of the Centers for Disease Control and Prevention*.

ability to recognize potential cases in the identification and treatment of diseases associated with biologic terrorism.

Critical Thinking

On the basis of your knowledge of inhalation anthrax, how does the clinical presentation from the index case measure up with the incubation period and final outcome?

In summary, officials believe that there were a total of five letters mailed, four of which were recovered. There were two known mailing dates, September 18 and October 9, 2001. The letter to the AMI building in Florida (see Fig. 7.5), where the index case originated, was not recovered. The September 18 letters went to the offices of NBC Studios and the *New York Post* in New York City. The October 9 letters were mailed to Senators Daschle and Leahy of the US Senate. The amount of formulated anthrax spores in these letters was estimated to be 1–2g. The letter to Senator Leahy (which was unopened at the time it was discovered) contained approximately 2g of highly weaponized anthrax spores.

Outbreaks of the disease were concentrated in six locations: Florida; New York; New Jersey; Capitol Hill in Washington, DC; the Washington, DC regional area, including Maryland and Virginia; and Connecticut. The anthrax incidents caused illness in 22 people: 11 with the cutaneous (skin) form of the disease and 11 with the inhalational (respiratory) form, 5 of who died. Demands on public health resources reached far beyond the six outbreaks of disease. Once officials realized that mail processed at contaminated postal facilities could be cross-contaminated and end up anywhere in the country, residents brought samples of suspicious powders to officials for testing and worried about the safety of their daily mail.

In dealing with this crisis, there were deficiencies in the local public health response and the federal government's ability to manage it. Public health officials did not fully appreciate the extent of communication, coordination, and cooperation needed among responders. There were difficulties in reaching clinicians to provide them with guidance. The Federal Bureau of Investigation (FBI) reached a conclusion in 2008 that the sole perpetrator was Dr. Bruce Ivins, an Army biodefense research scientist assigned to the US Army Research Institute of Infectious Diseases, Fort Detrick, MD. The conclusion of the FBI's investigation has been viewed by some experts as being technically flawed; therefore it is controversial.

RICIN AND THE AMATEUR BIOTERRORIST, UNITED STATES, 2003 AND 2004: INTENTIONAL RELEASE

In October 2003 a suspicious letter addressed to the US Department of Transportation was intercepted by US Postal Inspectors. Upon examination of the letter's contents postal inspectors recovered a warning: a metal vial containing ricin and a note threatening more attacks if laws restricting the activities of commercial truck drivers were not amended (see Fig. 7.6).

SPECIAL REWARD up to \$120,000

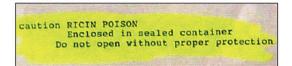
A reward of up to \$120,000 is being offered by the U.S. Postal Inspection Service, Federal Bureau of Investigation, and U.S. Department of Transportation-Office of Inspector General for information leading to the arrest and conviction of the person(s) responsible for mailing letters containing the poison ricin and ricin derivative. The vial pictured below was accompanied by a threatening letter addressed to the U.S. Department of Transportation and was discovered at the Greenville, SC, Post Office on October 15, 2003.

The person(s) responsible for these threats may be connected to the trucking or transportation industry, but you should report any potential leads.

Metal vial:



Typewritten on the exterior of the envelope was the following warning:



The following is a representation of the language contained in the threat letter.

to the department of transportation: I'm a fleet owner of a tanker company.

I have easy access to castor pulp. If my demand is dismissed I'm capable of making Ricin.

My demand is simple, January 4 2004 starts the new hours of service for trucks which include a ridiculous ten hours in the sleeper berth. Keep at eight or I will start dumping.

You have been warned this is the only letter that will be sent by me.

Fallen Angel

Public health information regarding ricin can be found at the Centers for Disease Control and Prevention Web site (www.cdc.gov)



Figure 7.6 Poster announcing a reward for anyone who might be able to provide information that would lead to the arrest of the person(s) responsible for the Fallen Angel ricin incident that occurred in October 2003. *Courtesy of the US Department of Justice*.

In February 2004 ricin was discovered in Senator William Frist's office in the Dirksen Office Building. After the toxin was discovered in a letter-opening machine in the senator's office, federal investigators examined some 20,000 pieces of mail, hoping to find the source of the ricin, but turned up nothing to lead them to a suspect. They were unable to determine whether the ricin had been there for hours, weeks, or even months before it was discovered by an intern in the office.

Conflicting reports on the handling of the response emerged. Some senate employees described the hours after the toxin was found as confused and chaotic. Some employees near Dr. Frist's office went home with no medical screening after the substance was found, and others went about their activities without being advised to seek decontamination.

The authorities said the substance was first seen about 3:00 pm on Monday when a hazardous materials team was dispatched to Dr. Frist's offices in the Dirksen Senate Office Building. After preliminary tests proved negative, an all-clear was given. Such an occurrence is not unusual for congressional offices, which frequently receive suspect mail that turns out to be harmless.

Critical Thinking

What is the risk to overreacting and carrying out containment activities every time a suspect item is discovered at government offices?

When follow-up tests detected the presence of ricin, the Capitol Police returned and began evacuating people to another area of the Dirksen building. By that time, staff members who were present said that many people had left for the day. Those who had been in the vicinity and remained in the building were directed to shower at a decontamination tent erected in a hallway between the Dirksen building and the adjacent Hart Senate Office Building. There they were interviewed by the police and allowed to go home.

Investigators have found nothing to explain how the potentially deadly powder wound up in the offices of the Senate Majority Leader. The investigation focused on a mysterious "Fallen Angel," who threatened to use ricin as a weapon unless new trucking regulations were rolled back. No obvious direct connection between the Frist case and the letters signed by Fallen Angel has been found (see Fig. 7.4). Those letters were discovered in mail facilities that serve the Greenville-Spartanburg International Airport in South Carolina and the White House.

EBOLA VIRUS OUTBREAK, WEST AFRICA, 2014: GEOPOLITICAL IMPLICATIONS

In early 2014 the World was introduced to the largest outbreak of Ebola virus disease (EVD) ever known. According to researchers, the index case for this outbreak came from a 1-year-old boy in the small village of Meliandou (Guéckédou Province), in the West

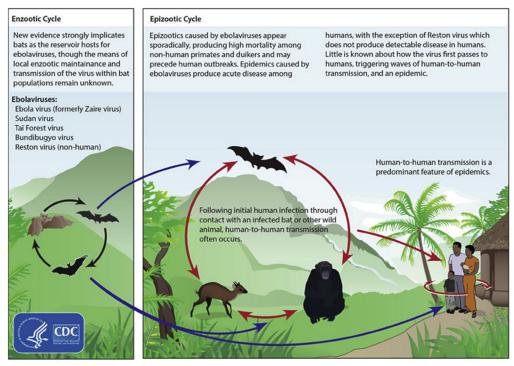


Figure 7.7 The enzootic (natural) and epizootic cycle (or natural history) of the Ebola virus. *Courtesy of the Centers for Disease Control and Prevention.*

African nation of Guinea. The researchers learned that children in Meliandou had been playing near the hollow of a large, dead tree. The tree had a colony of bats. The bats were believed to be infected with Ebola virus (Marí-Saéz et al., 2015). This has relevance because of what is currently believed to be the role of bats in the epizootic transmission cycle of Ebola virus (see Fig. 7.7). We also know that the 1-year-old boy mentioned previously died from a mysterious febrile illness, which spread throughout his family, to other villagers and then outside his village.

On March 23, 2014, the World Health Organization (WHO) was notified of an outbreak of EVD in Guinea. By that time it had spread to neighboring African countries (Liberia, Nigeria, Senegal, and Sierra Leone). Limited public health resources (see Fig. 7.8) and volunteer medical groups worked to quell the quickly spreading epidemic, but they were overwhelmed by the number of patients and patient contacts. It was not until August 8, 2014, that the WHO declared the epidemic to be a public health emergency of international concern (WHO Report, 2014). This begs the obvious question, "Why did it take nearly 5 months to make such a declaration?"

On September 20, 2014, a Liberian national, Thomas Eric Duncan, made his way from Liberia to Houston, Texas. Before getting on the plane in Liberia, Mr. Duncan



Figure 7.8 A sanitation team performs disinfection procedures in a village in West Africa before leaving the site. A strong bleach solution is sprayed on all personal protective gear to neutralize the virus and prevent the team from spreading the virus to themselves and other people. *Courtesy of the Centers for Disease Control and Prevention.*

assisted an ill pregnant woman by helping her out of a taxi and into a hospital. It is believed the woman was an EVD patient, but he was not aware of this. Regardless of what he knew, Mr. Duncan arrived in Houston feeling well with no fever or other symptoms. Six days later Mr. Duncan felt very ill, which prompted him to seek medical attention at a hospital in Houston, Texas. His travel history was not discussed at that time, so he was discharged from the emergency room (ER) with some antibiotics for what was believed to be a routine illness. He went back to the apartment, and a few days later his condition was so severe that he reported to the ER at Texas Health Presbyterian Hospital in Dallas where it became apparent that he was a suspect EVD patient. He was admitted to the intensive care unit and ended up in an isolation ward. His condition worsened and he later died. Unfortunately, infection prevention standards at the hospital were not entirely adequate. This resulted in two nurses (Nina Pham and Amber Vinson) being infected with Ebola virus. They were both treated successfully and fully recovered 2 weeks later.

The media and public reaction to the three cases in the United States (Duncan, Pham, and Vinson) was pronounced. Numerous politicians took a stance on mandatory quarantine procedures at the state and federal level. National and local media providers sought to hold the public's constant attention on the serious nature of "the deadly Ebola virus." It is safe to say that there was fear and some panic because of the politicization and dramatization of this limited outbreak. Meanwhile, state and local officials in Texas had an incident on their hands. Emergency management and public health agencies had to work together to ensure that the apartment where Duncan had been staying did not become the cause of more infections. All of Mr. Duncan's contacts had to be identified,



Figure 7.9 Hazardous materials professionals from the Cleaning Guys, LLC work within the hot and warm zone to decontaminate the apartment where Eric Thomas Duncan resided in Houston, Texas. *Provided by Erick McCallum, Cleaning Guys, LLC*.

placed under strict quarantine, and monitored. After their quarantine period the apartment became a hot zone that required thorough decontamination by a commercial hazmat clean-up group, Cleaning Guys, LLC (refer to Fig. 7.9). None of Mr. Duncan's contacts outside of the hospital became infected and the apartment he resided in and all its contents were rendered safe using technical decontamination procedures.

Critical Thinking

What has the 2014–15 EVD outbreak taught us about a few cases of viral hemorrhagic fever getting into the United States or any other developed country? Consider applying the criteria for Category A agents.

At the time of the preparation of this chapter, the outbreak had not been completely contained. As of August 2015 there have been a total of 15,190 confirmed cases with 11,288 fatalities (WHO Sitrep Ebola Summary; August 28, 2015). Currently, the outbreak is confined to just one country in West Africa: the putative source of the outbreak, Guinea. The fear is that EVD is now endemic in this region, with case numbers fluctuating with the seasons, but always there.

The EVD outbreak in West Africa was unprecedented in its scale and impact. Out of this human catastrophe has come renewed attention to global health security—its definition, meaning, and the practical implications for programs and policy. For example, how does a government begin to strengthen its core public health capacities as demanded by the international health regulations? What counts as a global health security concern? In the context of the governance of global health, including WHO reform, it will be important to distil lessons learned from the Ebola outbreak. *The Lancet* invited a group of respected global health practitioners to reflect on these lessons, to explore the idea of global health security, and to offer suggestions for next steps. Their contributions describe some of the major threats to individual and collective human health as well as the values and recommendations that should be considered to counteract such threats in the future. Many different perspectives are proposed. Their common goal is a more sustainable and resilient society for human health and well-being (Heymann et al., 2015). What will make for an interesting postoutbreak study are the geopolitical implications of a large-scale outbreak of a Category A agent, such as Ebola hemorrhagic fever. Remember that we will always be one simple border crossing or international flight away from the beginning of the next outbreak.

CONCLUSION

The six case studies briefly presented here should provoke the reader to delve more into the particulars of each incident. The Sverdlovsk anthrax incident illustrates the danger posed by bioweapons production. A seemingly simple accident involving the release of a small amount of formulated agent can have a dramatic effect. Imagine if the same thing occurred in the United States or Europe in the information age of which we are all part today. The Rajneeshee incident involving the intentional contamination of food with bacteria was the largest act of bioterrorism to occur in the United States. Acquisition of the agent, the ease of production, and the covert and simple nature of the attack emphasizes the indiscriminate and insidious nature of biological terrorism. Despite the best efforts of many people, it took more than a year and a confession of guilt from the perpetrators to convince officials that the incident was intentional.

The outbreak of pneumonic plague that took place in Surat, India, is a testimony to the importance of fast and decisive action to contain a natural outbreak of a highly contagious and deadly disease. Had this been related to an intentional act there would have been more index cases or victims initially to facilitate widespread disease. This emphasizes the importance of early detection and standard procedures for containment. The Amerithrax incident of 2001 showed us how vulnerable a nation is to a small amount of formulated biological material. Looking back on that time, the events, as they unfolded, seemed surreal. It was hard to believe that we were under attack and no one really knew for some time how widespread it was or when it would end. Many have criticized public officials for how they handled or mishandled the event. However, we believe that public health officials moved quickly to disseminate information and increase the awareness of the public (potential victims) and the vigilance of healthcare providers (alert guardians). Because of numerous evil documents circulated on the Internet, ricin production, possession, and dissemination now fits nicely into the toolbox of every amateur bioterrorist. Keeping things in perspective, ricin, in its crudest forms, is not a formidable threat, but it is deadly if delivered to the potential victim in the right way. Its production, possession, and dissemination are illegal and deserving of a rapid and formidable response. Persons that break these laws should be prosecuted to the fullest extent of the law.

The massive EVD outbreak of 2014 points out just how vulnerable underresourced countries are to hemorrhagic fever viruses. Once the genie is out of the bottle, so to speak, it is hard to put him back in. Lessons learned from this incident will point to the importance of global surveillance and health security. The "international community" will have to act more quickly to resource and assemble the teams of experts needed to quell the next outbreak in its early stages. Once a viral hemorrhagic fever leaves a small village and moves into a large metropolitan area, public health control measures become extremely difficult, if not impossible. Our hope is that EVD does not remain endemic in West Africa. Those countries affected will take years to recover economically from the outbreak.

ESSENTIAL TERMINOLOGY

- **Cluster**. A grouping of health-related events that are related temporally and in proximity. Typically, when clusters are recognized they are reported to public health departments in the local area.
- **Cordon sanitaire**. A French term that translates to "sanitary cord." It is used to denote an extreme use of quarantine in which public health authorities implement large-scale quarantine measures to contain the spread of disease. In this case, a small section of the city would have been under quarantine order. As one might imagine, this would be difficult to implement and enforce in a modern setting.
- **Fornite**. Any inanimate object that can mechanically transmit infectious agents from one host to another.

DISCUSSION QUESTIONS

- Does it seem to matter if an outbreak is derived from a natural, accidental, or intentional event? In what ways are they equivocal? In what ways are they different?
- With reference to the initial response, does it matter whether an outbreak is natural, accidental, or intentional? If yes, how does it matter and to whom? If not, why not?
- Would automated biosensor programs increase, decrease, or have no effect on the vigilance of medical practitioners presented with unusual disease outbreaks?

WEBSITES

The National Security Archive, November 15, 2001. Anthrax at Sverdlovsk. 1979. In:Wampler, Robert A., Blanton, Thomas S. (Eds.), US. Intelligence on the Deadliest Modern Outbreak, National Security Archive Electronic Briefing Book No. 61, vol. 5. Available at: www.gwu.edu/~nsarchiv/NSAEBB/NSAEBB61/ #8#8.

Hoffman, R., Norton, J., November–December 2002. Lessons learned from a full scale bio-terrorism exercise. Emerging Infectious Diseases 6 (6), 652–653. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2640923/pdf/11203432.pdf.

Mavalankar, D., 1995. Indian "plague" epidemic: unanswered questions and key lessons. Journal of the Royal Society of Medicine 88 (10), 547–551. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1295353/pdf/jrsoc-med00065-0007.pdf.

Blanchard, J., Haywood, Y., Stein, B., Tanielian, T., Stoto, M., Lurie, N., 2005. In their own words: lessons learned from those exposed to anthrax. American Journal of Public Health 95 (3), 489–495. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1449207/pdf/0950489.pdf.

World Health Organization. Ebola Virus Disease Outbreak. Available at: http://www.who.int/csr/disease/ebola/en/.

REFERENCES

- Bush, L., Abrams, B., Beall, A., Johnson, C., 2001. Index case of fatal inhalational anthrax due to bioterrorism in the United States. The New England Journal of Medicine 345, 1607–1610.
- von Bertallanfy, L., 1968. General System Theory. Brazillier, New York.
- Defense Intelligence Agency, March 21, 1980. Possible BW Accident Near Sverdlovsk. Intelligence Information Report.
- Heymann, D., Chen, L., Takemi, K., et al., 2015. Global health security: the wider lessons from the west African Ebola virus disease epidemic. Lancet. 385: 1884–1901.
- John, T., 1994. Learning from plague in India. Lancet 344, 972.
- Malecki, J., Wiersma, S., Chill, H., et al., 2001. Update: investigation of bioterrorism-related anthrax and interim guidelines for exposure management and antimicrobial therapy. Morbidity and Mortality Weekly Report 50 (42), 909–919.
- Marí-Saéz, A., Weiss, S., Nowak, K., Lapeyre, V., Zimmermann, F., Düx, A., Leendertz, F.H., 2015. Investigating the zoonotic origin of the West African Ebola epidemic. EMBO Molecular Medicine 7 (1), 17–23.
- Meselson, M., Guillemin, J., Hughes-Jones, M., et al., 1994. The Sverdlovsk anthrax outbreak of 1979. Science 266, 1202–1208.
- Meselson, M., September 1988. The Biological Weapons Convention and the Sverdlovsk Anthrax Outbreak of 1979 Federation of American Scientists Public Interest Report 41. p. 1.
- Sacks, O., 1973. Awakenings. Pan Books, London.
- Shah, G., 1997. Public Health and Urban Development: The Plague in Surat. Sage Publications Pvt. Ltd, New Delhi, India.
- Steinberg, F., 1995. Indian cities after the plague—what next? Trialog 43, 8-9.

- Wampler, R., Blanton, T. (Eds.), 2001. Anthrax at Sverdlovsk, 1979. The National Security Archive, vol. 5. U.S. Intelligence on the Deadliest Modern Outbreak. National Security Archive Electronic Briefing Book No. 61. Available at: http://nsarchive.gwu.edu/NSAEBB/NSAEBB61/.
- World Health Organization. Ebola Sitrep Summary Report. Available at: http://apps.who.int/gho/ data/view.ebola-sitrep.ebola-summary-latest?lang=en (accessed 28.08.15.).
- World Health Organization Ebola Response Team, 2014. Ebola virus disease in West Africa the first 9 months of the epidemic and forward projections. The New England Journal of Medicine 371, 148. Available at: http://www.nejm.org/doi/pdf/10.1056/NEJMoa1411100 (accessed 28.08.15.).