Anthrax: A Possible Case History

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Federal Bureau of Investigation (FBI) offices in five U.S. cities have received warnings of an imminent bioterrorist attack. Each threat indicated that a "shower of anthrax would rain on U.S. cities," unless certain demands were met immediately. One of these calls was in Northeast, a large city on the Eastern Seaboard with a metropolitan population of 2 million. The threats were credible, but no information was relayed to city officials in Northeast or elsewhere.

On the evening of November 1, a professional football game is being played in Northeast's outdoor stadium before an audience of 74,000. The evening sky is overcast, the temperature mild, a breeze blows from west to east. During the first quarter of the game, an unmarked truck drives along an elevated highway a mile upwind of the stadium. As it passes the stadium, the truck releases an aerosol of powdered anthrax over 30 seconds, creating an invisible, odorless anthrax cloud more than a third of a mile in breadth. The wind blows the cloud across the stadium parking lots, into and around the stadium, and onward for miles over the neighboring business and residential districts. After the anthrax release, the truck continues driving and is more than 100 miles away from the city by the time the game is finished. The anthrax release is detected by no one.

Approximately 16,000 of the 74,000 fans are infected by the anthrax cloud; another 4,000 in the business and residential districts downwind of the stadium also are infected. After the game, the fans disperse to their homes in the greater Northeast metropolitan area; some return to homes in neighboring states. A few are from other countries. The driver of the truck and his associates leave the country by plane that night. They will be many time zones away by the time the first symptoms of anthrax appear 2 days later.

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Two days after the game, hundreds of people in and around Northeast become ill with fever, cough, and (in some cases) shortness of breath and chest pain. Some of the sick self-administer over-the-counter cold remedies; some seek phone advice from physicians and nurses; others are seen in clinics, doctors' offices, and emergency departments throughout the city.

Influenza cases had been seen in Northeast 2 weeks before the game. Health-care providers seeing the new patients recommend bed rest and fluids for presumed flu. Specimens are sent to confirm influenza. A few of the sickest patients get chest radiographs to exclude pneumonia. Only in retrospect, after the source of illness is clear, will the widened mediastinum seen on a number of chest radiographs be recognized for the signal it carries. A few patients are hospitalized; some have blood cultures drawn. The 400 ill persons in the region are receiving care from so many different sources that the health emergency is not detected.

By November 4, nurses and physicians note the increased volume of serious upper respiratory illness, and some contact the city health department for treatment recommendations and a regional flu update. Blood cultures from the earliest patients grow gram-positive bacilli in seven laboratories around the city. The laboratories identify these as *Bacillus* species. No further identification is requested, and none is pursued.

By the evening of November 4, patients with the earliest symptoms are dying. The illness has been rapidly fatal, killing previously healthy young adults within 24 to 48 hours. Members of the medical community, now alarmed by these unexpected and unexplained deaths, urgently contact the state and city health departments. Health department officials contact the Centers for Disease Control and Prevention (CDC). By midnight November 4, 1,200 people around the city have fallen ill, 80 of whom have died.

Word that previously healthy persons are dying of a rapidly fatal illness spreads quickly among health-care providers in the state, and is

featured on local and national morning news shows. News media interview families of the deceased, physicians, and city health officials. Expert consultants appear on television to discuss potential diagnoses, including the new Spanish flu, Hong Kong bird flu, and many other infectious and noninfectious diseases. A rapid survey of city emergency departments and health clinics finds that persons of all ages and from all sectors of the city continue to come down with similar illness. The numbers have doubled since the previous day, inundating many health-care facilities.

The mayor convenes an emergency meeting of leading medical experts and health officials as reporters gather outside city hall. The assembled experts debate possible causes and responses to the illness. Many express great concern that a virulent strain of influenza or another highly contagious disease may be present. Isolation of all persons with fever, cough, or chest pain; expanded laboratory analyses; and rapid epidemiologic investigation are recommended. Blood and tissue specimens are sent to CDC for urgent analysis. CDC investigators are en route. During a news conference, the mayor describes the city's response to what appears to be a serious influenza outbreak, appeals for public calm, and is surprised by questions about the possibility of bioterrorism.

By noon November 5, intensive-care units and isolation beds across the city are full. Even patients receiving the most advanced medical care are dying. Patients are febrile, hypotensive, and seem to be in septic shock; some have meningitis. Still, there is no diagnosis. At some locations, the shock of rapid and unexplained deaths has created an atmosphere of desperation and confusion among hospital and clinic staff.

The recommended isolation protocols quickly fall apart as hospital and clinic staffs struggle to cope with the surge of patients. Fears of a contagious disease prompt hospital staff to don protective positive-pressure hoods; the news shows physicians working in this gear and explains that there are only two dozen or so such hoods available per hospital.

In the early evening of November 5, a university laboratory makes a preliminary diagnosis of anthrax from the blood culture of a young patient who died. The laboratory immediately notifies city and state health departments, which in turn notify CDC and FBI. The specimen is transferred to the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), where within hours experts report that rapid diagnostic tests support the preliminary diagnosis of anthrax.

The mayor of Northeast consults with officials from the city and state health departments, CDC, FBI, and USAMRIID. The working assumptions are that the disease in Northeast is anthrax and that it is the result of a bioterrorist attack. Widespread exposure to an anthrax aerosol is feared.

The mayor is outraged to learn that the FBI had not informed her of the credible anthrax threat to Northeast. She is also shocked that it has taken more than 80 deaths and hundreds of illnesses before anyone from the medical community came up with the diagnosis. She is informed that an anthrax vaccine exists, but it is unclear whether any will be made available for civilian use in Northeast. No one can yet estimate the probable scale of the epidemic or whether there has been a single or multiple attacks. CDC is seeking news of similar syndromes in other locations around the country. The mayor's medical advisors recommend that quinolone antibiotics be used for initial treatment of the sick. They also advise the same antibiotics for those exposed to anthrax but not yet sick, even though identifying the exposed will take time and requires more information. All that is known is that many (but not all) of the dying had been at the football game on November 1.

The mayor also is told that to prevent death, antibiotics must be given before symptoms occur, or at the latest, in the earliest hours after symptoms begin. Patients with serious symptoms are likely to die, no matter what anyone does. Available information suggests that the local supply of needed antibiotics will soon be exhausted; many local pharmacies were already emptied of antibiotics as the initial news of a lethal epidemic spread through the city. Given this shortage of antibiotics, one senior advisor asks the mayor to consider a triage plan that uses all available antibiotics to protect the exposed who are not yet sick. In this plan, antibiotics would be kept from those already sick and thus likely to die, regardless of treatment. The mayor requests immediate federal assistance in obtaining and distributing large supplies of antibiotics. Antibiotic shipments from other states are also urgently requested.

State officials notify hospitals around the city of the anthrax epidemic and warn them to prepare for a new surge of patients in the wake of the mayor's forthcoming TV address. Recommendations for the care of infected patients are sent to hospitals and clinics around the region.

The late night news is interrupted by the mayor announcing that anthrax had been released in the city. She outlines the recommended medical response and describes assistance Northeast is seeking from state and federal agencies. She urges that the needed antibiotics be taken by all those attending the football game. For those who attended the game and remain well, arrangements are being made to distribute antibiotics at 20 police stations and schools around the city starting immediately. Antibiotics will be distributed in packages sufficient for a 1-week supply. A second phase of distribution will commence with the arrival of new supplies of antibiotics. Eventually all those exposed will need to receive enough antibiotics to take for 60 days.

Persons feeling ill are instructed to report immediately to hospitals for treatment. The mayor reports that an official request for vaccine has been made to the federal government. She underscores that anthrax is not contagious. She again appeals for calm.

Tens of thousands rush to police stations and distribution centers before the antibiotics arrive. Communication between the distribution centers, the mayor's office, and the antibiotic suppliers is haphazard. No city plan exists or had even been considered for mass distribution of antibiotics. Some centers receive almost no antibiotics. At other centers, antibiotic supplies are rapidly exhausted.

At this point, there are effectively no antibiotics left in the city. Approximately 50,000 persons had obtained some quantity before supplies ran out, but there is no record of who has received them. Health-care facilities are unprepared to cope with the continually rising number of patients. By the early hours of November 6, 2,700 persons have become ill with anthrax, 300 of whom have died. Thousands more flood doctors' offices, clinics, and emergency departments, fearing that they are infected with anthrax.

On the morning of November 6, the mayor announces that schools and homeless shelters will be opened to the ill because hospitals can no longer accommodate new patients. The National Guard will keep order. The Office of Emergency Preparedness, Department of Health and Human Services, and the Federal Emergency Management Agency will provide some logistical support. The city has temporarily run out of antibiotics, but supplies from neighboring states are expected. Meanwhile, the media report that some of the dead were not at the football game and in fact were miles away from the stadium that day. Some reporters openly speculate that "antibiotics are being held back by city officials" and that "local authorities are losing control of the epidemic." They also report that false rumors of arriving antibiotic shipments have sparked mobs and violence at antibiotic distribution centers.

At midday November 6, epidemiologists report that some anthrax patients had not attended the game, suggesting that exposure had occurred over a wider area. In addition, computer models show that wind patterns may have blown anthrax spores downwind of the stadium for some miles. The antibiotic recommendations are now being expanded to include all persons living or working within an area defined by 8 miles east and 1 mile north or south of the stadium on November 1. The mayor is told by her advisors that, in fact, no antibiotic arrivals are imminent. Some states report they have no antibiotics to give, some are refusing to send shipments, and the federal government reports that it will be at least another 6 hours before its antibiotic resources arrive. Despite assurances that anthrax is not contagious, people with the ability to do so flee Northeast, causing traffic jams and increasing panic. Some train conductors, bus drivers, and pilots refuse to travel to Northeast, citing personal safety concerns and threatening to walk off the job if forced. As a result, train, bus, and plane traffic to and from Northeast is sharply disrupted. By midnight November 6, anthrax has sickened 3,200 people, 900 of whom have died.

Federal shipments of antibiotics have begun to arrive by November 7. The distribution centers, now increased to 40, continue to be variably stocked with medicine. A heavy National Guard presence is now evident at distribution centers to prevent violence. FBI officials report preliminary evidence that a truck was the source of the dispersal, though no suspects have been arrested and no group has

claimed responsibility. They confirm that threats of an anthrax attack were made in the week before the event. On televised interviews, families of the deceased promise legal action against the FBI for not revealing the threats, and against local and federal government for not supplying sufficient antibiotics and vaccine. Management of dead bodies becomes a growing crisis. Hospital and city mortuaries are full. Many funeral homes have closed. The state health department and CDC report that the deceased must be cremated. Some citizen and religious groups threaten that if cremation is enforced, there may not be full reporting of the dead, and private burial ceremonies would continue. By nightfall, 4,000 persons have fallen ill, 1,600 of whom have died.

By November 8, increasing numbers of the city's critical work force are absent, including police, firefighters, bus and subway operators, building managers, sewage treatment workers, electricity and water officials, and supermarket staff. Some are absent because of illness or death due to anthrax. Some skip work fearing contagious spread despite official statements to the contrary. Some simply fear violence in the city. Many of those with the means to leave the city do so.

National Guardsmen are able to fill some roles, but many tasks require specialized expertise. As a result, the public transit system is barely operational; some of the city's office buildings are shut down; response time for calls made to fire, police, and ambulance lengthens. Schools and universities are closed. State and city officials become increasingly concerned about an imperiled city infrastructure. Looting erupts.

The mayor holds a press conference to address false allegations that anthrax vaccine is being administered to select individuals in the city. She reports that federal authorities will make available some vaccine for those deemed at highest risk. But due to a national shortage of vaccine and military concerns that this attack may herald further attacks, there is only a highly limited amount of vaccine available. For the most part, the city will have to manage with antibiotics alone.

By evening, a total of 4,800 persons have become ill; 2,400 have died.

Aftermath

Of the 20,000 persons originally infected in Northeast, 4,000 died, most in the first 10 days after the attack. Some anthrax cases occurred in other cities, states, and countries where citizens attending that football game had returned home. Occasional cases occur beyond 10 days among persons refusing or discontinuing the long course of antibiotics. In all, approximately 250,000 persons receive antibiotics.

The media report that hundreds, if not thousands, needlessly died because of delays in antibiotic distribution, and further, that lifesaving antibiotics would have cost $100 per person—a price local and federal authorities had not been willing to pay. Military intervention in the form of martial law is avoided, despite calls by some federal authorities for a "modest military presence to keep peace and stability in a region clearly under attack." No group can be identified as the perpetrator, though FBI continues one of the largest investigations in its history. Many refuse to return to their homes downwind of the stadium and demand official compensation. Businesses downwind of the stadium are shut down. The stadium is largely abandoned. Newspapers brand the downwind area "the dead zone." Overall, city commerce suffers tremendous losses. The tourism industry collapses. City officials estimate it will be months or years before the city resumes a normal routine. Fear of anthrax may keep some away from Northeast indefinitely. On December 1, FBI receives a threat that anthrax will be released in five major U.S. cities over the next week.

This scenario is ominous. Such an epidemic would create extraordinary challenges for a modern American city. However, there is no need to give in to the ending of this story. Practical, modest preparedness efforts could make a difference and change the outcome. Many of the most useful efforts may be the result of ingenuity and depend on collaboration of experts from many disciplines.

Could the outcome have changed if state and local health officials had prior notification of the anthrax threats? Should laboratory practices be changed to increase the chance of early detection of anthrax? Should health-care workers become familiar with the early symptoms and signs of anthrax? What could hospitals do to prepare for epidemics of seriously ill patients? Could communities have plans for rapid mass antibiotic acquisition and distribution? Should anthrax vaccine be more widely available? How might health professionals and government officials

interact with the media to best inform the public and avoid misunderstanding and panic? What should the community, hospitals, and professional societies be doing? What should you be doing?

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