Ten years ago, just weeks after the September 11 attacks, the United States experienced a deliberate act of bioterrorism. Through use of the postal service, anthrax spores were widely disseminated, including to homes, the Senate, and major newsrooms, resulting in morbidity and mortality and effectively disrupting our way of life and revealing our vulnerability. Even though such attacks had been the subject of much writing and had been planned for, detection of and the appropriate response to an attack with an agent from the so-called “Category ‘A’ List” had only been considered in theoretical terms. What transpired during the following difficult weeks, including how public health and federal government agencies performed, has been both praised and criticized. An intertwined epidemiologic and criminal investigation of such magnitude was unprecedented in U.S. history. To address the question of whether we as a nation are now better prepared for future threats involving biologic agents, it is important to learn from the lessons of the 2001 anthrax attacks, including the critical role of clinicians in surveillance. As physicians involved in diagnosing anthrax in the index case and alerting authorities, we offer our perspective on these events a decade after their occurrence.

In the early morning of 2 October 2001, a confused and febrile Robert Stevens walked into the emergency department of JFK Medical Center, Palm Beach County, Florida, shortly after returning home from an automobile vacation trip to North Carolina. Responding to a request for a “stat” infectious diseases consult soon thereafter, Dr. Bush examined a by-then comatose man, interviewed his wife standing at the bedside, and hastened to the laboratory to inspect a Gram-stained sample of his cerebrospinal fluid. After visualization of numerous large, boxcar–shaped, gram-positive bacilli in a background of polymorphonuclear leukocytes (Figure), assurance was requested from the microbiology technologist to ascertain that the Gram stain was not underdecolorized. When it was determined that the bacilli were indeed gram-positive, anthrax was immediately and strongly suspected (1).

The subsequent expeditious identification of Bacillus anthracis in the cerebrospinal fluid began at the medical facility’s laboratory, where the pathologists (including Dr. Perez) reexamined the sample and sent it to a referral laboratory (Integrated Regional Laboratories, Fort Lauderdale, Florida) for additional workup. Sheep’s blood agar plates grew bacterial colonies from the sample in only 6 hours. We had requested placement of a penicillin disc on the plates to expedite the presumptive identification of B. anthracis, and the bacteria colonies displayed a prominent rim of growth inhibition around the antimicrobial disc. The next day, the Florida Department of Health confirmed the identification of the bacterium, according to the protocols of the Laboratory Response Network for Bioterrorism established by the Centers for Disease Control and Prevention (CDC) and the Association of Public Health Laboratories. Thus, within 48 hours of his presentation to the hospital, Mr. Stevens, a photo editor for a supermarket tabloid newspaper, became only the 19th known case of inhalational anthrax in the United States since 1900 and the first since 1976 (2).

Of the 18 previous cases of inhalational anthrax, all were associated with occupational exposure—the last 2 cases occurred in laboratory workers since 1950. Although Mr. Stevens’ infection was also due to an occupational exposure (in his newsroom office), it was not by a naturally occurring means but rather by an intentional criminal act of bioterrorism.

Given the significance of the inhalational anthrax diagnosis, Dr. Bush decided to promptly notify local health department officials. The hospital administration and staff struggled to communicate with a wide variety of local, state, and federal agencies while maintaining normal oper-
ations of the facility, despite the overwhelming presence of the media (3). Thus began one of the largest epidemiologic and criminal investigations in U.S. history.

It came as a surprise to us, particularly in the wake of the September 11 attacks, that the initial opinion of federal officials was that the exposure was an isolated case, not related likely to bioterrorism, and that because anthrax was not a person-to-person contagion (4), the public should not be alarmed. The surprise results from the fact that, just weeks before and immediately on the heels of September 11, the then—U.S. Secretary of the Department of Health and Human Services gathered government officials, along with a former co-founder of the Center for Civilian Bio-defense Strategies, for a series of urgent meetings to discuss the possibilities of a terrorism sequel. The collective sentiment of the group was that a bioterrorism event could occur and that the country was grossly unprepared for such an attack (5).

Contrary to the opinion that Mr. Stevens’ case was isolated, over the next 7 weeks 21 additional confirmed or suspected cases were found to have resulted from the deliberate use of the U.S. postal service to deliver anthrax spores as agents of biologic terrorism. The inhalational cases numbered 11, of which 5 persons—including Mr. Stevens—died; the cutaneous diagnoses consisted of 7 confirmed and 4 suspected cases. Four states (Florida, New York, New Jersey, and Connecticut) and Washington, DC, had confirmed anthrax cases, attesting to the surprisingly effective method of anthrax spore dispersion.

Ironically, the results of an experimental test of the Canadian National Defense to determine the risk to personnel opening threat letters containing anthrax spores was made available to interested parties in September 2001 (http://anthraxinvestigation.com/canadiananthraxstudiesp01 .pdf), just a few weeks before the U.S. attacks. The test showed that spores quickly disperse through a room, creating a serious threat not only to the person opening a letter but also to others in the same confined space. Before the 2001 U.S. postal service attacks, most estimates of the number of casualties that would occur from a deliberate anthrax attack were based on the belief that such an attack would involve an outdoor aerosol release of a large quantity of anthrax spores over a dense population. These estimations were largely based on information derived from the accidental aerosolized release of anthrax spores from a military microbiology facility in Sverdlovsk (in the former Soviet Union) in 1979 (6).

Unlike biological warfare, where the goal is the intentional use of a modified biological agent to cause massive loss of human life, some say bioterrorism is better defined as a method chiefly designed to disrupt our way of life and make us acutely aware of our vulnerability. Not discounting the loss of 5 human lives or the prolonged severe illness experienced by the 6 other victims of inhalational anthrax (some of whom have never fully recovered) (5, 7), the economic, social, and political consequences resulting from this covert act of bioterrorism were of enormous magnitude and, to some degree, still persist today as evidenced by changes in which we live our daily lives. For example, many people are still fearful of opening unrecognized mail.

Approximate calculations of the expenditures related to the anthrax attacks, which take into account the costs of cleanup and decontamination of the Senate Hart building and the Hamilton, New Jersey, and Brentwood, Washington, DC, postal facilities, along with the costs of laboratory tests (more than 1 million tests were done on 125 000 samples), drugs (more than 10 000 persons received ciprofloxacin as postexposure prophylaxis), other medical treatments, reduced postal revenue, and the costs for engaged personnel (Federal Bureau of Investigation [FBI], CDC, state and local authorities) exceed billions of dollars (5, 8).

One month after the initial attack, the Office of Public Health Preparedness was established within the U.S. Department of Health and Human Services. One U.S. senator stated that the FBI had responded to more than 7000 suspicious letters over a few months (5). Over 150 Laboratory Response Network reference laboratories, specialized centers capable of responding to biologic and chemical terrorism and possessing biosafety level-3 capabilities, are currently in operation, compared with 20 or fewer such laboratories in 2001. The fiscal year 2012 federal budget for civilian biodefense totals $6.42 billion, nearly 11 times greater than that of 2001.

The 2001 anthrax attacks also opened what was perhaps the largest epidemiologic investigation of an infectious diseases outbreak in the history of U.S. public health. Except for the 1984 investigation of the deliberate Rajneeshee salmonella contamination of salad bars in Oregon, resulting in food poisoning of more than 750 individuals (9), no local, state or federal probe into an outbreak had been so intimately linked to a parallel and concomitant criminal inquiry. On the morning of 4 October 2001, immediately following the official CDC announcement of the inhalational anthrax case at our medical center, the collective representatives of the various health agencies huddled, planned, and analyzed the gathering of scientific data and postexposure prophylaxis strategies, while their FBI counterparts, including an agent who specialized in bioterrorism, began creating a profile of an individual, or group of individuals, who might have both the knowledge and means of carrying out an act of bioterrorism using anthrax. The discovery of anthrax spores on the computer keyboard of Robert Stevens at his workplace in the America Media building, just 3 days after his fatal diagnosis, together with the finding of a trace amount of anthrax in a previously opened letter sent to NBC News in New York City, proved to be the crucial pieces of epidemiologic evidence confirming that anthrax had indeed been disseminated through the mail. The search for the anthrax-containing letter at the NBC offices had been instituted after diagnosis of cutaneous anthrax in a 38-year old assistant to Tom Brokaw was confirmed.
More than 8 years later, on 19 February 2010, the 92-page “Amerithrax Investigative Summary,” based on some 2700 pages of documents, was finally published. It officially closed the FBI’s investigation. It concluded that Bruce Ivins, a microbiologist and leading research scientist studying vaccines and cures for exposure to anthrax at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), was the sole perpetrator, acting alone in planning and executing these acts of terrorism. The Bureau reported that the anthrax spores in the letters were genetically connected to unique anthrax spores that Ivins had developed and maintained in his laboratory at USAMRIID. Although the FBI stated that its investigation went beyond scientific evidence and included interviews and other information as part of what it considers a firm case incriminating Ivins, on 15 February 2011 a panel of scientific experts assembled by the National Academy of Sciences, at the request of the FBI, independently evaluated the Bureau’s genetic analysis of the anthrax spores. In doing so, this group of highly trained personnel advised that the scientific evidence put forth by the FBI was insufficient to prove that Ivins was the culprit. Furthermore, recently filed official papers have acknowledged that the “hot suite” sealed area in Ivins’ laboratory did not contain the equipment needed to turn liquid anthrax into the refined anthrax powder that was present in the letters, and that the laboratory lacked the facilities in 2001 to manufacture the kind of spores found in the letters (10, 11). Bruce Ivins’ suicide in 2008 precluded a legal resolution of his guilt or innocence.

So, what have we learned? Clearly, many aspects of the 2001 anthrax attacks went well: the laboratory’s ability to quickly identify the pathogen, the successful and expedient deployment of the National Pharmaceutical Stockpile for postexposure prophylaxis, the decrease in mortality from inhalation anthrax compared with historical rates through rapid diagnosis and multidisciplinary care, and the willingness of many medical personnel and lay volunteers to freely accept risk and responsibility during a time of fear and uncertainty. However, there were also many lessons learned: 1) the realization that scientific knowledge about anthrax is old, outdated, and inaccurate (for example, the relative ease of passage of anthrax spores through unopened envelopes and the much smaller quantity of spores necessary to result in clinical disease after exposure) (12); 2) the confusion and delay in administering an anthrax vaccine for postexposure prophylaxis owing to the lack of timely availability; and 3) the hoarding of ciprofloxacin and other antibiotics, enabled by physicians, to thousands of persons far beyond the population considered immediately at risk (the “worried well”). Although specific data are unavailable, some sources reported increases in antibiotic sales of 300% to 600% (13). Perhaps most important, we now have a much better appreciation and understanding of real-time disease recognition and communication in describing what a diagnosis of inhalation anthrax might imply and making clear who ought to be in charge, particularly with regard to legal authority and medical decision making.

For years before the 2001 anthrax attacks, and to a greater extent since, the CDC has relied on syndromic surveillance systems to enhance early detection of illnesses caused by biologic agents that could cause a bioterrorism attack. The fundamental objective of such surveillance is to identify illness clusters early, even before diagnoses are confirmed and reported to public health agencies, to mobilize the most rapid response possible and thus limit morbidity and mortality (14). As we now know, this program was not successful in October 2001. In fact, before the diagnosis of the index case of anthrax in Florida, 4 individuals in New York City had been seen and treated for skin lesions that were later established to be cutaneous anthrax. In considering whether we as a nation are now better prepared, it is important to remember that identification of the U.S. index case of anthrax bioterrorism was made possible through the “on-the-ground” ability of individual clinicians and laboratory personnel to recognize a potential case of bioterrorism.

To this day, Dr. Bush is often asked the question, “What made you think of anthrax?” After 10 years, the answer has remained the same: “What would have transpired if I had not?” Despite our significant advances in technology and the development of systems designed for bioterrorism preparedness, we firmly believe that an astute clinician will once again be the first to recognize the next patient with an illness resulting from deliberate exposure to a biologic agent. It has been said that luck is where the road of opportunity crosses the road of preparation. In public health this intersection is often at the bedside.

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