Epidemiology of Bioterrorism

Julie A. Pavlin
Walter Reed Army Institute of Research, Washington, D.C., USA

Since the discovery of Iraq's biological weapons program, concern regarding the threat of biological warfare has increased (1). Anthrax immunizations; increased nuclear, biological, and chemical defense training; improved detection systems and protective gear; and increased vigilance have been instituted to protect the military.

However, the military is not the only population at risk for biological attack. To effectively counter the potentially devastating effects of an attack, we need to understand the basic epidemiologic principles of biological agents used as weapons.

A biological agent is commonly portrayed as a genetically engineered organism resistant to all known vaccines and drugs, highly contagious, and able to harm thousands of people. However, alleged attacks by the Aum Shinrikyo did not result in a single illness from a biological agent (2), and the successful 1984 contamination of salad bars in The Dalles, Oregon, by a religious cult involved a common salmonella strain that was not lethal or contagious and was susceptible to antibiotics (3).

Therefore, our level of suspicion and diligence in identifying and reacting to a biological attack must remain high, since the attack may not follow an expected pattern. Furthermore, a small outbreak of illness could be an early warning of a more serious attack, and recognition and prompt institution of preventive measures (such as effective vaccines and antibiotics) could save thousands of lives.

To facilitate the rapid identification of a bioterrorist attack, all health-care providers and public health personnel should have basic epidemiologic skills and knowledge of what to expect in such a setting.

Address for correspondence: Julie A. Pavlin, Department of Field Studies, Division of Preventive Medicine, Walter Reed Army Institute of Research, Washington, D.C. 20307-5100, USA; fax: 202-782-0613; e-mail: pavlinj@wrsmtp-ccmail.army.mil.

Differential Diagnosis

Any small or large outbreak of disease should be evaluated as a potential bioterrorist attack. This initial investigation does not have to be time consuming or involve law enforcement. A look at the facts surrounding the outbreak to determine if anything seems unusual or indicative of bioterrorism should suffice. Since a disease outbreak can be the result of intentional contamination, the differential diagnosis of an outbreak should first be considered. The possibilities include a spontaneous outbreak of a known endemic disease, a spontaneous outbreak of a new or reemerging disease, a laboratory accident, or an intentional attack with a biological agent. Epidemiologic tools can assist in differentiating between these possibilities.

The cause of a disease or even the occurrence of something unusual may be very difficult to determine, especially if the initial cases are few. Surveillance needs to be more than routine. Not only unusually high rates of illness but also unusual diseases should signal a warning. For example, even one case of inhalation anthrax should cause immediate concern and action.

Unlike chemical terrorism, biological terrorism is not immediately obvious but may appear insidiously, with primary-care providers witnessing the first cases. However, it may not even be emergency room personnel who first detect a problem. The first to notice could be a hospital laboratory seeing unusual strains of organisms, or the county epidemiologist keeping track of hospital admissions, or even pharmacists distributing more antibiotics than usual, 911 operators noticing an increase in respiratory distress calls, or funeral directors with increased business. All epidemiologic data should be tracked and aggressively followed to ensure the most rapid recognition and response.

Epidemiologic Approach

The basic epidemiologic approach in the evaluation of a potential bioterrorist or biowarfare attack is not different from any standard epidemiologic investigation. The first step is to use laboratory and clinical findings to confirm that a disease outbreak has occurred. A case definition should be constructed to determine the number of cases and the attack rate. The use of objective criteria in the development of a case definition is very important in determining an accurate case number, as both additional cases may be found and some may be excluded, especially as the potential exists for hysteria to be confused with actual disease. The estimated rate of illness should be compared with rates during previous years to determine if the rate constitutes a deviation from the norm.

Once the case definition and attack rate have been determined, the outbreak can be characterized in the conventional context of time, place, and person. These data will provide crucial information in determining the potential source of the outbreak.

Epidemic Curve

Using data gathered on cases over time, an epidemic curve can be calculated. The disease pattern is an important factor in differentiating between a natural outbreak and an intentional attack. In most naturally occurring outbreaks, numbers of cases gradually increase as a progressively larger number of people come in contact with other patients, fomites, and vectors that can spread disease. Eventually, most of the population has been exposed and is immune to further disease, and the number of cases, or epidemic curve, gradually decreases. Conversely, a bioterrorism attack is most likely to be caused by a point source, with everyone coming in contact with the agent at approximately the same time. The epidemic curve in this case would be compressed, with a peak in a matter of days or even hours, even with physiologic and exposure differences. If the biological agent is contagious, it is possible to see a second curve peak after the first, as original cases expose originally unexposed persons to the agent. The steep epidemic curve expected in a bioterrorism attack is similar to what would be seen with other point source exposures, such as foodborne outbreaks. Therefore, the compressed epidemic curve is still not pathognomonic for an intentional bioterrorism attack.

If a specific group has been exposed, the epidemic curve may indicate the time of exposure. From this information, a possible incubation period can be calculated, which can assist in determining the potential cause of illness, as well as suggesting a possible intentional attack (if the incubation period is shorter than usual as a result of an unusually high inoculum or more effective exposure route). Calculating the incubation period may also help determine if the disease is spread from person to person, which is extremely important to effective disease control measures.

Epidemiologic Clues

As steep epidemic curves can be seen in natural point-source exposures, additional characteristics of the outbreak should be investigated in determining whether it is the result of a biological attack (4,5). None of the following clues alone constitute proof of intentional use of a biological agent, but together they can assist greatly in determining if further investigation is warranted. 1) The presence of a large epidemic, with greater case loads than expected, especially in a discrete population. 2) More severe disease than expected for a given pathogen, as well as unusual routes of exposure, such as a preponderance of inhalational disease as was seen in Sverdlovsk after the accidental release of aerosolized *Bacillus anthracis* spores (6). 3) A disease that is unusual for a given geographic area, is found outside the normal transmission season, or is impossible to transmit naturally in the absence of the normal vector for transmission. 4) Multiple simultaneous epidemics of different diseases. 5) A disease outbreak with zoonotic as well as human consequences, as many of the potential threat agents are pathogenic to animals. 6) Unusual strains or variants of organisms or antimicrobial resistance patterns disparate from those circulating. 7) Higher attack rates in those exposed in certain areas, such as inside a building if the agent was released indoors, or lower rates in those inside a sealed building if an aerosol was released outdoors. 8) Intelligence that an adversary has access to a particular agent or agents. 9) Claims by a terrorist of the release of a biologic agent. 10) Direct evidence of the release of an agent, with findings of equipment, munitions, or tampering.

Even with the presence of more than one of the above indicators, it may not be easy to determine that an attack occurred through nefarious means. For example, it took months to determine that the outbreak of salmonellosis in Oregon was caused by intentional contamination of salad bars (3). Other outbreaks, such as the hantavirus outbreak in the Four Corners area of the United States, have been thought of as possible results of intentional contamination (7). Even if no conclusive answer can be derived quickly, the means employed in determining the cause of an attack will still provide medical personnel with information that may prevent illness and death.

Recommendations for Preparedness

Improved awareness and readiness should a bioterrorism attack occur include education of all medical personnel, especially primary-care providers and emergency personnel first to see patients affected by a biological attack. Training should include basic epidemiologic principles as well as clinical information on diagnosing and treating agents that pose the highest threat. Training should be refreshed periodically to ensure that skills remain current.

Improved surveillance efforts should be instituted with as close to real-time data gathering as possible. All facets of surveillance should be used, to include emergency visits, laboratory data, pharmacy use, school absenteeism, or any other data that correlate with an increase in infectious disease. Robust surveillance systems are essential to detecting any emerging or reemerging disease. Quick recognition of any change in disease patterns will facilitate determining the source and preventing further exposure, which should be the key driving force behind any epidemiologic investigation. Through strong epidemiologic training, a close attention to disease patterns, and a healthy respect for the threat of biological terrorism, potential problems can be discovered rapidly, and actions can be taken to decrease the impact of disease, regardless of its origin.

Major Pavlin is chief of the Field Studies Department, Division of Preventive Medicine, Walter Reed Army Institute of Research. She has worked in the area of medical biodefense education. Currently she is developing national and international surveillance systems for emerging diseases with the Department of Defense's Global Emerging Infections Surveillance and Response System.

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