Introduction

In September 2001, an unknown person (or persons) sent anthrax spores to several locations by way of the US Postal Service. This biological-agent (bioagent) attack infected 22 people—11 with inhalational anthrax and 11 with cutaneous anthrax. Five people infected with inhalational anthrax died. The American Medical Association recommends “…early antibiotic administration” for inhalational anthrax; however, physicians prefer to diagnose a disease (or medical condition) before administering antibiotics. Initial symptoms of inhalational anthrax are fever, malaise, fatigue, occasional cough, and chest discomfort. The flu-like symptoms of inhalational anthrax may cause physicians to misdiagnose inhalational anthrax as influenza.

Covert dissemination of a bioagent in a public place can go undetected for several days or weeks. There is no immediate impact because of the bioagent’s incubation period and the time between exposure and the appearance of symptoms. The covert release of a bioagent could result in a large number of casualties and tax the health care system of the United States. Simultaneous releases of a bioagent at or near US military installations could have a devastating effect.

It is necessary to immediately detect and characterize a bioagent to provide effective treatment and determine what levels of medical resources are required to treat casualties. A networked system of real-time bioagent detectors could provide early warning of an attack by bioterrorists. This article discusses the most likely bioagents and the methods of employment bioterrorists may use. It will state the indicators of a covert agent release and compare the current state-of-the-art biological detectors.

The Threat

What is bioterrorism? The Centers for Disease Control and Prevention define it as “…the intentional or threatened use of viruses, bacteria, fungi, or toxins from living organisms to produce death or disease in humans, animals, or plants.” There are many potential bioagents; however, there are six types that experts agree might be used: anthrax, botulinum toxin, pneumonic plague, smallpox, tularemia, and viral hemorrhagic fevers (Ebola) (see the table on page 22). Other potential bioagents exist, but the types listed pose a risk to national security. These bioagents were chosen because they—

- Are easily disseminated as aerosols or through transmission from person to person, producing a high mortality rate and the potential for a major impact to public health.
- Require special action for public health preparedness.
- Have the potential for causing public panic and social disruption.

Medical experts have estimated the number of casualties that would occur in the event of a covert release of bioagents. The World Health Organization (WHO) estimates that releasing 50 kilograms of anthrax spores over an urban population of 5 million people would sicken 250,000 and kill 100,000. WHO estimates that a point source release of botulinum toxin would kill or incapacitate...
10 percent of persons within 0.5 kilometer downwind of the release point, and an aerosol dispersal of 50 kilograms of tularemia over a metropolitan area of 5 million inhabitants would incapacitate 250,000 persons and result in 19,000 deaths. Typical smallpox epidemics have resulted in mortality rates of 30 percent. Covert dissemination of a bioagent in a public place will not have an immediate impact because of the delay between exposure and the onset of symptoms.

**Indicators of a Bioterrorist Attack**

The current US agent detection system relies on local health providers to detect and report the outbreak of disease. And the initial detection of a covert release of a bioagent will probably occur at the local level. Disease surveillance systems at the state and local health agencies must be capable of detecting unusual patterns of disease. Components of a public health response to bioterrorism are disease detection and health surveillance, rapid laboratory analysis, and epidemiological investigation and implementation of control measures. However, traditional methods for the detection and identification of bioagents require at least a day for completion. Detecting and responding quickly to bioterrorism is essential. Without special preparation, an attack with bioagents could overwhelm the local civilian and military health systems. Large numbers of patients would seek medical attention, resulting in the need for medical supplies, diagnostic tests, and hospital beds. Those at risk in the public health system include emergency responders, health care workers, public health officials, and civilian and military personnel on military installations.

### Potential Threat Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Mortality Rate (Percent)</th>
<th>Incubation Period</th>
<th>Contagious</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anthrax (bacillus anthracis)</td>
<td>90 to 100</td>
<td>7 days</td>
<td>No</td>
<td>Symptoms include fever, malaise, cough, difficulty breathing, toxemia, cyanosis, and terminal shock.</td>
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<tr>
<td>Botulinum toxin (clostridium botulinum)</td>
<td>60 to 100</td>
<td>12 to 72 hours</td>
<td>No</td>
<td>Symptoms include blurred vision, difficulty talking and swallowing, dry mouth, and muscle weakness. Severe symptoms include paralysis of the arms, trunk, and legs.</td>
</tr>
<tr>
<td>Pneumonic plague (yersinia pestis)</td>
<td>100</td>
<td>1 to 6 days</td>
<td>Yes</td>
<td>Symptoms include high fever, chills, headache, cough with bloody sputum, severe pneumonia, and sepsis.</td>
</tr>
<tr>
<td>Smallpox (variola major)</td>
<td>30</td>
<td>12 to 14 days</td>
<td>Yes</td>
<td>Initial symptoms include malaise, fever, chills, vomiting, headache, and backache. Severe symptoms (2–3 days later) include flat, red spots that progress to puss-filled lesions on the skin and lining of the throat and mouth.</td>
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<tr>
<td>Tularemia (francisella tularensis)</td>
<td>30 to 40</td>
<td>1 to 14 days</td>
<td>No</td>
<td>Symptoms include fever, chills, fatigue, chest discomfort, dry cough, and swollen lymph nodes.</td>
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<tr>
<td>Viral hemorrhagic fevers (filo and arena viruses)</td>
<td>50 to 90 (Ebola)</td>
<td>2 to 21 days (Ebola)</td>
<td>Yes</td>
<td>Symptoms include high fever, severe prostration, slight rash, and bleeding (the symptoms may vary depending on the virus).</td>
</tr>
</tbody>
</table>
People seeking medical treatment for symptoms of respiratory illness will likely be the first evidence of a covert release of aerosolized anthrax. Patients infected with anthrax can recover from the disease if antibiotics are administered before the onset of symptoms. However, early diagnosis of anthrax is difficult, especially before any symptoms are evident. Laboratory tests take from six to twenty-four hours, and the test results are only preliminary findings. Early identification of a botulism outbreak depends on the ability of medical personnel to recognize the signs and symptoms of the disease. Aerosol dissemination may be difficult to recognize because a large number of people in the same geographical area will be exposed to the botulinum toxin almost simultaneously. Laboratory tests to confirm botulism can take from one to two days.

An outbreak of pneumonic plague would result in symptoms that resemble severe pneumonia. An indicator of a bioterrorist dissemination of pneumonic plague would be the occurrence of cases in locations where pneumonic plague has not occurred naturally. The sudden appearance of large numbers of previously healthy patients with fever, cough, shortness of breath, and chest pain suggests exposure to anthrax or pneumonic plague. A confirmatory test is required, but laboratory tests for plague take from one to six days. Early administration of antibiotics is helpful in treating plague victims.

An aerosol release of the smallpox virus would disseminate widely because the virus is stable, meaning it remains active in aerosol form. Smallpox is also transmittable from person to person. Initially, the smallpox victim has a high fever, abdominal pain, and severe headache. A rash will appear within one or two days from the onset of symptoms. Since smallpox is a viral infection, there is no antibiotic treatment available. Health care workers can only provide supportive therapy and palliative care. A covert release of aerosolized tularemia in a densely populated area would result in large numbers of people showing respiratory illness. Antibiotics are useful in the treatment of tularemia; however, the symptoms of tularemia also resemble those of respiratory illness. Laboratory identification of tularemia is difficult because the tests screen for the common pathogens that cause respiratory illness.

**Biosensors**

The Department of Defense is currently working on a biological detection system. This system is a network of sensors and communication links that fill the need for automated bioagent detectors for real-time sample collection, detection, and identification in the field. Such a system has the potential for application in the United States and could be linked into the public health detection and surveillance system. At the heart of the biological detection system is a biosensor.

There are three types of biosensors: chemical mass spectrometry systems, biochemical systems, and biological tissue-based systems. Chemical mass spectrometry systems break down a sample into its component amino acids, biochemical systems detect a DNA sequence or protein, and biological tissue-based systems detect how a bioagent or toxin affects live mammalian cells.

Chemical mass spectrometry systems reduce dependence on live tissue and other biological reagents that must be preserved. Mass spectrometry involves heating a liquid sample until it evaporates and then bombarding the vaporized liquid with electron beams so that the molecules fragment and assume an electrical charge. The charged fragments are then accelerated through an electric field that sorts them by mass and charge and permits the calculation of molecular weights. Mass spectrometry has two advantages:

- It is rapid, with a total detection time of only five minutes (including preparation time).
- It is sensitive enough to detect and identify mixtures of closely related bacterial spores.

Biochemical systems rely on the uniqueness of nucleic acid sequences in self-replicating organisms. A detection method driven by a polymerase chain reaction (PCR) relies on comparing DNA taken from microorganisms in a sample with the DNA of known bioagents. The advantage of using PCR is its ability to produce many copies of the target nucleic acid sequence, allowing for the identification of a pathogen from a small sample in a relatively short time span. The disadvantage of using PCR is the requirement for repeated cycles of samples to be heated close to the boiling point of water and then cooled. This process requires a disproportionate amount of energy to heat and cool the samples. Biological tissue-based systems rely on natural and unique phenomena in organisms. Any chemical compound that triggers an immune response from live tissue can act as an antigen. Antibodies generated from a particular pathogen are specific and will only bind to that pathogen and not to any other pathogen. Immunological detection has the additional advantage of being able to detect both microorganisms and biological toxins, which lack DNA. The drawback of
antibody tests is that they require prior knowledge of the bioagent.

Lawrence Livermore National Laboratory (LLNL) is developing two types of biodetectors for real-time sample collection, detection, and identification in the field. One system uses a miniature flow cytometer. The flow cytometer uses an immunoassay system to look at proteins on the surface of cells. To maximize the detection potential and give faster results, the PCR unit and flow cytometer are being multiplexed to handle multiple samples at once. In 1996, LLNL delivered to the Army a portable, battery-powered, real-time biodetector based on PCR technology. The technologies exist which may be used in a nationwide system of biodetectors.

Conclusion

This article has addressed the bioagents that terrorists would most likely employ in an attack. Bioterrorists will probably disseminate these agents as aerosols to cause the largest number of casualties. Current detection and identification methods rely on the public health system using epidemiological methods to determine that a bioterrorist attack occurred. Using real-time, networked detectors will speed the identification of bioagents. Early detection and identification will save lives by allowing the packages of bioagent-specific medical supplies to be sent to the attack areas. It is imperative that the sustaining base refine and field a system of networked biodetectors placed in and around population centers and military installations.

References


Mr. Kushnir is the Chief of the Environmental Sciences Committee, US Army Logistics Management College, Fort Lee, Virginia. He holds a bachelor’s degree in chemistry from Adelphi University, Garden City, New York, and a master’s degree in chemistry from St. John’s University, New York. Mr. Kushnir is a retired US Army Reserve chemical officer.