Bioterrorism: Priority Agents

Unless you’ve been living on Mars with a broken interplanetary radio, you’re aware of the two October cases of inhalational anthrax in Florida — the first in the United States since 1976 — and of cases of cutaneous anthrax in New York City. Anthrax is a disease of such rarity in the U.S. that any case appropriately triggers conjecture about bioterrorism, and in these cases, ongoing investigation by public-health and criminal-justice officials has not quelled the suspicion.

Faithful readers of these pages have been apprized of the possibility of bioterrorism, i.e., the deliberate use of microorganisms to cause disease with the intention of achieving a political end. Unfortunately, we don’t know where, when, or with what agent a bioterrorist might strike. And because it is impractical to maintain stocks of antibiotics and vaccines sufficient to protect every citizen in every locale from every possible biological agent for an indefinite period of time, the only workable, long-term strategy is to be able to detect an event as early as possible, to respond quickly, and to bring resources to bear efficiently.

The cornerstone of our disease-surveillance system is a cadre of physicians, physician assistants, nurse practitioners, and clinical laboratorians who will recognize the public-health implications of reportable diseases, clusters of illnesses, and some unusual illnesses, and who will notify health department officials so that public-health investigation and action can be undertaken expeditiously. The importance of alert clinicians is underscored by the recent diagnosis and reporting of inhalational anthrax by the Florida physician who spotted the causative agent on Gram-stained cerebrospinal fluid.

Although nearly any microbe could be put to nefarious use, CDC has classified 6 diseases as “Category A,” i.e., highest priority, because they can be easily disseminated or transmitted person to person; cause high mortality, with potential for major public-health impact; might cause public panic and social disruption; and require special action for public-health preparedness. The following is a quick overview of the Category A diseases, suspicion of any of which should prompt an immediate call to the local health department.

**Anthrax.** A nonspecific prodrome (i.e., fever, dyspnea, cough, and chest discomfort) follows inhalation of infectious spores. Approximately 2–4 days after initial symptoms, sometimes after a brief period of improvement, respiratory failure and hemodynamic collapse ensue. Inhalational anthrax also might include thoracic edema and a widened mediastinum on chest radiograph.

Gram-positive bacilli can grow on blood agar, whereas Gram-negative rods may be seen on Gram stain, mucus, or pus. Inhalation and/or ingestion of spores, cutaneous contact with infected animal, and inhalation and/or ingestion of infected fleas are modes of transmission.

**Plague.** Clinical features of pneumonic plague include fever, cough with mucopurulent sputum (Gram-negative rods may be seen on Gram stain), hemoptysis, and chest pain. A chest radiograph will show evidence of bronchopneumonia.

**Botulism.** Clinical features include symmetric cranial neuropathies (i.e., drooping eyelids, weakened jaw clench, and difficulty swallowing or speaking), blurred vision or diplopia, symmetric descending weakness in a proximal-to-distal pattern, and respiratory dysfunction from respiratory muscle paralysis or upper airway obstruction without sensory deficits. Inhalational botulism would have a similar clinical presentation as anthrax.

**Tularemia.** Clinical features of tularemia include fever, malaise, lymphadenopathy, and skin rash. Tularemia is caused by *Francisella tularensis*, a Gram-negative rod that infects a wide range of animals, including ticks, rabbits, deer, and beavers. The most common mode of transmission is by skin contact with infected animals or their products. Inhalation and ingestion also are possible modes of transmission.

**Hemorrhagic Fever.** Hemorrhagic fevers are caused by viruses that infect a wide range of animals, including bats, rodents, and ticks. The viruses are transmitted to humans by direct contact with infected animals or their products, by vector-borne transmission, or by inhalation or ingestion of contaminated water. Anthrax, tularemia, botulism, and hemorrhagic fever are listed in the table below.

### Microbiology and Epidemiology of Selected BT Agents

<table>
<thead>
<tr>
<th>Agent</th>
<th>Microbiology</th>
<th>Reservoir</th>
<th>Incubation</th>
<th>Transmission</th>
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<tbody>
<tr>
<td>Anthrax</td>
<td><em>Bacillus anthracis</em>, a spore-forming Gram-positive rod</td>
<td>livestock and wildlife, spores visible in soil for years</td>
<td>Average: 1-7 days Range: 1-60 days</td>
<td>Inhalation and/or ingestion of spores, cutaneous contact with infected animal</td>
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<tr>
<td>Plague</td>
<td><em>Yersinia pestis</em>, a Gram-negative rod</td>
<td>wild rodents</td>
<td>1-7 days (longer in immunocompromised individuals)</td>
<td>Bubonic: bites from infected fleas, pneumonic: person-to-person by respiratory droplets</td>
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<tr>
<td>Smallpox</td>
<td><em>Variola virus</em>, an orthopoxvirus</td>
<td>officially, only in designated freezers</td>
<td>7-19 days</td>
<td>Respiratory</td>
</tr>
<tr>
<td>Botulism</td>
<td>Neurotoxins produced by the anaerobic Gram-positive rod <em>Clostridium botulinum</em></td>
<td>spores, ubiquitous in soil</td>
<td>12-36 hours to several days</td>
<td>Ingestion of preformed toxin</td>
</tr>
<tr>
<td>Tularemia</td>
<td><em>Francisella tularensis</em>, a Gram-negative rod</td>
<td>wild animals (rabbits, beavers, various ticks)</td>
<td>Average: 3-5 days Range: 1-14 days</td>
<td>Tick bites, handling or eating insufficiently cooked meats, drinking contaminated water, inhalation of contaminated soil</td>
</tr>
<tr>
<td>Hemorrhagic fever</td>
<td><em>Ebolavirus</em></td>
<td>Unknown. Bats?</td>
<td>Average: 5-10 days Range: 2-19 days</td>
<td>Contact with body fluid of infected person</td>
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foodborne botulism; however, the gastrointestinal symptoms that accompany foodborne botulism may be absent. Smallpox (variola). The acute clinical symptoms of smallpox resemble other acute viral illnesses, such as influenza, beginning with a 2- to 4-day nonspecific prodrome of fever and myalgias before rash onset. Several clinical features can help clinicians differentiate varicella (chickenpox) from smallpox. The rash of varicella is most prominent on the trunk and develops in successive groups of lesions over several days, resulting in lesions in various stages of development and resolution. In comparison, the vesicular/pustular rash of smallpox is typically most prominent on the face and extremities, and lesions develop at the same time. Smallpox (variola). The acute clinical symptoms of smallpox resemble other acute viral illnesses, such as influenza, beginning with a 2- to 4-day nonspecific prodrome of fever and myalgias before rash onset. Several clinical features can help clinicians differentiate varicella (chickenpox) from smallpox. The rash of varicella is most prominent on the trunk and develops in successive groups of lesions over several days, resulting in lesions in various stages of development and resolution. In comparison, the vesicular/pustular rash of smallpox is typically most prominent on the face and extremities, and lesions develop at the same time.

Inhalational tularemia. Inhalation of F. tularensis causes an abrupt onset of an acute, nonspecific febrile illness beginning 3-5 days after exposure, with pleuropneumonitis developing in a substantial proportion of cases during subsequent days. Hemorrhagic fever (such as would be caused by Ebola or Marburg viruses). After an incubation period of usually 5-10 days (range: 2-19 days), illness is characterized by abrupt onset of fever, myalgia, and headache. Other signs and symptoms include nausea and vomiting, abdominal pain, diarrhea, chest pain, cough, and pharyngitis. A maculopapular rash, prominent on the trunk, develops in most patients approximately 5 days after onset of illness. Bleeding manifestations, such as petechiae, ecchymoses, and hemorrhages, occur as the disease progresses.

ADDITIONAL RESOURCES

A wealth of information, in addition to valuable bioterrorism-related links, is available on our web site http://www.ohd.hr.state.or.us/acd/bioterr/home.htm.

REFERENCES