1. DISEASE REPORTING

1.1 Purpose of Reporting and Surveillance

Rapid detection of anthrax-related illness to allow expeditious treatment of those who are ill, prompt identification of the source of infection, including identification of intentional release of anthrax in the context of a terrorist attack, and rapid implementation of control measures.

1.2 Laboratory and Physician Reporting Requirements

Immediate reporting of suspected anthrax infection by health care providers by laboratory personnel.

1.3 Local Health Department Reporting and Follow-Up Responsibilities

Notify ACDP immediately of any suspected anthrax infection. Coordinate with ACDP and other agencies as necessary to determine source of infection as well as to carry out contact investigation and prophylaxis for others who appear to have been exposed. (Realistically, if we have an event, the place is going to be swarming with CDC and other federal folks. We won't have to do this on our own.)

2. THE DISEASE AND ITS EPIDEMIOLOGY

2.1 Etiologic Agent

*Bacillus anthracis*: an aerobic, non-motile, spore-forming, encapsulated, gram positive, rod-shaped bacterium.

2.2 Description of Illness

Anthrax typically presents as one of three clinical syndromes, depending on the route of exposure.

1. Cutaneous anthrax.

   Cutaneous disease is characterized by development of one or more painless, itchy papules on the skin, typically on exposed areas such as the face, neck, forearms, or hands. Within 24 hours, the papule enlarges to form a skin ulcer. This subsequently crusts over, forming the painless black eschar that is the hallmark of the cutaneous form of the disease. Localized swelling, inflammation of the lymph channels, painful regional lymph node swelling, and systemic symptoms also occur. The untreated case fatality rate is 20%; with appropriate therapy, death is rare.

2. Inhalational anthrax.

   Inhalational disease typically progresses through two distinct stages. The first, lasting from several hours to several days, involves influenza-like symptoms such as fever, cough, shortness of breath, headache, chills, and at times, abdominal or chest discomfort. The second stage involves abrupt onset of sweats, spiking fever, severe respiratory distress, and shock. Of 11 people who developed inhalational disease during the 2001 anthrax attacks, five (45%) died. Therapy must be started early in the course of illness to be effective.


   Gastrointestinal anthrax is a form of the disease rarely seen in the U.S. It presents with nausea, vomiting, and malaise, then progresses to bloody diarrhea, acute abdomen, and sepsis. The case fatality rate is greater than 60%. While antibiotic use may decrease this, the nonspecific initial presentation makes diagnosis difficult in the absence of a known exposure or cluster of disease.

2.3 Reservoirs

   Historically, anthrax has come from contact with:
Anthrax

- Herbivores (cattle, sheep, goats, etc.) ill with the disease
- Contaminated products (wool, goat hair, meat, hides, etc.) from ill herbivores.

While dormant anthrax spores are found in the soil of many areas in the US and other parts of the world, infection resulting from direct inhalation of natural spores in soil is felt to be very rare.

From a BT perspective, the main concern is specially processed spores which, when released, have a higher potential for causing infection. The extent of stockpiling of such weapons by nations and/or terrorist groups is unknown.

2.4 Modes of Transmission
- Spore contact with the skin.
- Inhalation of spores
- Eating contaminated food, typically meat from an infected animal.

2.5 Period of Communicability
Anthrax is not known to spread person-to-person.

2.6 Incubation Period
- Inhalational: 2–60 days
- Cutaneous: 1–12 days
- Gastrointestinal: 1–7 days.

2.7 Treatment
ACDP will get up-to-date information on prophylaxis to you as needed.
See Tables 1–3 on pages 6–8.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Confirmed Case Definition
A clinically compatible illness with one of the following:
- Culture and identification of \( B. \text{anthracis} \) from clinical specimens by the Laboratory Response Network (LRN);
- Demonstration of \( B. \text{anthracis} \) antigens in tissues by immunohistochemical staining using both \( B. \text{anthracis} \) cell wall and capsule monoclonal antibodies;
- Evidence of a four-fold rise in antibodies to protective antigen between acute and convalescent sera or a fourfold change in antibodies to protective antigen in paired convalescent sera using Centers for Disease Control and Prevention (CDC) quantitative anti-PA IgG ELISA testing;
- Documented anthrax environmental exposure AND evidence of \( B. \text{anthracis} \) DNA (for example, by LRN-validated polymerase chain reaction) in clinical specimens collected from a normally sterile site (such as blood or CSF) or lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal).

3.2 Probable Case Definition
A clinically compatible illness that does not meet the confirmed case definition, but with one of the following:
- Epidemiological link to a documented anthrax environmental exposure;
- Evidence of \( B. \text{anthracis} \) DNA (for example, by LRN-validated polymerase chain reaction) in clinical specimens collected from a normally sterile site (such as blood or cerebrospinal fluid) or lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal);
- Positive result on testing of clinical serum specimens using the Quick ELISA Anthrax-PA kit;
- Detection of Lethal Factor (LF) in clinical serum specimens by LF mass spectrometry
- Positive result on testing of culture from clinical specimens with the RedLine Alert test.
3.3 **Suspect Case Definition**

Clinically compatible illness in the absence of definitive, presumptive, or suggestive laboratory evidence of *B. anthracis*, or epidemiologic evidence relating it to anthrax.

3.4 **Services Available at the Oregon State Public Health Laboratory**

OSPHL offers LRN-validated PCR testing. They can do confirmatory culture testing as well.

### 4. CASE INVESTIGATION

4.1 **Identify Source of Infection**

Treat any case of anthrax as a potential bioterrorism incident (until this can be ruled out). Any resulting investigation is potentially both a public health and a criminal investigation. Immediately interview all cases, suspect or confirmed, to identify the route and venue of exposure. Consider directed environmental sampling of a suspect venue to localize the exposure.

4.2 **Identify Potentially Exposed Persons**

Once the route and venue of exposure have been established:

1. Determine the time and spatial extent of the exposure.
2. In circumscribed exposures, develop a list of persons with suspected exposure, using:
   - interviews with those known to be exposed,
   - review of attendee lists of any functions where exposure is suspected to have occurred,
   - credit card receipts from such events, and
   - any other evidence available.
3. Contact all persons on list to assess for illness and to discuss possible prophylaxis.
4. When broad, outdoor dissemination and resultant widespread exposure are suspected, collect information about activities and areas visited preceding symptom onset in those who are ill. For gastrointestinal anthrax, explore the seven (7) days prior to onset. For cutaneous disease, go back 14 days. For inhalational disease, go back 60 days prior to onset.

In coordination with ACDP, CDC, and other potentially affected nearby jurisdictions, make a best estimate of the area of exposure to guide prophylaxis efforts for the population at risk.

### 5. CONTROLLING FURTHER SPREAD

5.1 **Education**

When contacting potentially exposed persons, educate them about possible symptoms of anthrax disease, including specific conditions that should prompt immediate medical evaluation, such as:

- fever,
- cough,
- shortness of breath,
- vomiting,
- diarrhea, or
- appearance of a painless sore on the skin.

Describe possible adverse reactions to any medicine given for prophylaxis, and reinforce the possibility of spore germination and resultant disease if medications are not continued for the full course.

5.2 **Decontamination**

Decontamination of buildings containing weaponized *B. anthracis* is not easy. Expert advice would be required. The decision to decontaminate potentially exposed individuals is based upon the credibility of the threat, as established by the FBI and other law enforcement agencies, and the potential for exposure(s) of the people at the scene. In general, personal decontamination should consist of soap and water on exposed skin and removal of potentially contaminated outer garments and shoes. Once home, a shower to wash off any lingering sores could also be worthwhile.
Anthrax

Depending upon the situation, clothing may be collected as evidence (and the individual supplied with an over-garment), may be removed and bagged for decontamination at home or a commercial facility (and the individual supplied with an over-garment), or may be worn home and laundered or dry cleaned. If more extensive exposure to anthrax is reported, all potentially contaminated garments should be removed, bagged and laundered, and exposed person should take a full shower, washing thoroughly with soap and warm water.

5.3 Isolation
Not indicated.

5.4 Prophylaxis
1. Post-exposure
Although not currently licensed for use in the post-exposure setting, anthrax vaccine was used under an investigational new drug protocol in response to the 2001 attacks. Several antimicrobials can be used for prophylaxis in those who have been exposed to anthrax. If this becomes necessary, ACDP will provide up-to-date guidelines.

2. Pre-exposure
An inactivated cell-free vaccine exists and can be given as a six-dose series with annual boosters. It is currently recommended only for those with regular occupational exposure to *B. anthracis* and is also used by the US military. It is not generally recommended for public health workers or the general public.

6. MANAGING SPECIAL SITUATIONS
See tables at the end of this section.

6.1 Response Following Discovery of a Suspicious Substance in a Community

1. Evaluation by law enforcement
   Upon discovery of a suspicious substance (white powder or otherwise), 911 should be contacted immediately. If there is evidence of explosion or illness or injury, the 911 dispatcher should immediately call both local law enforcement and fire/paramedical services. If there is no evidence of explosion or acute illness, 911 dispatcher should call local law enforcement. Local law enforcement should then assess whether or not a "credible threat" exists. They may then call in a hazardous materials (haz-mat) team to aid in a safety assessment, but the initial key step in the "response cascade" is a threat assessment by law enforcement. **If this has not occurred, refer the person contacting you to local law enforcement (or 911) to begin this process.** After this evaluation, there are two possible situations in which public health might be involved:
   - Law enforcement concludes that there is no credible threat.
     - In this case, the local health department could be contacted to help in explaining risk (or the lack of it), providing information about the incident, etc.
     - Provide information/explanation of situation if requested.
     - Consult with ACDP/Preparedness Surveillance Epidemiology Team (PSET) as needed to draft statements.
   - Law enforcement concludes that there is a credible threat.
     - Law enforcement will retain custody of the suspicious substance.
     - FBI will arrange for further evaluation through OSPHL or CDC.

6.2 Public Health Response in the Setting of a Credible Threat

1. Communicate periodically with ACDP/PSET to review available information.
2. ACDP should contact OSPHL, give them information about the incident, and let them know that FBI may be contacting them about specimen testing, if this has not happened already.
3. Consider developing a press release outlining the steps being taken to investigate the event, reviewing that all such events are taken seriously, and that any threat or intentional release of a suspicious substance, even as a hoax, is a crime.
4. There are two principal situations that might arise from completion of laboratory analysis to detect
• OPHD will coordinate with local health departments and emergency management personnel to arrange for prophylaxis as indicated.

6.3 Positive Signal at a U.S. Postal Service Biohazard Detection System (BDS) Program Facility

1. Five counties (Deschutes, Jackson, Lane, Marion, and Multnomah) have postal facilities that conduct on-going, real-time PCR testing for anthrax.

2. In 2006, CDC issued guidance that, due to the high specificity of this BDS testing, a positive signal should trigger decontamination and prophylaxis of those potentially exposed, rather than waiting for confirmatory testing.

3. BDS-specific response plans have been developed by U.S. Postal Service, the participating facilities, and the counties where these facilities are located. These plans can be used to guide response in the setting of a positive BDS signal.

UPDATE LOG

2003. Original guideline released
April 2011. Info on use of vaccine in post-exposure setting, background information under “Description of Illness,” and information on managing special situations were revised. (R. Leman)

January 2013. Updated treatment recommendations based on CDC guidance. Added case investigation (Sec 4) outlining strategies when broad outdoor dissemination suspected. Added information to Decontamination Section (See 5.2) Added info on response to positive signal from Postal Service Biohazard Detection System Program facility to "Managing Special Situations" (Sec 6). (R. Leman)
### Table 1. Recommended therapy for inhalational anthrax infection in the contained casual setting. a,b

<table>
<thead>
<tr>
<th>Category</th>
<th>Initial IV therapy&lt;sup&gt;cd&lt;/sup&gt;</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Ciprofloxacin 400 mg every 12 hours (recommended unless contraindicated) or Ciprofloxacin 500 mg twice daily or Doxycycline 100 mg every 12 hours&lt;sup&gt;i&lt;/sup&gt; and 1 or 2 additional antimicrobials&lt;sup&gt;d&lt;/sup&gt;</td>
<td>IV treatment initially before switching to oral antimicrobial therapy when clinically appropriate: Ciprofloxacin 500 mg twice daily or Doxycycline 100 mg twice daily. Continue oral and IV treatment for 60 days&lt;sup&gt;j&lt;/sup&gt;</td>
</tr>
<tr>
<td>Children</td>
<td>Ciprofloxacin 10-15 mg every 12 hours (recommended unless contraindicated) or Doxycycline for those aged: Ciprofloxacin 10-15 mg every 12 hours or Doxycycline 100 mg twice daily for those aged: Ciprofloxacin 10-15 mg every 12 hours or Doxycycline 100 mg twice daily</td>
<td>IV treatment initially before switching to oral antimicrobial therapy when clinically appropriate: Ciprofloxacin 10-15 mg every 12 hours (recommended unless contraindicated) or Doxycycline 100 mg twice daily. Continue oral and IV treatment for 60 days&lt;sup&gt;j&lt;/sup&gt;</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Same as for nonpregnant adults Ciprofloxacin recommended in pregnancy prior to third trimester</td>
<td>IV treatment initially before switching to oral antimicrobial therapy when clinically appropriate. Oral therapy regimens are the same as for nonpregnant adults</td>
</tr>
<tr>
<td>Immunocompromised persons</td>
<td>Same as for non-immunocompromised adults and children</td>
<td>IV treatment initially before switching to oral antimicrobial therapy when clinically appropriate. Oral therapy regimens are the same as for nonpregnant adults</td>
</tr>
</tbody>
</table>

a. This table is adapted with permission from *Morbidity and Mortality Weekly Report*. For gastrointestinal oropharyngeal anthrax, use regimens recommended for inhalational anthrax.
b. Roxibacumab, a monoclonal antibody, is now approved for treatment of inhalational anthrax.
c. Steroids may be considered as an adjunct therapy for patients with severe edema and for meningitis based in experience with bacterial meningitis of other etiologies. Early aggressive drainage of pleural effusions recommended for inhalational anthrax.
d. Other agents with *in vitro* activity include rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and clarithromycin. Because of concerns of constitutive and inducible β lactamases in *Bacillus anthracis*, penicillin and ampicillin should not be used alone. Consultation with an infectious disease specialist is advised. Given risk of meningeal involvement with systemic anthrax, choose agents with adequate penetration.
e. Initial therapy may be altered based on the clinical course of the patient; 1 or 2 antimicrobial agents may be adequate as patient improves.
f. If meningitis is suspected, doxycycline may be less optimal because of poor central nervous system penetration.
g. If intravenous (IV) ciprofloxacin is not available, oral ciprofloxacin may be acceptable because it is rapidly and well absorbed from the gastrointestinal tract with no substantial loss by the first-pass metabolism. Maximum serum concentrations are attained 1 to 2 hours after oral dosing but may not be achieved if vomiting or ileus is present.
h. In children, ciprofloxacin dosage should not exceed 1 g/d.
i. The American Academy of Pediatrics recommends treatment of young children with tetracyclines for serious infections (i.e., Rocky Mountain spotted fever).
j. Because of potential persistence of spores after an aerosol exposure, antimicrobial therapy should be continued for 60 days.
### Anthrax

Table 2. Recommended therapy for inhalation anthrax infection the mass casualty setting*

<table>
<thead>
<tr>
<th>Category</th>
<th>Initial oral therapy</th>
<th>Alternative therapy if strain is proved susceptible</th>
<th>Duration after exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Ciprofloxacin 500 mg twice daily</td>
<td>Doxycycline 100 mg every 12 hours&lt;sup&gt;a&lt;/sup&gt; Amoxicillin 500 mg orally every 8 hours&lt;sup&gt;d&lt;/sup&gt;</td>
<td>60 days</td>
</tr>
<tr>
<td>Children</td>
<td>Ciprofloxacin 20-30 mg/kg per day orally taken in 2 daily doses, not to exceed 1g/d&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Doxycycline&lt;sup&gt;f&lt;/sup&gt; or Amoxicillin: &gt;20 kg: 500 mg orally every 8 hours&lt;sup&gt;d&lt;/sup&gt; &lt;20 kg: 40 mg/kg orally in 3 doses every 8 hours&lt;sup&gt;d&lt;/sup&gt;</td>
<td>60 days</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>Ciprofloxacin 500 mg orally every 12 hours</td>
<td>Doxycycline or Amoxicillin 500 mg orally every 8 hours&lt;sup&gt;d&lt;/sup&gt;</td>
<td>60 days</td>
</tr>
<tr>
<td>Immunocompromised persons</td>
<td>Same as for non-immunocompromised adults and children</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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a. Some of these recommendations are based on animal studies or in vitro studies and are not approved by the US Food and Drug Administration.
b. In vitro studies suggest ofloxacin (400 mg orally every 12 hours), or levofloxacin, 500 mg orally every 24 hours could be substituted for ciprofloxacin.
c. In vitro studies suggest that 500 mg of tetracycline orally every 6 hours could be substituted for doxycycline. In addition, 400 mg of gatifloxacin or moxifloxacin, both fluoroquinolones with mechanisms of action consistent with ciprofloxacin, taken orally could be substituted.
d. According to the Centers for Disease Control and Prevention recommendations, amoxicillin is suitable for postexposure prophylaxis only after 10 to 14 days of fluoroquinolones or doxycycline treatment and then only if there are contraindications to these 2 classes of medications (e.g., pregnancy, lactating mother, age > 18 year or intolerance of other antibiotics). f. If meningitis is suspected, doxycycline may be less optimal because of poor central nervous system penetration.
e. Doxycycline could also be used if antibiotic susceptibility testing, exhaustion of drug supplies, or adverse reactions preclude use of ciprofloxacin. For children heavier than 45 kg, the adult dosage should be used. For children 45 kg or lighter use 2.5 mg/kg of doxycycline every 12 hours.
f. Ciprofloxacin is preferred. If there is a contraindication to fluoroquinolone use, doxycycline can be substituted.
Table 3. Recommended therapy for cutaneous anthrax infection associated with a bioterrorism attack

<table>
<thead>
<tr>
<th>Category</th>
<th>Initial oral therapy</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Ciprofloxacin 500 mg twice daily&lt;sup&gt;b&lt;/sup&gt; or Doxycycline 100 mg twice daily&lt;sup&gt;b&lt;/sup&gt;</td>
<td>60 days</td>
</tr>
<tr>
<td>Children</td>
<td>Ciprofloxacin 10-15 mg every 12 hours (not to exceed 1 g/d)&lt;sup&gt;b&lt;/sup&gt; or Doxycycline for those aged: &gt;8 y and weight &gt;45 kg: 100 mg every 12 hours &gt;8 y and weight ≤45 kg: 2.2 mg/kg every 12 hours ≤8 y: 2.2 mg/kg every 12 hours</td>
<td>60 days</td>
</tr>
<tr>
<td>Pregnant women&lt;sup&gt;e&lt;/sup&gt;</td>
<td>Ciprofloxacin 500 mg twice daily or Doxycycline 100 mg twice daily</td>
<td>60 days</td>
</tr>
<tr>
<td>Immunocompromised persons</td>
<td>Same as for non-immunocompromised adults and children</td>
<td></td>
</tr>
</tbody>
</table>

<sup>a</sup> This table is adapted with permission from *Morbidity and Mortality Weekly Report*. Cutaneous anthrax with signs of systemic involvement, extensive edema, or lesions on the head or neck require intravenous therapy and a multidrug approach is recommended.

<sup>b</sup> Ciprofloxacin or doxycycline should be considered first-line therapy. Amoxicillin can be substituted if a patient cannot take a fluoroquinolone or tetracycline class drug. Adults are recommended to take the 500 mg of amoxicillin orally 3 times a day. For children, 80 kg/mg of amoxicillin can be divided into 3 doses in 8-hour increments is an option for completion of therapy after clinical improvement. Oral amoxicillin dose is based on the need to achieve appropriate minimum inhibitory concentration levels.

<sup>c</sup> Previous guidelines have suggested treating cutaneous anthrax for 7 to 10, but 60 days is recommended for bioterrorism attacks, given the likelihood of exposure to aerosolized *Bacillus anthracis*.

<sup>d</sup> The American Academy of Pediatrics recommends treatment of young children with tetracycline for serious infections (e.g., Rocky Mountain spotted fever).

<sup>e</sup> Although tetracyclines or ciprofloxacin are not recommended during pregnancy, their use may be indicated for life-threatening illnesses. In this setting, barring contraindications, ciprofloxacin would be preferred.