

Anthrax

1. DISEASE REPORTING

A. 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 context of a bioterrorist attack, and rapid implementation of control measures.

B. Laboratory and Physician Reporting Requirements

Immediate reporting of suspected anthrax infection by health care providers and within 24 hours by lab personnel.

C. Local Health Department Reporting and Follow-up Responsibilities

Notify OHS immediately of any suspected anthrax infection. Coordinate with OHS and other agencies as necessary to determine source of infection as well as to carry out tracing and prophylaxis of 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

A. Etiologic Agent

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

B. Description of Illness

Anthrax typically presents as one of 3 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 lymph channels, painful regional lymph node enlargement, and systemic symptoms can 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.

3. Gastrointestinal anthrax

Gastrointestinal anthrax is a rare form of the disease never documented 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.

C. Sources of Infection

Historically, Anthrax has come from contact with:

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

D. Modes of Transmission

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

E. Period of Communicability

Anthrax is not known to spread person-to-person.

F. Incubation period

- Inhalational: 2–60 days
- Cutaneous: 1–12 days
- Gastrointestinal: 3–7 days

G. Treatment

OHS/ACDP will get up-to-date information on treatment and prophylaxis to you p.r.n.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

A. Confirmed Case Definition

Clinically compatible illness (cutaneous, inhalational, or gastrointestinal) that was either:

1. lab confirmed by isolation of *B. anthracis* from a patient's clinical specimens, **or**
2. associated with other lab evidence of *B. anthracis* infection based on at least two supportive tests, such as PCR, time-resolved fluorescent antibody testing, or immunohistochemistry (IHC) staining.

B. Presumptive Case Definition

Clinically compatible illness in a person who:

1. shares a common exposure with a lab-confirmed case **or**
2. on lab examination has a Gram stain demonstrating large, encapsulated, Gram-negative rods or a culture from a sample other than a nasal swab that grows non-beta hemolytic, non-motile, catalase-positive colonies of characteristic morphology on sheep blood agar.

C. Suspect Case

A patient with a clinically compatible illness with no alternative diagnosis and no isolation of *B. anthracis*, but with either:

1. lab evidence of *B. anthracis* by one supportive lab test, **or**
2. an epidemiological link to an environmental *B. anthracis* exposure.

D. Services Available at the Oregon State Public Health Laboratory

OSPHL offers PCR and time-resolved fluorescence testing, each of which can provide rapid, presumptive diagnosis of anthrax. They can do confirmatory culture testing as well.

4. CASE INVESTIGATION

A. 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.

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B. 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. Develop a list of persons with suspected exposure, using:
 - a. interviews with those known to be exposed,
 - b. review of attendee lists of any functions where exposure is suspected to have occurred,
 - c. credit card receipts from such events, and
 - d. any other evidence available.
3. Contact all persons on list to assess for illness and to discuss possible prophylaxis.

5. CONTROLLING FURTHER SPREAD

A. 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.

B. Decontamination

Decontamination of buildings containing weaponized *B. anthracis* is not easy. Expert advice would be required.

C. Isolation

Not indicated.

D. 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, OHS 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

A. Response Following Discovery of a Suspicious Substance

1. Evaluation by local 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. 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

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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:

- a. Law enforcement concludes that there is no credible threat.
 - i. 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.
 - ii. Provide information/explanation of situation if requested.
 - iii. Consult with OHS/ACDP/Bioterrorism Response Team as needed to draft statements.
- b. Law enforcement concludes that there is a credible threat.
 - i. Law enforcement will retain custody of the suspicious substance.
 - ii. FBI will arrange for further evaluation, which may be done at state or federal labs.

B. Public Health Response in the Setting of a Credible Threat

1. Communicate periodically with OHS/ACDP/Bioterrorism Response Team to review available information.
2. ACDP should contact OSPHL, give them available information about the incident, and let them know that specimens will be arriving and when.
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 bioterrorist agents:
 - a. The analysis is negative (no biologic agent is detected).
 - i. Develop press release outlining the findings of the investigation and negative results of the laboratory analysis.
 - b. The analysis is positive (a biologic agent is detected).
 - i. OSPHL will notify OHS, FBI, and the Office of Emergency Management of the findings.
 - ii. OHS will inform the local health department.
 - iii. Press release will be developed (for presentation by people higher up the ladder than us) outlining the findings of the investigation so far and their implications.
 - iv. Pursue case investigation to identify people who have been exposed to the substance should be pursued as outlined in Section 4, “Case Investigation.”
 - v. OHS will coordinate with local health departments and emergency management personnel to arrange for prophylaxis as indicated.

See the following pages for treatment tables.

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Table 1

Recommended therapy for inhalational anthrax infection in the contained casualty setting ^{a,b}		
Category	Initial IV therapy ^{c,d}	Duration
Adults	Ciprofloxacin 400 mg every 12 hours or Doxycycline 100 mg every 12 hours ^f and 1 or 2 additional antimicrobials ^d	IV treatment initially ^e 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 ⁱ
Children	Ciprofloxacin 10-15 mg/kg every 12 hours ^{g,h} or Doxycycline ^{f,i} for those aged >8 y and weight >45 kg: 100 mg every 12 hours >8 y and weight ≤45 kg: 2.2 mg/kg every 12 hours ≤8 y: 2.2 mg/kg every 12 hours and 1 or 2 additional antimicrobials ^d	IV treatment initially ^e before switching to oral antimicrobial therapy when clinically appropriate: Ciprofloxacin 10-15 mg/kg every 12 hours ^h or Doxycycline for those aged >8 y and weight >45 kg: 100 mg twice daily >8 y and weight ≤45 kg: 2.2 mg/kg twice daily ≤8 y: 2.2 mg/kg twice daily Continue oral and IV treatment for 60 days ⁱ
Pregnant women	Same for nonpregnant adults	IV treatment initially ^e before switching to oral antimicrobial therapy when clinically appropriate ^b ; oral therapy regimens are the same for nonpregnant adults
Immunocompromised persons		Same for nonimmunocompromised adults and children
<p>a. This table is adapted with permission from <i>Morbidity and Mortality Weekly Report</i>. For gastrointestinal and oropharyngeal anthrax, use regimens recommended for inhalational anthrax.</p> <p>b. Ciprofloxacin or doxycycline should be considered an essential part of first-line therapy for inhalational anthrax.</p> <p>c. Steroids may be considered as an adjunct therapy for patients with severe edema and for meningitis based on experience with bacterial meningitis of other etiologies.</p> <p>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 <i>Bacillus anthracis</i>, penicillin and ampicillin should not be used alone. Consultation with an infectious disease specialist is advised.</p> <p>e. Initial therapy may be altered based on clinical course of the patient; 1 or 2 antimicrobial agents may be adequate as the patient improves.</p> <p>f. If meningitis is suspected, doxycycline may be less optimal because of poor central nervous system penetration.</p> <p>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 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.</p> <p>h. In children, ciprofloxacin dosage should not exceed 1 g/d.</p> <p>i. The American Academy of Pediatrics recommends treatment of young children with tetracyclines for serious infections (i.e., Rocky Mountain spotted fever).</p> <p>j. Because of the potential persistence of spores after an aerosol exposure, antimicrobial therapy should be continued for 60 days.</p> <p>k. Although tetracyclines are not recommended during pregnancy, their use may be indicated for life-threatening illness. Adverse effects on developing teeth and bones of fetus are dose related; therefore, doxycycline might be used for a short time (7–14 days) before 6 months of gestation. The high death rate from the infection outweighs the risk posed by the antimicrobial agent.</p>		

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Table 2

Recommended therapy for inhalational anthrax infection in the mass casualty setting or for postexposure prophylaxis ^a			
Category	Initial oral therapy ^b	Alternative therapy if strain is proved susceptible	Duration after exposure
Adults	Ciprofloxacin 500 mg orally every 12 hours	Doxycycline 100 mg orally every 12 hours ^c Amoxicillin 500 mg orally every 8 hours ^d	60 days
Children	Ciprofloxacin 20-30 mg/kg per d orally taken in 2 daily doses, not to exceed 1 g/d ^e	Weight \geq 20 kg: Amoxicillin 500 mg orally every 8 hours ^d Weight <20 kg: Amoxicillin 40 mg/kg orally in 3 doses every 8 hours ^d	60 days
Pregnant women ^f	Ciprofloxacin 500 mg orally every 12 hours	Amoxicillin 500 mg orally every 8 hours ^d	60 days
Immunosuppressed persons		Same for nonimmunosuppressed adults and children	
<p>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.</p> <p>b. In vitro studies suggest ofloxacin (400 mg orally every 12 hours, or levofloxacin, 500mg orally every 24 hours) could be substituted for ciprofloxacin.</p> <p>c. In vitro studies suggest that 500mg of tetracycline orally every 6 hours could be substituted for doxycycline. In addition, 400mg of gatifloxacin or monifloxacin, both fluoroquinolones with mechanisms of action consistent with ciprofloxacin, taken orally daily could be substituted.</p> <p>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 <18years or intolerance of other antibiotics).</p> <p>e. Doxycycline could also be used if antibiotic susceptibility testing, exhaustion of drug supplies, adverse reactions preclude use of ciprofloxacin. For children heavier than 45 kg, adult dosage should be used. For children lighter than 45 kg, 2.5 mg/1g of doxycycline orally every 12 hours should be used.</p> <p>f. See 'Management of Pregnant Population' for details.</p>			

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Table 3

Recommended therapy for cutaneous anthrax infection associated with a bioterrorism attack^a		
Category	Initial oral therapy^b	Duration^c
Adults	Ciprofloxacin 500 mg twice daily ^b or Doxycycline 100 mg twice daily ^b	60 days
Children^d	Ciprofloxacin 10–15 mg/kg every 12 hours (not to exceed 1 g/d) ^b or Doxycycline for those aged ^d >8 y and weight >45 kg: 100 mg every 12 hours >8 y and weight ≤45 kg: 2.2 mg/kg every 12 hours ≤8 y: 2.2 mg/kg every 12 hours	60 days
Pregnant women^e	Ciprofloxacin 500 mg twice daily or Doxycycline 100 mg twice daily	60 days
Immuno-compromised persons	Same for nonimmunocompromised adults and children	
<p>a. This table is adapted with permission from the <i>Morbidity and Mortality Weekly Report</i>. 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.</p> <p>b. 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 500 mg of amoxicillin orally 3 times a day. For children, 80 mg/kg of amoxicillin to 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.</p> <p>c. Previous guidelines have suggested treating cutaneous anthrax for 7 to 10 days, but 60 days is recommended for bioterrorism attacks, given the likelihood of exposure to aerosolized <i>Bacillus anthracis</i>.</p> <p>d. The American Academy of Pediatrics recommends treatment of young children with tetracyclines for serious infections (e.g., Rocky Mountain spotted fever).</p> <p>e. Although tetracyclines or ciprofloxacin is not recommended during pregnancy, their use may be indicated for life-threatening illness. Adverse effects on developing teeth and bones of a fetus are dose related; therefore, doxycycline might be used for a short time (7-14 days) before 6 months of gestation.</p>		