ANTHRAX PROPHYLAXIS (BIOTERRORISM)

I. DEFINITION:
A. Presentation: Anthrax is an acute infectious disease caused by the spore-forming bacterium *Bacillus anthracis*. Anthrax is a disease of warm-blooded animals that can infect humans. Symptoms and incubation period vary depending on how the disease was contracted. Anthrax infection can occur in four forms: inhalational, cutaneous (skin), gastrointestinal and injection. Person-to-person spread of anthrax most likely does not occur. Severe disease causes shock, hemorrhagic meningitis and multi-organ failure.

B. Occurrence: Although anthrax can be found anywhere in the world, it is most common in agricultural regions where it occurs in wild and domestic animals, including, cattle, sheep, goats, camels, antelopes and other herbivores. Areas of the world currently listed as high risk are South and Central America, southern and eastern Europe, central and southwestern Asia, sub-Saharan Africa, and the Caribbean.

C. Bioterrorism agent: *B. anthracis* is considered a potential bioterrorism (BT) agent, and CDC has classified anthrax as a category A biological warfare agent. If the OSDH is responding to a large-scale BT event where individuals may have been exposed to anthrax, updated/current post-exposure prophylaxis (PEP) guidance will be distributed through the appropriate chain of command.

II. CLINICAL FORMS:
A. Inhalational (also known as pulmonary):

Inhalational anthrax is the most lethal form of anthrax and results from inhalation of spores of *Bacillus anthracis*. Inhalational anthrax is the most likely scenario in a BT event. Symptoms begin with a brief prodrome resembling a viral respiratory illness and may include fever, malaise, and mild cough or chest pain, followed over 3 – 4 days by development of hypoxia and dyspnea, with radiographic evidence of mediastinal widening, and death shortly thereafter. The incubation period of inhalational anthrax among humans typically ranges from 1 - 43 days but may occur up to 60 days. Host factors, infectious dose, and chemoprophylaxis may affect the length of the incubation period. Case-fatality estimates for inhalation anthrax are greater than 85%, however early diagnosis with initiation of aggressive therapy may reduce mortality.

B. Cutaneous:

Cutaneous anthrax follows deposition of the organism onto the skin, occurring most often on exposed areas of the hands, arms, or face. Risk is increased when broken skin is present prior to the exposure. An area of local edema becomes a pruritic macule or papule, which enlarges and ulcerates with black eschar after 2 - 6 days. Small, 1-3 mm vesicles may surround the ulcer. A painless, depressed, black eschar usually with surrounding moderate to severe edema subsequently develops. Clients may also have fever, malaise, headache, and regional lymphadenopathy, and can progress to septicemia. The incubation period for cutaneous disease is reported to be 1 - 12 days. More than 95% of all naturally occurring anthrax infections worldwide are cutaneous. The case fatality rate for cutaneous anthrax is 5 - 20% without, and <1% with, antibiotic treatment.
C. Gastrointestinal:

Gastrointestinal anthrax is caused by consuming raw or undercooked contaminated meat from an anthrax-infected animal. It is characterized by severe abdominal pain, nausea and vomiting, followed by fever and signs of septicemia. Gastrointestinal anthrax has an incubation period of 1 - 6 days. An oropharyngeal form is less common, and is characterized by lesions, necrotic ulcers and swelling in the oropharynx and neck. Lower bowel inflammation typically causes nausea, loss of appetite, and fever followed by abdominal pain, hematemesis, and bloody diarrhea. The case fatality rate is estimated to be 40%. The effect of early antibiotic treatment on the case-fatality rate is not established.

D. Injection:

Injection-related anthrax has been recognized in northern Europe since 2009, and has been attributed to contaminated heroin. Injection anthrax is more severe than cutaneous anthrax, and symptoms may be more similar to systemic anthrax infection. Symptoms include severe soft tissue infection, significant soft tissue edema, compartment syndrome and/or necrotizing fasciitis. Eschar may not be present.

III. MANAGEMENT:

A. Place client information in PHOCIS and open a limited service record (Consent for Service, ODH 303C, Progress note, ODH 303G and PHOCIS demographic print out).

B. Initial screening of clients during a BT event:

1. Asymptomatic client WITHOUT known exposure to anthrax
   a. Educate the client about the rarity of infection without known exposure.
   b. Explain that there is no screening test available for the detection of anthrax infection in an asymptomatic person.
   c. Provide client with anthrax fact sheet.

2. Asymptomatic client WITH known/suspected exposure to anthrax during/following a bioterrorism event
   a. Perform decontamination per established protocol.
   b. Conduct an individual risk assessment based on the current scenario, and consult with the Acute Disease Service (ADS) Epidemiologist-on-Call at (405) 271-4060 to determine if post-exposure prophylaxis (PEP) is recommended.
   c. In the case of *B. anthracis* exposure associated with a BT event, the CDC has recommended the following measures for decontamination of patients:
      - Remove contaminated clothing carefully
      - Store clothing in labeled plastic bags
      - Handle clothing minimally to avoid agitation
      - Instruct patients to shower thoroughly with soap and water
3. **Post-exposure Prophylaxis (PEP) Recommendations:**

   a. Consult with Acute Disease Service (ADS) Epidemiologist-on-Call at (405) 271-4060 to determine if PEP is recommended. If a known/suspected BT event has occurred, follow guidance established for that event, and consult the ADS epi-on-call if needed.

   b. PEP is used when a BT event is suspected or confirmed, and the client is likely to have been exposed. **Prescribing of PEP without credible evidence of an exposure is not indicated.** See the table in this document below to determine which antibiotic to issue.

   Post-exposure prophylaxis for inhalation anthrax involves BOTH antibiotics and anthrax vaccination.

   1) Oral antimicrobial agents approved by the US FDA and recommended by CDC for anthrax PEP include ciprofloxacin, doxycycline, levofloxacin, moxifloxacin, clindamycin, amoxicillin and penicillin (see table). The recommended duration of PEP antimicrobial therapy is 60 days, regardless of anthrax vaccination history. **In the event of a large scale event, a 10 day supply of medication may be provided at the initial visit to the dispensing site.**

      a) Clinicians may choose to use oral amoxicillin as an alternative for PEP for certain patient groups (e.g., children, pregnant or nursing women) if the associated strain is sensitive to amoxicillin (MIC ≤0.125 mcg/mL)

      b) Ciprofloxacin is preferred over doxycycline for first-line anthrax PEP for pregnant, postpartum, and lactating women.

   2) In the post-exposure setting, ACIP recommends that anthrax vaccine (Anthrax Vaccine Absorbed or AVA) be administered in three subcutaneous doses (at 0, 2, and 4 weeks) in conjunction with a 60 day course of antimicrobial therapy.

   3) ACIP recommends the use of AVA for both pregnant and lactating women, as well as the consideration of vaccine use among children exposed to *B. anthracis* spores.

   c. Raxibacumab is a monoclonal antibody that neutralizes *B. anthracis* toxins, and can be used as treatment or prophylaxis of inhalational anthrax when alternative preventive therapies are not available or are not appropriate. Raxibacumab is given as a single dose following premedication with diphenhydramine. A supply of raxibacumab, is held in the US Strategic National Stockpile (SNS) for use by the CDC in the event of an anthrax emergency. It is not included in routine mass PEP recommendations.

   d. Anthrax is not spread from person to person, therefore, PEP is not recommended for family members or other personal contacts of exposed persons unless they were similarly exposed.

   e. During Mass Antibiotic Prophylaxis Clinics, when possible, all family members should receive the same medications. For example, if one family member is allergic to ciprofloxacin, but all family members can take doxycycline, then all family members would receive doxycycline, the secondary drug of choice. It is important to note that this might not be possible with a family with multiple drug allergies and issues.
f. If antibiotics are in limited supply the State Health Officer or designee will determine the number of doses to be issued. The remainder of the doses to cover 60 days of treatment will be issued as soon as supplies allow.

4. Symptomatic clients with or without potential or known exposure are to be referred to their health care provider for diagnosis and treatment. Identification of symptomatic clients is to be immediately reported to the ADS Epidemiologist-on-Call at (405) 271-4060 for investigation.

C. Counseling and Education:

At time of issuance of oral antibiotics, it is important that clients are provided with educational materials and counseled that all medications may have undesirable side effects. It is critical that clients inform the public health nurse of any troublesome reactions and NOT discontinue the antibiotic prophylaxis without medical consult.
<table>
<thead>
<tr>
<th>Population</th>
<th>Antimicrobials for 60-day duration* PEP</th>
<th>AVA dosage</th>
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<tbody>
<tr>
<td>Adults (18-65 years)</td>
<td><strong>Ciprofloxacin</strong>, 500 mg every 12 hours for 60 days OR <strong>Doxycycline</strong>, 100 mg every 12 hours for 60 days</td>
<td>3-dose subcutaneous (SC) series: first dose administered as soon as possible, second and third doses administered 2 and 4 weeks after the first dose</td>
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<td></td>
<td>A 10 day supply of medication will be provided at the initial visit to the dispensing site. Note: ciprofloxacin is preferred over doxycycline for first-line anthrax PEP</td>
<td>Recommendations for use of AVA in children are made on an event-by-event basis</td>
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</tbody>
</table>
| Children (one month of age and older)**      | **Ciprofloxacin**<br>
\* < 31 kg (67 lb.): 15 mg/kg every 12 hours for 60 days OR<br>
\* > 31 kg (67 lb.): give 500 mg PO every 12 hours for 60 days<br>
Not to exceed 500 mg/dose or 1 g daily OR<br>
** Doxycycline**<br>
\* < 35 kg (76 lb.): 2.2 mg/kg every 12 hours for 60 days (not to exceed 100 mg/dose) OR<br>
\* > 35 kg (76 lb.): 100 mg/dose every 12 hours for 60 days. Not to exceed 100 mg/dose or 200 mg daily<br>
A 10 day supply of medication will be provided at the initial visit to the dispensing site. | Recommendations for use of AVA in children are made on an event-by-event basis |
| Pregnant Women** and breastfeeding mothers   | **One of the following for 60 days:**<br>
\* Ciprofloxacin, 500 mg orally twice daily<br>
A 10 day supply of medication will be provided at the initial visit to the dispensing site. | Recommendations for use of AVA in children are made on an event-by-event basis |
|                                              | **Doxycycline**, 100 mg orally twice daily<br>
Amoxicillin**, 500 mg orally every 8 hours | 3-dose subcutaneous (SC) series: first dose administered as soon as possible, second and third doses administered 2 and 4 weeks after the first dose |

*Preferred drugs are indicated in **boldface.** Alternative drugs are listed in order of preference for treatment for patients who cannot take first-line treatment or if first-line treatment is unavailable.

Table: Recommended oral antimicrobial agent and anthrax vaccine adsorbed (AVA) dosages for Post-exposure prophylaxis (PEP) after exposure to aerosolized *Bacillus anthracis* spores

**Note:** Doses are provided for children with normal renal and hepatic function. Doses may vary for those with some degree of organ failure.

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* Based on in vitro susceptibility data rather than studies of clinical efficacy.

†Antimicrobials should continue for 14 days after administration of the third dose of vaccine.

‡Levofloxacin is a second-line antimicrobial agent for PEP for persons aged ≥6 months with medical issues (e.g., tolerance or resistance to ciprofloxacin) that indicate its use. Safety data on extended use of levofloxacin in any population for >28 days are limited; therefore, levofloxacin PEP should only be used when the benefit outweighs the risk.

††Use of tetracyclines and fluoroquinolones in children can have adverse effects. These effects must be weighed carefully against the risk for developing life-threatening disease. If exposure to B. anthracis is confirmed, children may be treated initially with ciprofloxacin or doxycycline as prophylaxis. However, amoxicillin is preferred for antimicrobial PEP in children when susceptibility testing indicates that the B. anthracis isolate is susceptible to penicillins.

§§In 1991, The American Academy of Pediatrics (AAP) amended the recommendation to allow treatment of young children with tetracyclines for serious infections such as Rocky Mountain spotted fever for which doxycycline might be indicated. Doxycycline is preferred for its twice daily dosage and low incidence of gastrointestinal side effects.

***If susceptibility testing demonstrates an amoxicillin MIC ≤0.125 μg/mL, oral amoxicillin should be used to complete therapy.

The antimicrobial choice for initial prophylactic therapy among pregnant women is ciprofloxacin. Doxycycline should be used with caution in asymptomatic pregnant women and only when other appropriate antimicrobial drugs are contraindicated. Although tetracyclines are not recommended during pregnancy, their use might be indicated for life-threatening illness.

REFERENCES:


Anthrax Post Exposure Prophylaxis Screening Questionnaire and Algorithm

### Doxycycline Dominant Dispensing Algorithm

**Evaluate for Doxycycline**

- **Is this person allergic to Doxycycline, Tetracycline, or any other “cycline” drugs?**
- **Is this person Pregnant?**

  - All “no”

  - **Does this person have difficulty swallowing pills?**
    - **Is this person both <76 lbs. & < 18 years of age?**
      - All “no”

  - **Dispense Doxycycline & FDA approved Doxycycline fact sheet**

**Evaluate for Ciprofloxacin**

- **Is this person allergic Ciprofloxacin, Levoquin or any other “floxacin” drug?**
- **Does this person have seizure disorder or epilepsy?**
- **Is this person currently taking Tizanidine (Zanaflex)?**
- **Is this person both <76 lbs. & < 18 years of age?**
- **Does this person have difficulty swallowing pills?**

  - All “no”

  - **Dispense Ciprofloxacin & FDA approved Ciprofloxacin fact sheet**

- **“Yes” to any**

  - **Refer to clinician**

  - **Dispense Doxycycline & FDA approved Doxycycline fact sheet and include the following:**
    - FDA Pamphlet on preparing doxycycline for children and adults who cannot swallow pills.