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MEDICAL TREATMENT AND RESPONSE TO SUSPECTED
ANTHRAX:
INFORMATION FOR HEALTH CARE PROVIDERS
DURING BIOLOGIC EMERGENCIES

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The Purpose of this document is to provide New York City medical care providers with diagnostic and patient management information regarding anthrax:

ALL SUSPECT CASES OF ANTHRAX MUST BE REPORTED IMMEDIATELY TO THE NEW YORK CITY DEPARTMENT OF HEALTH COMMUNICABLE DISEASE PROGRAM

During Business Hours: Please call one of the following temporary numbers:
(212) 295-5658, (212) 295-5671, (212) 295- 5670, and (212) 295- 5665
After Hours: Please call the Poison Control Center: (212)764-7667 or (800) 222-1222

I. KEY SUMMARY POINTS

- Epidemiology:**
- Anthrax can be transmitted by inhalation, ingestion or direct inoculation into the skin.
 - The spore form of anthrax is highly resistant to physical and chemical agents; spores can persist in the environment for years.
 - Inhalational anthrax is not transmitted person-to-person. There is a potential risk of secondary infection with cutaneous anthrax if there is direct contact with drainage from an open sore.
- Clinical:**
(Inhalational)
- Inhalational anthrax presents as acute hemorrhagic mediastinitis.
 - Biphasic illness, with initial phase characterized by nonspecific flu-like illness followed by acute phase characterized by severe respiratory distress and toxemia (sepsis).
 - Incubation period is 1-5 days (may be as long as 60 days).
 - Chest x-ray findings: **Mediastinal widening in a previously healthy febrile patient is highly suggestive of anthrax.**
 - Mortality rate for inhalational anthrax may approach 90%, unless appropriate antibiotic treatment is initiated within the first few days of illness.

Diagnosis:

- Gram stain shows gram-positive bacilli, occurring singly or in chains, often with squared off ends. In advanced disease, a gram stain of unspun blood may be positive.
- Distinguishing characteristics on culture include: non-hemolytic, non-motile, encapsulated bacteria that are susceptible to gamma phage lysis
- Confirmatory testing is available at the New York City Department of Health (NYC DOH) Public Health Laboratories and at other national reference laboratories.
- Clinical laboratory specimens should be handled in Biosafety Level 2 facilities.

Treatment:

- Prompt initiation of antibiotic therapy is essential.
- Antibiotic susceptibility testing is KEY to guiding treatment; susceptibility testing is currently only available through the CDC.
- Ciprofloxacin, or any other quinolone used for treatment of pulmonary infections, is the antibiotic of choice if the isolate is resistant to penicillins and tetracyclines or for empiric therapy while awaiting susceptibility results (alternative: doxycycline). Multi-drug regimens are recommended for inhalational and severe cutaneous anthrax infections, with either ciprofloxacin or doxycycline being the primary medication, *plus* one or more of the following: penicillin, ampicillin, imipenem, rifampin, clindamycin, vancomycin, chloramphenicol, or clarithromycin.
- Females who are pregnant (or who think that they might be pregnant) and children less than 8 years old also should be treated empirically with a quinolone (alternative: doxycycline), while awaiting susceptibility results.
- Antibiotic treatment should continue for 60 days for inhalational anthrax or for a cutaneous case that occurred after aerosol exposure.

Prophylaxis:

(Indicated for prevention of inhalational disease after an aerosol exposure)

- Start antibiotic prophylaxis immediately after exposure with either ciprofloxacin (or other quinolone used for treatment of pulmonary infections) or doxycycline. (If strain is penicillin-susceptible, without evidence of penicillinase activity, therapy can be switched to penicillin or amoxicillin.) Prophylaxis should continue for 60 days.

Patient Isolation:

- Standard precautions. Patients with anthrax of any form do not require isolation rooms.

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II. Introduction/Epidemiology

Anthrax is a disease caused by *Bacillus anthracis*, which can infect many warm-blooded animals, including humans. Transmission usually occurs through contact with infected animals (herbivores, such as cows, sheep or goats) or contaminated animal products. Humans become infected by inoculation, inhalation, or ingestion of the bacterium, resulting primarily in infections of the skin and rarely, the lungs or the gastrointestinal tract. The bacillus produces a resistant spore that could be dispersed as a small particle aerosol. **In the event of a biologic terrorist attack, aerosolization is a likely mode of transmission, and inhalational anthrax would be the predominant form of disease affecting persons exposed to the aerosol.** However, the 2001 outbreak of intentional anthrax also involved cutaneous anthrax due to direct contact with threat letters contaminated with anthrax spores.

The spore form of *B. anthracis* is highly resistant to physical and chemical agents. The organism has been shown to persist for years in factories contaminated during the processing of infected animal products. Soil is a major reservoir for anthrax spores in areas where animal outbreaks have occurred.

Although human anthrax is infrequent and sporadic in the United States and most other industrialized countries, human cases (primarily cutaneous) continue to be reported from Africa, Asia, Europe, and the Americas. Although anthrax-contaminated soil exists in many foci throughout the United States, the number of cases reported annually has declined throughout the last five decades; 6 human cases (all cutaneous anthrax) were reported between 1981-2000. Two naturally occurring cutaneous cases were reported in the United States in 2001; both were associated with animal exposure. Prior to the 2001 outbreak of intentional anthrax, the last inhalational case in the United States occurred in 1978. There had been no reports of anthrax in New York City in over 50 years until the intentional outbreak of cutaneous anthrax in 2001.

A suspected case of anthrax in a patient without a clear exposure history (e.g., no travel to an area with endemic anthrax, or no exposure to imported animal products) may be the first clue of a bioterrorist attack. Even a single, suspect case should prompt immediate notification of the Communicable Disease Program: (phone numbers listed above).

Person-to-person transmission of anthrax is extremely rare, and has only been suggested in cutaneous anthrax with a potential risk of secondary infection if there is direct contact with drainage from an open sore. Person-to-person transmission of inhalational anthrax has never been reported.

III. Significance as a Potential Bioterrorist Agent

- ◆ Anthrax has been weaponized by several countries during the last 50 years. (United States, former Soviet Union, Iraq)
- ◆ Anthrax is easy to cultivate and spores are readily produced; however, production of weapons-grade anthrax spore requires technical sophistication to ensure a high proportion of spores within the 1-5 micron size required to reach the alveoli and terminal bronchioles.
- ◆ Anthrax spores are highly resistant to heat and disinfection.
- ◆ If aerosolized spores are inhaled, a severe hemorrhagic mediastinitis with accompanying sepsis, can occur with mortality rates in advanced disease approaching 90%, unless appropriate treatment is initiated within the first few days of illness.
- ◆ Currently, anthrax vaccine is in limited supply in the United States and generally not available to the public.
- ◆ Anthrax has now been successfully used in the United States as a biologic weapon. The perpetrators have not yet been apprehended, so there is a risk of continued attacks in the future.

IV. Clinical Manifestations

During an act of bioterrorism, release of an aerosol would be the route of transmission with the highest potential morbidity and mortality. Most exposed individuals would likely present with symptoms of inhalational anthrax with only a few, if any, having the cutaneous form of the disease. Gastrointestinal anthrax would be much less likely, unless a food or beverage item was contaminated with a significant number of anthrax spores.

Inhalational Anthrax presents as acute hemorrhagic mediastinitis (often with pleural effusions) after inhalation of airborne particles contaminated with *B. anthracis* spores.

Incubation period - illness usually occurs within 1-5 days of exposure (may be as long as 60 days). In the 2001 intentional outbreak due to letters contaminated with anthrax spores, the median incubation period from time of exposure to onset of symptoms was 4 days (range 4-7 days).

Symptoms - Typically biphasic illness

Initial Phase is characterized by flu-like symptoms:

- mild, nonspecific respiratory illness
- malaise, fatigue, myalgia, headache
- low-grade fever, drenching sweats
- nonproductive cough
- chest tightness or discomfort
- rhonchi may be heard; exam otherwise normal

Acute Phase develops after 2-5 days, it may be preceded briefly by 1 -2 days of improvement (although this was not reported among the 10 inhalational cases associated with the 2001 intentional outbreak).

Characteristic findings include:

- Acute, severe respiratory distress
- high fever or hypothermic shock
- dyspnea, cyanosis, stridor and profuse diaphoresis
- subcutaneous edema of chest and neck
- moist crepitant rales
- pleural effusions, may be hemorrhagic
- x-ray findings: **mediastinal widening in an otherwise healthy, febrile person is a highly suggestive sign**; pleural effusions are often present. In previous outbreaks, pulmonary infiltrates were rare. However, 7 of the 10 cases in the 2001 intentional outbreak had infiltrates present on chest radiography.

Shock develops rapidly, sometimes accompanied by evidence of hemorrhagic meningitis, and patients usually die within 24 hours of onset of the acute phase. In prior outbreaks, mortality rates approached 90% despite appropriate antibiotic therapy. In the 2001 outbreak, the case fatality rate was 40%; surviving patients all received combination antibiotic therapy effective against *B. anthracis* within the first 5 days of illness onset.

The differential diagnosis of acute mediastinitis includes: esophageal perforation; trauma; contiguous spread from a head, neck or thoracic infection; and post-surgical infections after cardiothoracic procedures.

Anthrax should be strongly considered in any previously healthy patient with acute mediastinitis, especially in the absence of a recent history of chest or upper gastrointestinal trauma or surgery.

Early Symptoms of Inhalational Anthrax among 2001 Outbreak-related Cases

The 10 cases of inhalational anthrax in the United States during the 2001 intentional outbreak all had prodromal illnesses lasting 3-7 days before being admitted to a hospital. While initial symptoms varied, all 10 cases reported chills and fever and a feeling of fatigue and/or malaise.

Other common early pre-hospitalization symptoms included:

- Minimal or nonproductive cough in 90%
- Shortness of breath in 80%
- Nausea or vomiting in 80%
- Chest discomfort/pleuritic pain in 60%
- Headache in 50%

Less common symptoms included:

- Sore throat in 20%
- Rhinorrhea in 10%

Lastly, on admission, a common finding among the 2001 inhalational anthrax cases was a rapid heart rate out of proportion to the patient's temperature.

Inhalational anthrax can often be clinically distinguished from common respiratory viruses such as influenza. Persons with common respiratory viruses rarely report shortness of breath (6% of cases), but they often have upper respiratory symptoms such as sore throat (64-84% of cases) and rhinorrhea (68-79% of cases). In addition, chest x-rays are more likely to be normal among persons with respiratory viral infections.

The diagnosis of inhalational anthrax requires a very high index of suspicion, most often based on epidemiologic evidence of a potential exposure. In the initial stages after a bioterrorist attack, a recognized source of exposure would likely be absent -- clinical suspicion is of utmost importance.

Cutaneous Anthrax: characterized by the development of a rapidly progressing ulcer with a black scab known as an eschar, often surrounded by significant edema and erythema.

Incubation period - ranges from 1-15 days but is commonly < 7 days

Symptoms - an evolving skin lesion, usually located on the exposed parts of the body (face, neck, arms), with a varying degree of associated edema. The skin lesion typically progresses as follows:

Small, painless, pruritic papule \equiv small ring of vesicles that coalesce into a single large vesicle \equiv within 1-2 days, the vesicle ruptures to form depressed ulcer \equiv 1-3 cm blackened eschar develops in center (3-10 days from onset of lesion) \equiv eschar falls off (after 1-2 weeks) leaving a permanent scar. The lesion is usually painless and the surrounding tissue is often erythematous and markedly edematous.

The primary differential diagnosis is a spider bite; however, spider bites, such as from brown recluse spiders are usually quite painful unlike cutaneous anthrax lesions.

The cutaneous lesion may be accompanied by systemic symptoms including fever, headache, myalgias, and regional lymphangitis/lymphadenopathy. Lesions on the face and neck may be associated with significant edema and impingement of the trachea from neck swelling can occur. "Malignant edema" describes a syndrome with marked edema, induration and multiple bullae at the site of inoculation associated with generalized toxemia. Septicemia is rare. Untreated cutaneous anthrax has a case fatality rate up to 20%, but fatalities are rare (< 1%) with effective antibiotic treatment.

Gastrointestinal Anthrax: occurs after the ingestion of contaminated uncooked food, particularly raw or undercooked meat from infected animals. There has never been a case of gastrointestinal anthrax reported in the United States.

Incubation period - ranges from 2-7 days

Symptoms - Two clinical presentations, intestinal and oropharyngeal, have been described. The symptoms of intestinal anthrax are initially nonspecific and include nausea, vomiting, anorexia and fever. As the disease progresses, severe abdominal pain, hematemesis and bloody diarrhea develop, occasionally accompanied by ascites. The patient may present with the findings of an acute surgical abdomen. Oropharyngeal anthrax is associated with cervical edema and necrosis. A lesion, resembling a cutaneous anthrax lesion, may be seen in the oral cavity on the posterior wall, the hard palate or the tonsils. Patients typically complain of fever, dysphagia and lymphadenopathy. Toxemia, shock and cyanosis characterize the terminal stages of both forms of the disease. The case fatality rate for gastrointestinal anthrax ranges from 25 to 60%.

Meningitis: Meningitis occurs in less than 5% of cases, and may be a complication of any form of anthrax (inhalational, gastrointestinal or cutaneous). It is usually hemorrhagic, and rarely presents without a primary focus.

Incubation period - concurrent with, or one to several days after the onset of cutaneous, inhalational or gastrointestinal anthrax.

Symptoms - abrupt onset of meningeal symptoms including nausea, vomiting, myalgia, chills and dizziness. Laboratory findings are notable for a hemorrhagic meningitis. Encephalomyelitis and cortical hemorrhages have been reported; death occurs in 1-6 days.

V. Laboratory Diagnosis

Laboratory work with clinical specimens must be done under Biosafety Level 2 conditions. If infection with *Bacillus anthracis* is suspected, please immediately call the Communicable Disease Program to arrange for submission of specimens to an appropriate reference laboratory for confirmatory testing.

Culture is the definitive test for anthrax.

Bacillus anthracis can be isolated from blood, pleural fluid, CSF, ascitic fluid, vesicular fluid or lesion exudate. Sputum cultures are rarely positive. When culturing a lesion, collect either vesicular fluid or exudate from the ulcer. If there is no visible exudate, lift the edge of the eschar with a pair of forceps and collect the fluid near the edge. Cultures of a cutaneous lesion are most likely to be positive if obtained early in the course of illness, and prior to the initiation of antibiotics.

Blood cultures may be positive for bacterial growth in 12-48 hours using standard culture media; however, the ability of most clinical microbiology laboratories to definitively identify *B. anthracis* may be limited. Many automated identification systems cannot identify this organism.

Microscopy

< **Gram stain**

< Gram stain should be performed on vesicular fluid or exudate from ulcerative lesions for suspected cutaneous anthrax, pleural fluid for suspected inhalational anthrax, and CSF for suspected meningial anthrax. **In advanced disease, a gram stain of unspun blood may be positive.** The Gram stain shows large, gram positive bacilli, usually occurring singly or in chains, often with squared-off ends.

< **Direct Fluorescent Antibody (DFA) Test**

< Rapid diagnostic staining technique for cell wall and capsular antigens. This test has been used to examine exudate from cutaneous lesions, CSF and tissue and to confirm anthrax in a culture of a suspicious *Bacillus species*. It generally would not be helpful for inhalational anthrax because respiratory/pleural fluid specimens are usually negative in the early stages of disease when rapid diagnosis is most critical. This test is currently available only at national, state and local public health reference laboratories, such as the NYC DOH Public Health Laboratory.

< **Rapid diagnostic tests**

- < An ELISA assay for antibodies against protective antigen and PCR for detection of nucleic acid can provide a preliminary diagnosis of anthrax within several hours. Currently, serologic testing and PCR testing are available at CDC; the NYCDOH will facilitate specimen shipments through the NYC Public Health Laboratory.

Evaluation of a Blood Culture that is Suspicious for Anthrax: The following summarized the steps needed to presumptively identify anthrax, and its morphological and chemical characteristics in the microbiology laboratory:

- Overnight incubation on a blood or nutrient agar isolation plate
- Gram stain shows large gram positive rods with square or concave ends
- Blood agar colonies are non-hemolytic, rough, gray-white, tenacious colonies with comma-shaped protrusions
- Subculture to blood agar plates to test for lysis with gamma phage and penicillin susceptibility. (**NOTE: Although naturally-occurring anthrax is penicillin-sensitive, in the event of a bioterrorist event, an anthrax strain resistant to penicillin may have been released.**)
- Test for lack of growth on phenylethyl alcohol blood agar, lack of gelatin hydrolysis, and lack of salicin fermentation
- The bacterial capsule can be demonstrated on nutrient agar containing 0.7% sodium bicarbonate incubated overnight in a candle jar. Examine for capsule with methylene blue or India ink.

To distinguish *Bacillus anthracis* from other *Bacillus species*: Distinguishing features include that *Bacillus anthracis* is non-hemolytic, non-motile, encapsulated and susceptible to gamma phage lysis.

Summary: *Bacillus anthracis* is a gram positive bacillus that is white or gray in color, nonhemolytic or weakly so, nonmotile, gamma phage susceptible and usually penicillin susceptible, and able to produce the characteristic capsule.

Serology - not helpful for rapidly establishing the diagnosis during the acute illness as paired sera is required; with acute specimen obtained within 5 days of onset and convalescent sera obtained 2 weeks after the acute specimen.

Autopsy Findings - identifying thoracic hemorrhagic necrotizing lymphadenitis and hemorrhagic necrotizing mediastinitis in a previously healthy patient is highly suggestive of inhalational anthrax. Hemorrhagic meningitis would also be a distinct clue to the diagnosis of anthrax.

****NOTE: In the context of a bioterrorist event, the anthrax strain may be penicillin-resistant. There are currently no NCCLS standards for susceptibility testing for *B. anthracis*. As soon as *B. anthracis* is suspected or identified, microbiology laboratories must immediately alert the Communicable Disease Program at 212-295-5658 or 212-295-5665 and the NYC DOH Bioterrorism Laboratory at (212) 447-6907 or (212) 444-6941. After hours, please call the Poison Control Center: (212) 764-7667.**

Confirmatory and susceptibility testing will be arranged at the CDC. The results of susceptibility testing are crucial in guiding both therapy and prophylaxis for potentially infected persons.

VI. Handling Laboratory Specimens

Biosafety Level 2 practices, containment equipment and facilities are recommended for procedures on clinical materials suspected as being positive for anthrax (vegetative form of *Bacillus anthracis*). However, a Biosafety Level 3 laboratory is required for handling anthrax spores ((e.g., *contaminated powders*)). Laboratory staff handling specimens from persons who might have anthrax are recommended to wear surgical gloves, protective gowns and shoe covers. Laboratory tests should be performed in Biological Safety Level 2 cabinets and blood cultures should be maintained in a closed system. Every effort should be made to avoid splashing or creating an aerosol, and protective eye wear and masks should be worn if work cannot be done in a Biological Safety Level 2 cabinet. A full-face mask respirator with a HEPA (high efficiency particulate air) filter is an acceptable alternative to masks and protective eye wear.

Accidental spills of potentially contaminated material should be decontaminated immediately by covering liberally with a disinfectant solution (5% hypochlorite or other OSHA-approved solutions), **left to soak for 30 minutes**, and wiped up with absorbent material soaked in disinfectant. All biohazardous waste should be decontaminated by autoclaving. Contaminated equipment or instruments may be decontaminated with a hypochlorite solution, hydrogen peroxide, iodine, peracetic acid, 1% glutaraldehyde solution, formaldehyde, ethylene oxide, copper irradiation or other OSHA-approved solutions, or by autoclaving or boiling for 10 minutes.

VII. Treatment

The key to successful treatment is prompt administration of an effective antibiotic regimen at the first suspicion of anthrax. During a biologic emergency, before susceptibility is determined (which may take several days), assume penicillin- and tetracycline-resistance and treat empirically with intravenous ciprofloxacin, in combination with at least one or more of the following antibiotics: penicillin, ampicillin, imipenem, rifampin, clindamycin, vancomycin, chloramphenicol, or clarithromycin. Although not yet FDA approved, other quinolones used for treatment of pulmonary infections (e.g., ofloxacin or levofloxacin) would be reasonable alternatives. Penicillin is the antibiotic of choice for treating infections with penicillin-sensitive anthrax, if there is no evidence of penicillinase activity.

Treatment for Non-Pregnant Adults:

INHALATIONAL AND GASTROINTESTINAL ANTHRAX:

For **penicillin-resistant anthrax and initial empiric therapy**, administer ciprofloxacin at 400 mg IV every 8 to 12 hours (Although not yet FDA approved for treatment of anthrax, alternative quinolone options include: ofloxacin 400 mg IV every 12 hours or levofloxacin 500 mg IV every 24 hours). If the isolate is tetracycline-susceptible, doxycycline 200 mg initially, followed by 100mg IV every 12 hours is equally efficacious. In the setting of suspected anthrax meningitis, consider adding vancomycin 1gm IV every 12 hours.

Multi-drug regimens are recommended for inhalational and severe cutaneous anthrax infections, with either ciprofloxacin or doxycycline being the primary medication, *plus* one or more of the following: penicillin, ampicillin, imipenem, rifampin, clindamycin, vancomycin, chloramphenicol, or clarithromycin.

For **penicillin-susceptible anthrax**, administer Penicillin G IV 80,000 units/kg body weight in the first hour followed by a maintenance dose of 320,000 units/kg body weight/day. The average adult dose is 4 million units every 4 hours; can also be administered as 2 million units every 2 hours.

Patients can be switched to alternative effective regimens, once the results of antibiotic sensitivity testing are known. Because testing showed that the strain responsible for the 2001 anthrax outbreak contained both a cephalosporinase and an inducible penicillinase, clinicians were recommended to avoid treating solely with penicillins. Patients can be switched to oral therapy (e.g., amoxicillin) when clinically improved.

Supportive therapy is often required (e.g., volume expanders, vasopressor agents, oxygen, and mechanical ventilation). A tracheotomy may be needed if cervical edema compromises the airways.

Continue antibiotic treatment for 60 days.

CUTANEOUS ANTHRAX:

Mild disease

For **penicillin-susceptible anthrax**, administer potassium penicillin V orally at 30 mg/kg body weight/day in four equal portions every 6 hours, or amoxicillin 500 mg orally every 8 hours.

For penicillin-resistant anthrax or initial empiric therapy, administer ciprofloxacin 500 mg orally every 12 hours. Another quinolone (e.g., ofloxacin or levofloxacin) or (if tetracycline-susceptible) doxycycline 100 mg orally every 12 hours, would be reasonable alternatives. Treatment regimens should be adjusted based on the results of antibiotic sensitivity testing.

Extensive lesions or if blood cultures are positive

For penicillin-susceptible anthrax, administer penicillin G IV 2-4 million units every 4-6 hours.

For penicillin-resistant anthrax or initial empiric therapy, administer ciprofloxacin 400 mg IV every 12 hours. Another quinolone (e.g., ofloxacin or levofloxacin) or (if tetracycline-susceptible) doxycycline 100 mg IV every 12 hours, would be reasonable alternatives. Treatment regimens should be adjusted based on the results of antibiotic sensitivity testing.

Extensive cutaneous lesions and those involving the head and neck should be treated with multi-drug regimens. When the edema and systemic symptoms have improved, patients may be switched to oral regimens. The skin lesions will continue to evolve despite the use of effective antibiotics but severe edema and systemic symptoms will be prevented. Glucocorticoids for the first 3-4 days of treatment may reduce morbidity and mortality in severe cutaneous anthrax (malignant edema), particularly in the setting of laryngeal edema.

Duration of Therapy for Cutaneous Anthrax:

In the absence of an aerosol exposure, therapy should be continued for 14 days. If an aerosol exposure occurred, oral therapy should be continued for 60 days.

ALTERNATIVE ANTIBIOTIC OPTIONS:

The following drugs have been shown to have in vitro activity against anthrax and could be used as potential alternative agents in the event of an emergency, when the preferred antimicrobials are unavailable or in short supply:

erythromycin	aminoglycosides	vancomycin
imipenem	cephalothin/cefazolin	chloramphenicol
clindamycin	tetracycline	extended -spectrum penicillins

***** In vitro testing suggests that *B. anthracis* is generally resistant to sulfamethoxazole, trimethoprim, cefuroxime, cefotaxime, ceftriaxone, ceftazidime, and aztreonam. Therefore, these antibiotics should not be used for treatment or prophylaxis of anthrax infection.*****

THERAPY IN PEDIATRIC PATIENTS AND PREGNANT WOMEN:

For penicillin-resistant anthrax and empiric therapy: Although ciprofloxacin is generally not recommended for children less than 16 years of age due to concerns about the development of arthropathy, the high mortality rate from anthrax infection weighs heavily in favor of using ciprofloxacin for empiric therapy, pending susceptibility results. Ciprofloxacin should be given at 20-30 mg/kg/day orally or IV in 2 divided doses, not to exceed 1 gm/day. Although not yet FDA-approved for treatment of anthrax, other quinolones (e.g., ofloxacin or levofloxacin) MAY be reasonable alternatives. During the 2001 outbreak, multi-drug regimens were recommended, as in adults.

For penicillin-susceptible anthrax (no evidence of an inducible penicillinase):

Penicillin G is the drug of choice for **children**. The recommended intravenous dose for children with severe cutaneous anthrax, inhalation anthrax, or gastrointestinal anthrax is 250,000 units/kg body weight/day administered every 4 hours. Oral formulations can be used for milder disease or when IV therapy is not available.

If quinolone supplies are exhausted and the patient is penicillin or quinolone allergic, or the anthrax strain is penicillin-resistant, doxycycline would be the preferred alternative agent (5 mg/kg/day IV or orally divided every 12 hours). Although doxycycline is not routinely administered to children < 8 years of age because of the risk of discoloration of teeth, the high mortality rate from systemic anthrax makes use of this agent the greater priority.

Penicillin G is the drug of choice for **pregnant women**, if the isolate is penicillin-susceptible and there is no evidence of an inducible penicillinase. The dosing schedule is as outlined for adults above. Ciprofloxacin, although not routinely prescribed during pregnancy, is the preferred alternative drug for initial empiric therapy or for penicillin-resistant strains, as tetracyclines can result in rare but serious liver toxicity during pregnancy. If doxycycline is used because of exhaustion of quinolone supplies or severe allergy to either penicillin or ciprofloxacin, liver function tests should be monitored.

VACCINATION:

Anthrax vaccine is currently in short supply and generally is not available for the public

VIII. Isolation of Patients

All staff should observe **Standard Precautions** when caring for patients with suspected or confirmed anthrax. In addition, the following is advised:

Patients do not require isolation rooms.

For cutaneous anthrax, contact precautions should be observed for patients with skin lesions.

Masks are not necessary, since patients with inhalational anthrax typically do not have pneumonia and do not produce aerosols containing sufficient spore counts to cause secondary infections.

Hands should be washed after touching the patient or potentially contaminated articles and before taking care of another patient.

IX. Disposal of Infectious Waste

Use of tracking forms, containment, storage, packaging, treatment and disposal methods should be based upon the same rules as all other regulated medical wastes.

X. Autopsy and Handling of Corpses

All postmortem procedures should be performed using Standard Precautions.

All persons performing or assisting in postmortem procedures must wear mandated personal protective equipment, as required by OSHA guidelines.

Instruments should be autoclaved or sterilized with a 10% bleach solution or other OSHA-approved solutions. Surfaces contaminated during postmortem procedures should be decontaminated with an appropriate chemical germicide such as iodine or 5% hypochlorite.

XI. Management of Exposed Persons – Prophylaxis

In the event of an intentional release of *Bacillus anthracis* spores, public health authorities will attempt to determine the time and place of the event, in order to identify the at-risk populations requiring post-exposure prophylaxis. This will enable public health interventions to be focused on those persons most likely to have been exposed.

Since inhalational anthrax does not spread from person to person, household and other contacts of exposed persons do not require prophylaxis, unless they too were potentially exposed to the aerosolized anthrax spores released at the time of the attack.

During the 2001 anthrax outbreak, clinicians used nasal swabs extensively to determine whether individuals had been exposed to inhaled anthrax spores. Testing is most likely to be positive within the first 48 hours after exposure, and nasal swabs are less likely to be positive once clinical symptoms develop. In addition, a negative nasal swab does not rule out an exposure. Nasal swabs can be useful as part of epidemiologic and environmental investigations conducted by public health authorities; however, they should not be used to assist with clinical decision-making for an individual patient, given their poor positive and negative predictive values.

Inhalational exposures: In animal studies, initiation of antibiotic therapy quickly after exposure has been shown to markedly reduce the mortality of inhalational anthrax. A combination of antibiotics (for 30 days) and vaccination (at 0, 2 and 4 weeks) is currently recommended. However, due to a nationwide shortage, anthrax vaccine is not available to the public. Antibiotic susceptibility information on clinical isolates should guide prophylactic antibiotic choices.

Recommendations for prophylaxis of potentially exposed adults

For **penicillin-resistant** strains or initial empiric prophylaxis in potentially exposed adults, the recommended prophylactic regimen is ciprofloxacin 500 mg orally every 12 hours. Other oral quinolones (e.g., ofloxacin or levofloxacin) or doxycycline would be reasonable alternatives.

For **penicillin-susceptible** strains, potassium penicillin V (30 mg/kg/day in 4 divided doses) or amoxicillin (500 mg orally every 8 hours) are the preferred regimens.

Prophylactic regimens should be adjusted based on the results of antibiotic sensitivity testing of clinical isolates.

Recommendations for prophylaxis of potentially exposed children, and pregnant and lactating women

For penicillin-resistant anthrax, or while still awaiting the results of antibiotic sensitivity testing, administer ciprofloxacin (20-30 mg per kg of body mass per day divided every 12 hours). Another quinolone (e.g., ofloxacin or levofloxacin) would be a reasonable alternative. Doxycycline (5 mg per kg of body mass per day divided every 12 hours) may be used if a quinolone is unavailable or contraindicated, in spite of the risk for dental discoloration, given the potential seriousness of anthrax infection.

For penicillin-sensitive anthrax, all children should be treated with a penicillin antibiotic (for children weighing at least 20 kg, amoxicillin 500 mg po every 8 hours; for children < 20 kg, amoxicillin 80 mg per kg per day in divided doses every 8 hours).

Recommendations for potentially exposed pregnant women: Prophylaxis recommendations are the same as for other adults. However, given the potential for liver toxicity following tetracycline administration, doxycycline would be recommended only when other options are unavailable or contra-indicated due to allergic reactions, adverse effects, or interference with other medication.

Duration of antibiotic prophylaxis: Antibiotic prophylaxis should be continued for 60 days or until an exposure has been ruled out. If anthrax vaccine is available, then antibiotic prophylaxis should continue for 30 days, or until three doses of anthrax vaccine have been administered (Days 0, 14 and 28).

Exposures through cuts, abrasions or injections: Immediately wash the potentially exposed part, and apply a disinfectant solution. The patient should be educated about the signs and symptoms of cutaneous anthrax and instructed to immediately seek medical attention if a suspect skin lesion develops. If a suspicious skin lesion is seen, promptly begin therapy as outlined under the treatment section for "Cutaneous anthrax-mild disease"; continue therapy for 14 days. Anthrax vaccine is not indicated.

Ingestional exposures: Treat as for exposure by cuts or abrasions.

All persons exposed to aerosolized anthrax should be instructed to watch for signs/symptoms of influenza-like illness for at least 7 days. If such symptoms occur, patients should be evaluated immediately by a physician for the possible institution of intravenous antibiotic therapy. The initial clinical work-up should include blood cultures, as well as gram stain and culture of pleural and cerebrospinal fluid, if clinically indicated, and a chest x-ray and/or a CT scan to evaluate for the presence of mediastinal adenopathy and/or pleural effusions.

Anthrax vaccine : An aluminum hydroxide-absorbed, cell-free killed vaccine for anthrax has been developed and used primarily by the military and laboratory workers. The vaccine efficacy against cutaneous anthrax has been documented for humans; evidence for protection against inhalational and gastrointestinal anthrax is limited to animal studies.

For prophylaxis, the vaccine is given parenterally (0.5mL subcutaneously) in three doses 2 weeks apart (Days 0, 14 and 28). Currently, there are limited vaccine supplies in the United States, and distribution is restricted to the military or persons at high-risk due to occupational exposures. (NOTE: Data from animal studies suggest that two doses of anthrax vaccine given two weeks apart may be sufficient, and in the setting of limited vaccine supplies may be a practical alternative).

Adverse reactions to anthrax vaccine are not common. About 6% of patients may develop a local reaction and 2-3% experience mild systemic symptoms.

No studies have investigated the safety of anthrax vaccine in pregnant women or children. Pregnant women should be vaccinated against anthrax only if the potential benefits of vaccination outweigh the potential risks to the woman and fetus.

XII. Reporting to the Health Department

Human and animal anthrax are reportable diseases in New York City and New York State. All suspect human cases should be reported immediately by phone:

During business hours

< Report suspect cases of human anthrax to:

1st: New York City Department of Health at (*temporary numbers*):
(212) 295-5658, (212) 295-5665, (212) 295- 5670, (212) 295-5671, or (212) 295- 5675, or the Poison Control Center, at (212) 764-7667

2nd: New York State Department of Health at **518-473-4439**.

- < Report cases of animal anthrax to:
- 1st: New York City Department of Health, Veterinary Public Health Services **212-676-2120**
 - 2nd: New York State Public Health Veterinarian at **518-474-4436**
 - 3rd: New York State Division of Animal Industry at **518-457-3502**

After business hours

- < Human and animal cases call
- 1st: New York City Department of Health's Poison Control Center at **212- POISONS** (212-764-7667); or
 - 2nd: New York State Department of Health at **518-465-9720**

XIII. References

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Table 1: Inhalational Anthrax Treatment and Prophylaxis

	Therapy †	Prophylaxis *
Adult Doses		
Empiric or Penicillin-Resistant **	Ciprofloxacin 400mg IV q 8-12h (Alternative quinolones*** include: ofloxacin 400mg IV q 8-12h or levofloxacin 500mg IV q 24h Doxycycline 200mg IV x 1, then 100mg IV q 12h (if tetracycline-susceptible)	Ciprofloxacin 500mg po bid (Alternative quinolones include: ofloxacin 400mg po q 8-12h or levofloxacin 500mg po q 24h Doxycycline 100mg po bid (if tetracycline susceptible)
Penicillin-Susceptible (No evidence of an inducible penicillinase)	Penicillin G 80,000 units per kg in 1st hour followed by 320,000 units/kg/ day. (Average adult dose is 4 million units q 4hr or 2 million units q 2h)	Penicillin VK 30mg/kg/d in 4 divided doses Amoxicillin 500mg po q 8h
Pediatric Doses		
Empiric or Penicillin-Resistant	Ciprofloxacin 20-30mg/kg/day IV in 2 divided doses (maximum daily dose not to exceed 1 gram/d) Doxycycline 2.5 mg/kg/d IV q 12h (if tetracycline-susceptible)	Ciprofloxacin 10-15mg/kg po q 12h Doxycycline: >8 yrs and >45kg: 100 mg po q 12h >8 yrs and ≤45 kg: 2.5 mg/kg po q 12h ≤8 yrs: 2.2 mg/kg po BID (if tetracycline-susceptible)
Penicillin-Susceptible (No evidence of an inducible penicillinase)	Penicillin G 250,000 units/kg per day IV administered every 4 hours	Penicillin VK 30 mg/kg per day po administered in 4 divided doses Amoxicillin 500mg po q 8h if > 20kg or 80mg/kg per day po divided in 3 doses if < 20kg

† During the 2001 anthrax outbreak, multi-drug regimens were recommended for inhalational and severe cutaneous anthrax infections, with either ciprofloxacin or doxycycline being the base medication, *plus* one or more of the following added: penicillin, ampicillin, imipenem, rifampin, clindamycin, vancomycin, chloramphenicol, or clarithromycin.

* Antibiotic prophylaxis should be continued for 60 days if anthrax vaccine is not available (or if vaccine is available, antibiotics should be continued until 3rd dose of vaccine has been administered at 4 weeks).

** In pregnant women, penicillin-resistant anthrax should be treated with ciprofloxacin. If doxycycline is used, liver function tests should be monitored closely.

*** Although not yet FDA approved for treatment or prophylaxis of anthrax, limited in vitro data suggests that other quinolones would be effective alternatives.