

Outline

- Introduction
- Epidemiology
- Clinical Features
- Differential Diagnosis
- Laboratory Diagnosis
- Treatment and Prophylaxis
- Complications
- Infection Control
- Pearls and Pitfalls
- References

Immediately report any suspected or confirmed cases of anthrax to:

**SFDPH Communicable Disease Control
(24/7 Tel: 415-554-2830)**

- By law, health care providers must report suspected or confirmed cases of anthrax to their local health department immediately [within 1 hr].
- SFDPH Communicable Disease Control can facilitate specialized testing and will initiate the public health response as needed.

Also notify your:

- Infection Control Professional
- Clinical Laboratory

INTRODUCTION

Anthrax is an acute infection caused by *Bacillus anthracis*, a large, gram-positive, spore-forming, aerobic, encapsulated, rod-shaped bacterium. Spores germinate and form bacteria in nutrient-rich environments, whereas bacteria form spores in nutrient-poor environments. The anthrax bacillus produces high levels of two toxins: Edema toxin causes massive edema at the site of germination, and lethal toxin leads to sepsis. Severity of anthrax disease depends on the route of infection and the presence of complications, with case-fatality ranging from 5% to 95% if untreated.¹⁻³

The Working Group for Civilian Biodefense considers *B. anthracis* to be one of the most serious biological threats. Anthrax has been weaponized and used. It can be fairly easily disseminated and causes illness and death. Of the potential ways that *B. anthracis* could be used as a biological weapon, an aerosol release is expected to have the most severe medical and public health outcomes.¹

EPIDEMIOLOGY

Anthrax as a Biological Weapon

Anthrax was successfully used as a biological weapon in the United States in October 2001. Cases resulted from direct or indirect exposure to mail that was deliberately contaminated with anthrax spores. In total, 22 cases were identified, 11 with inhalational (five fatal) and 11 with cutaneous anthrax (seven confirmed, four suspected).

Several countries have had anthrax weaponization programs in the past, including the United States. In 1979 an outbreak of anthrax in the Soviet Union resulted from accidental release of

anthrax spores from a facility producing weaponized anthrax. Of 77 reported human cases, all but two were inhalational, and there was an 86% fatality rate.⁴

Experts believe that an aerosol release of weapons-grade spores is the most likely mechanism for use of anthrax as a biological weapon in the future. Anthrax spores could also be used to deliberately contaminate food and water. Spores remain stable in water for several days and are not destroyed by pasteurization.¹

An intentional release of anthrax may have the following characteristics:¹⁻³

- Multiple similarly presenting cases *clustered in time*:
 - Severe acute febrile illness or febrile death
 - Severe sepsis not due to predisposing illness
 - Respiratory failure with a widened mediastinum on CXR
- Atypical host characteristics: unexpected, unexplained cases of acute illness in previously healthy persons who rapidly develop a progressive respiratory illness
- Multiple similarly presenting cases *clustered geographically*:
 - Acute febrile illness in persons who were in close proximity to a deliberate release of anthrax
- Absence of risk factors: patients lack anthrax exposure risk factors (e.g., veterinary or other animal handling work, meat processing, work that involves animal hides, hair, or bones, or agricultural work in areas with endemic anthrax)

Intentionally released anthrax spores may be altered for more efficient aerosolization and lethality (e.g., highly concentrated, treated to reduce clumping and reduce particle size, genetically modified to increase virulence, resist antimicrobials and reduce vaccine efficacy).

Naturally Occurring Anthrax

Reservoir

The natural reservoir for *B. anthracis* is soil, and the predominant hosts are herbivores (cattle, sheep, goats, horses, pigs, and others) that acquire infection from consuming contaminated soil or feed. Anthrax spores can persist in soil for years and are resistant to drying, heat, ultraviolet light, gamma radiation, and some disinfectants.⁵ Anthrax in animals is endemic in many areas of the world and anthrax outbreaks in animals occur sporadically in the United States.

Mode of transmission

Anthrax is generally a zoonotic disease. Humans become infected through contact with infected animals and animal products through several mechanisms:^{1, 5, 6}

- contact with infected animal tissues (e.g., veterinarians, animal handlers, meat processors, and other processes that involve animal hides, hair, and bones) or contaminated soil
- ingestion of contaminated, undercooked meat from infected animals
- inhalation of infectious aerosols (e.g., those generated during processing of animal products, such as tanning hides, processing wool or bone)

Person-to-person transmission of *B. anthracis* does not occur with gastrointestinal (GI) or inhalational anthrax, but has been reported rarely with cutaneous anthrax.¹

Worldwide Occurrence

Worldwide, approximately 2000 cases are reported annually. Anthrax is more common in developing countries with less rigorous animal disease control programs. Cases of human anthrax are most often reported in South and Central America, Southern and Eastern Europe, Asia, Africa, the Caribbean, and the Middle East.¹ The largest reported outbreak of human anthrax occurred in Zimbabwe (1979-1985), which involved more than 10,000 individuals and was associated with anthrax disease in cattle.²

United States Occurrence

Naturally occurring anthrax is rare in the United States, with approximately 1-2 cases reported each year. The majority of anthrax cases in the United States are cutaneous and acquired occupationally in workers who come in contact with animals or animal products. Only 19 cases of naturally occurring inhalational anthrax have been reported since 1900, and there have been no confirmed gastrointestinal cases.^{2, 7} Recent cases of naturally occurring anthrax include:

- In 2006, a New York City resident contracted inhalational anthrax while making drums from goat hides imported from Africa. The untanned hides were contaminated with anthrax spores, which may have been aerosolized during removal of hair.⁷ The CDC believes that this was an isolated case and considers handling animal skins or making drums to be a low risk for cutaneous anthrax and extremely low risk for inhalational anthrax.⁸
- In 2002, two cases of cutaneous anthrax were reported. A laboratory worker from a Texas lab that processed environmental *B. anthracis* specimens contracted cutaneous anthrax through direct contact with a contaminated surface.⁹ The second case occurred in a veterinarian who contracted the infection from a cow during necropsy.¹⁰
- Two cases of human cutaneous anthrax were reported following epizootics in North Dakota (2000) and southwest Texas (2001). Both cases resulted from exposure during disposal of infected animal carcasses.¹¹

Occurrence in California and San Francisco

From 1994 to 2007, no cases of anthrax were reported in California.¹²⁻¹⁵ However, in 2001 an outbreak of bovine anthrax caused the death of 21 beef cattle in a rural section of Santa Clara County.

CLINICAL FEATURES

There are three primary clinical types of anthrax disease, inhalational, cutaneous and gastrointestinal, which result from the way infection is acquired. Anthrax meningitis, which generally occurs as a complication of these primary forms of disease, is most likely to be seen with inhalational anthrax.

Anthrax infection is a severe clinical illness and can be life-threatening. Case fatality varies by the clinical type of disease. Overall case-fatality rates have declined because of more prompt administration of antibiotics and improved supportive care. Compared to historical rates, mortality has decreased from 86-95% to 45% for inhalational anthrax, 5-20% to less than 1% for cutaneous anthrax, and 25-60% to 12% for gastrointestinal anthrax. Anthrax meningitis case-fatality rates approach 95% even with antibiotic treatment.^{2, 3, 16}

In the event of bioterrorism, the method of dissemination would influence the type of clinical disease that would be expected. Following an aerosol release, the majority of cases would be inhalational with some cutaneous cases whereas use of a small volume powder could result in both inhalational and cutaneous anthrax cases (as seen in the 2001 attacks). Gastrointestinal cases might occur following contamination of food or water.

Inhalational Anthrax

Inhalational anthrax is caused by inhalation of spores that reach the alveoli, undergo phagocytosis and travel to regional lymph nodes. The spores then germinate to become bacterial cells, which multiply in the lymphatic system and cause lymphadenitis of the mediastinal and peribronchial lymph nodes. The bacteria release toxins that cause hemorrhage, edema, and necrosis. Bacteria entering the bloodstream lead to septicemia, septic shock, and death. Systemic infection following inhalational anthrax is almost always fatal.¹

One of the key clinical features of inhalational anthrax is evidence of pleural effusion and mediastinal widening on CXR or chest computed tomographic (CT) scan. Based on experience from the 2001 attacks, chest CT (without contrast) was found to be more sensitive than CXR for identification of mediastinal widening typical of inhalational anthrax.³

CLINICAL FEATURES: INHALATIONAL ANTHRAX^{1, 2, 6, 17}	
Incubation Period	1-6 days (range <1 day to 8 weeks)
Transmission	Inhalation of aerosolized spores
Signs and Symptoms	<ul style="list-style-type: none"> Initial presentation: Non-specific symptoms (low-grade fever, chills, nonproductive cough, malaise, fatigue, myalgias, profound sweats, chest discomfort) Intermediate presentation: Abrupt onset of high fever, dyspnea, progressive respiratory distress, confusion, nausea or vomiting Fulminant disease progression, if untreated
Progression and Complications	<ul style="list-style-type: none"> Severe respiratory distress (dyspnea, stridor, cyanosis), which may be preceded by 1-3 days of improvement Pleural effusions Meningitis Shock
Laboratory and Radiographic Findings	<ul style="list-style-type: none"> Chest CT or radiograph: mediastinal widening (often), pleural effusions that are commonly hemorrhagic (often), infiltrates (rare) Gram-positive bacilli on unspun peripheral blood smear or CSF Elevated transaminases Hypoxemia Metabolic acidosis Total WBC count normal or slightly elevated with elevated percentage of neutrophils or band forms
CSF, cerebrospinal fluid; WBC, white blood (cell) count.	

Cutaneous Anthrax

In cutaneous anthrax, spores or bacilli are introduced through cuts or breaks in the skin. Spores germinate at the site of contact and release toxins, causing development of a lesion and edema. Organisms may be carried to regional lymph nodes and cause painful lymphadenopathy and lymphangitis. Septicemic complications of cutaneous anthrax occur in 10-20% of untreated cases.¹⁻³

CLINICAL FEATURES: CUTANEOUS ANTHRAX^{1, 2, 6, 17}	
Incubation Period	3-4 days (range 1–12 days)
Transmission	<ul style="list-style-type: none"> • Direct skin contact with spores; in nature, contact with infected animals or animal products (usually related to occupational exposure) • Bite of infective arthropod (rare)
Signs and Symptoms	<ul style="list-style-type: none"> • Local skin involvement after direct contact with spores or bacilli (commonly seen on hands, forearms, head, and neck) • Skin lesion with the following progression: 1) Development of a papular lesion and localized itching, 2) papule turns into vesicular or bulbous lesion accompanied by painless edema, 3) lesion becomes necrotic and vesicles may surround the ulcer, and 4) lesion develops painless black eschar within 7–14 days of initial lesion • Lymphadenopathy and lymphangitis • Fever and malaise (common)
Progression and Complications	<ul style="list-style-type: none"> • Bacteremia • Meningitis • Extensive edema causing airway compression • Sepsis
Laboratory Findings	<ul style="list-style-type: none"> • Bacilli may be seen on Gram stain of subcutaneous tissue

Pediatric considerations: A case of cutaneous anthrax occurred in a 7-month old during the anthrax attack of 2001. This case was difficult to recognize and rapidly progressed to severe systemic illness despite timely antibiotic treatment. Clinical features included a painless draining lesion with edema that developed into an eschar, fever, leukocytosis, severe microangiopathic hemolytic anemia, renal failure, and coagulopathy.¹⁸

Gastrointestinal Anthrax

Gastrointestinal (GI) anthrax results from ingestion of *B. anthracis* bacteria, such as may be found in poorly cooked meat from infected animals. The incubation period for GI anthrax is 1-7 days. Two clinical presentations have been described: intestinal and oropharyngeal.

With *intestinal anthrax*, intestinal lesions occur in the ileum or cecum and are followed by regional lymphadenopathy. Symptoms of intestinal anthrax are initially nonspecific and include low-grade fever, malaise, nausea, vomiting, anorexia and fever. As disease progresses, abdominal pain, hematemesis, and bloody diarrhea develop. The patient may present with findings of an acute abdomen. After 2-4 days, ascites develop and abdominal pain lessens. Hematogenous spread with

resultant septicemia can occur. Mesenteric adenopathy on CT scan is likely, and mediastinal widening on CXR is possible.^{1, 2, 5, 6}

In *oropharyngeal anthrax*, a mucosal ulcer occurs initially in the mouth or throat, associated with fever, throat pain, and dysphasia. This is followed by cervical edema and regional lymphadenopathy. Ulcers may become necrotic with development of a white patch covering the ulcer. Swelling can become severe enough to affect breathing. Hematogenous spread, septicemia, and meningitis can occur.^{1, 2, 5, 6}

Gram stain of ascitic fluid, oropharyngeal ulcers, or unspun peripheral blood may show Gram-positive rods. Leukocytosis with left shift may be present. *B. anthracis* can be cultured from oropharyngeal swabs and stool specimens.⁶

Anthrax Meningitis

Anthrax meningitis can occur as a complication of cutaneous, inhalational, or GI anthrax, but is most commonly seen with inhalational anthrax (up to 50%). Patients may or may not present with symptoms of the primary site of infection. In addition to typical symptoms of bacterial meningitis, anthrax meningitis may involve hemorrhage or meningoenzephalitis. Case fatality with anthrax meningitis is greater than 90%. Even one case of anthrax meningitis should alert public health authorities to identify the source of exposure and investigate the possibility of bioterrorism.³

Anthrax and Pregnant Women

Maternal and perinatal complications are not completely understood, because anthrax infection during pregnancy is rare. Preterm delivery may be one of the major complications.¹⁹

DIFFERENTIAL DIAGNOSIS

Because of its mild, nonspecific nature in the early states, a high index of suspicion is necessary to make a timely diagnosis of anthrax. Screening protocols and clinical prediction tools have been proposed and partially evaluated.²⁰ Prompt administration of antibiotics can be critical to patient survival; therefore, clinicians should administer appropriate antibiotics when the diagnosis is suspected.¹

Differential: Inhalational Anthrax^{1, 2, 5, 6, 21}

Early disease mimics influenza and other respiratory infections. However nasal symptoms are typically not present and rapid diagnostic tests, such as nasopharyngeal swabs for detection of respiratory virus antigens, would typically be negative.

Key features that distinguish *inhalational* anthrax from other conditions are:

- CXR is abnormal even during early stages of influenza like illness
- CXR or chest CT show widened mediastinum and pleural effusion but minimal or no pneumonitis

Features that distinguish *inhalational* anthrax from influenza:

- Neurological symptoms without headache (e.g., confusion, syncope) and nausea/vomiting are more common in inhalational anthrax
- Rhinorrhea and pharyngitis were uncommon in inhalational anthrax cases from 2001 U.S. attack

Other conditions to consider are:

- bacterial pneumonia (*Mycoplasma*, *Staphylococcus*, *Streptococcus*, *Haemophilus*, *Klebsiella*, *Moraxella*, *Legionella*)
- *Chlamydia* infection
- influenza
- other viral pneumonia (respiratory syncytial virus [RSV], cytomegalovirus [CMV], hantavirus)
- Q fever
- pneumonic plague
- tularemia
- primary mediastinitis
- ruptured aortic aneurysm
- histoplasmosis
- coccidioidomycosis
- silicosis
- sarcoidosis

Differential: Cutaneous Anthrax^{3, 5, 6}

Key features that distinguish *cutaneous* anthrax are:

- painlessness of the lesion itself
- large extent of local edema

Other conditions to consider:

- ecthyma gangrenosum
- ulceroglandular tularemia
- bubonic plague
- cellulitis (staphylococcal or streptococcal)
- brown recluse spider bite
- necrotizing soft tissue infections, (e.g., *Streptococcus*, *Clostridium*)
- Coumadin or heparin necrosis
- rickettsial infection
- necrotic herpes simplex infection
- orf virus infection
- glanders
- cutaneous leishmaniasis
- cat scratch fever
- melioidosis

Differential: Gastrointestinal Anthrax^{2, 5}

The differential diagnosis for the *intestinal* form of the disease includes:

- typhoid fever
- intestinal tularemia
- acute bacterial gastroenteritis (e.g., *Campylobacter*, *Shigella*, toxicogenic *Escherichia coli*, *Yersinia*)
- bacterial peritonitis
- peptic or duodenal ulcer
- any other causes of acute abdomen

The differential diagnosis for the *oropharyngeal* form of the disease includes:

- streptococcal pharyngitis
- infectious mononucleosis
- diphtheria
- pharyngeal tularemia
- other causes of pharyngitis (e.g., enteroviral vesicular, herpetic, anaerobic or Vincent's angina, *Yersinia enterocolitica*)

Differential: Anthrax Meningitis^{3, 5}

A key feature that distinguishes anthrax meningitis is bloody cerebrospinal fluid (CSF) containing gram-positive bacilli.

Other conditions to consider are:

- subarachnoid hemorrhage
- bacterial meningitis
- aseptic meningitis

LABORATORY AND RADIOGRAPHIC FINDINGS

The diagnosis of anthrax requires a high index of suspicion because the disease often presents with nonspecific symptoms. Routine laboratory and radiographic findings for specific clinical presentations of anthrax are listed in the clinical features tables.

Initial identification and diagnosis of the organism relies on evaluation of infected tissue (blood, sputum, CSF, fluid collected from an unroofed vesicle, ulcer, eschar, or skin lesion scraping, or stool). The gold standard for anthrax diagnosis is direct culture of clinical specimens onto blood agar with demonstration of typical Gram stain, motility, and biochemical features. Blood cultures, which are positive nearly 100% of the time in inhalational anthrax, should be obtained prior to antibiotic administration because there is rapid sterilization of blood after a single dose of antibiotics. Because laboratories may view gram-positive bacilli as contaminants and because *B. anthracis* may be a risk to laboratory personnel, clinicians should notify the laboratory when anthrax is suspected.^{1-3, 5}

If you are testing or considering testing for anthrax, you should:

- **IMMEDIATELY notify SFDPH Communicable Disease Control (24/7 Tel: 415-554-2830).**
SFDPH can authorize and facilitate testing, and will initiate the public health response as needed.
- **Inform your lab that anthrax is under suspicion. Labs may view Gram-positive bacilli as contaminants and may not pursue further identification unless notified.**

Although rapid diagnostic tests are not widely available, the public health laboratory system may be able to provide this testing on clinical specimens. Other tests available through the public health

laboratory system include polymerase chain reaction (PCR), serologic tests, and immunohistochemistry.²²

Testing for Exposure to aerosolized Anthrax

Nasal swab cultures have been used to study environmental exposure to aerosolized anthrax, they are not recommended for use in the clinical setting. The sensitivity, specificity, and predictive value of nasal swab cultures is not known.⁶

TREATMENT AND PROPHYLAXIS

These recommendations are current as of this document date. SFDPH will provide periodic updates as needed and situational guidance in response to events (www.sfcddcp.org).

Treatment of Confirmed or Suspected Anthrax

This section refers to individuals with suspected or confirmed anthrax disease.

The basic components of treatment for anthrax consist of hospitalization with intensive supportive care and IV antibiotics. After obtaining appropriate cultures, antimicrobials should be started *immediately* on suspicion and prior to confirmation of the diagnosis.¹ Patients with inhalational anthrax who received antibiotics within 4.7 days of exposure had a 40% case fatality, compared to a 75% case-fatality in those with treatment initiated after 4.7 days.²¹

Because susceptibility data will be delayed, initial antibiotics must be chosen empirically. Recommendations for initial empiric therapy of suspected or confirmed anthrax disease are described below. Empiric therapy with at least two agents is recommended because of the potential for infection with strains of *B. anthracis* engineered to be penicillin- and/or tetracycline-resistant.¹ Antibiotic resistance to amoxicillin is of greater concern than resistance to doxycycline or ciprofloxacin; therefore, amoxicillin is not recommended as a first-line agent unless the strain has been proven susceptible. Therapy may be switched to oral antimicrobials when clinically indicated. Therapy should be continued for a total duration of 60 days because spores can persist and then germinate for prolonged periods. There is a possibility that spores could germinate and cause illness up to 100 days after exposure.¹

Contained casualty setting: Parenteral antimicrobial therapy with at least two agents is recommended for *inhalational and GI anthrax* when individual medical management is available. After clinical improvement is noted, treatment can be switched to oral therapy with ciprofloxacin or doxycycline, based on susceptibilities and clinical considerations. Draining of pleural effusions has also been associated with reduced mortality.²¹

Cutaneous anthrax can be treated with oral antibiotics. If in addition to cutaneous lesions there are signs of systemic disease or extensive edema, or if lesions are present on the head or the neck, then the multidrug IV regimen is recommended.

ANTHRAX: TREATMENT AND POST-EXPOSURE PROPHYLAXIS RECOMMENDATIONS^A

	INITIAL IV THERAPY ^{B,C} FOR INHALATIONAL, GI ANTHRAX, OR CUTANEOUS ANTHRAX WITH COMPLICATIONS ^D	INITIAL THERAPY FOR CUTANEOUS ANTHRAX ^{B,D}	THERAPY FOR ANTHRAX IN THE MASS CASUALTY SETTING, OR POSTEXPOSURE PROPHYLAXIS, OR AFTER CLINICAL IMPROVEMENT ON IV THERAPY ^{E,F}
Adult	<p>Ciprofloxacin, 400 mg IV q12 hr or</p> <p>Doxycycline^G, 100 mg IV q12 hr</p> <p>AND</p> <p>One or two additional antimicrobials (agents with <i>in vitro</i> activity include rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and clarithromycin)^H</p>	<p>Ciprofloxacin, 500 mg orally q12 hrs for 60 days or</p> <p>Doxycycline, 100 mg orally q12 hrs for 60 days</p>	<p>Ciprofloxacin^I, 500 mg orally twice daily for 60 days or</p> <p>Doxycycline^J, 100 mg orally twice daily for 60 days</p>
Children	<p>Ciprofloxacin^{K,L}, 10 mg/kg IV q12 hrs (max 400 g/dose) or</p> <p>Doxycycline^{G,L,M}: ≥45 kg, 100 mg IV q12 hr <45 kg, give 2.2 mg/kg IV q12 hrs (max 200 mg/day)</p> <p>AND</p> <p>One or two additional antimicrobials (agents with <i>in vitro</i> activity include rifampin, vancomycin, penicillin, ampicillin, chloramphenicol, imipenem, clindamycin, and clarithromycin)^H</p>	<p>Ciprofloxacin, 15 mg/kg orally q12 hrs (max 500 mg/dose) for 60 days or</p> <p>Doxycycline^{G,L,M}: ≥45 kg, give 100 mg orally q12 hrs for 60 days <45 kg, give 2.2 mg/kg orally q12 hrs (max 200 mg/day) for 60 days</p>	<p>Ciprofloxacin^I, 15 mg/kg orally twice daily (max 500 mg/dose) for 60 days or</p> <p>Doxycycline^J: ≥45 kg, give 100 mg orally twice daily for 60 days <45 kg, give 2.2 mg/kg orally twice daily (max 200 mg/day) for 60 days or</p> <p>Amoxicillin^N >20 kg: 500 mg orally three times daily for 60 days ≤20 kg: 80 mg/kg/day orally in three divided doses every 8 hrs for 60 days</p>
Pregnant women	Same as for non-pregnant adults ^O	Same as for non-pregnant adults ^O	Same as for non-pregnant adults or Amoxicillin ^N 500 mg orally three times daily for 60 days
Immuno-compromised Persons	Same as for non-immunocompromised persons and children	Same as for non-immunocompromised persons and children	Same as for non-immunocompromised persons and children

^A The treatment recommendations included in this table are adapted from guidance developed during the 2001 anthrax outbreaks. Therapy recommendations in other situations should be guided by antimicrobial susceptibility results.^{1,2,6,17}

^B Ciprofloxacin or doxycycline should be considered an essential part of first-line therapy for inhalational anthrax.

^C Steroids may be considered an adjunct therapy for patients with severe edema and for meningitis based on experience with bacterial meningitis of other etiologies.

^D Cutaneous anthrax cases with signs of systemic involvement, extensive edema, or lesions on the head or neck require intravenous therapy, and a multidrug approach is recommended.

^E Initial therapy may be altered based on clinical course of patient; one or two antimicrobial agents (eg, ciprofloxacin or doxycycline) may be adequate as patient improves.

^F If pharmaceutical resources permit in a mass casualty setting, therapy with at least two agents is recommended over monotherapy.

^G If meningitis is suspected, doxycycline may be less optimal because of poor central nervous system penetration.

^H Because of concerns of constitutive and inducible beta-lactamases in *Bacillus anthracis* isolates, penicillin and ampicillin should not be used alone. Consultation with an infectious disease specialist is advised.

^I In vitro studies suggest that ofloxacin (400 mg orally every 12 hours) or levofloxacin, (500 mg orally every 24 hours) could be used in place of ciprofloxacin – if supplies were limited in a mass casualty or post-exposure prophylaxis situation. FDA has approved levofloxacin for PEP in adults and children.

^J In vitro studies suggest that 500 mg of tetracycline orally every 6 hours could be used in place of doxycycline – if supplies were limited in a mass casualty or post-exposure prophylaxis situation.

^K If intravenous 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 1-2 hours after oral dosing but may not be achieved if vomiting or ileus is present.

^L Tetracycline and quinolone antibiotics are generally not recommended during pregnancy or childhood; however their use may be indicated for life-threatening illness. Ciprofloxacin may be preferred in pregnant women and children up to 8 years of age because of the known adverse event profile of doxycycline (e.g., tooth discoloration). Doxycycline may be preferred in children 8 years and older because of the adverse event profile of ciprofloxacin (e.g., arthropathies).

^M American Academy of Pediatrics recommends treatment of young children with tetracyclines for serious infections (eg, Rocky Mountain spotted fever).

^N Amoxicillin is not approved by the FDA for post-exposure prophylaxis or treatment of anthrax. However, CDC has indicated that if the isolate is determined to be susceptible to amoxicillin, it could be used for pregnant women and children for post-exposure prophylaxis or for completion of 60 days antibiotic therapy after initial treatment with ciprofloxacin or doxycycline. Amoxicillin resistance to anthrax is of greater concern than that of doxycycline or ciprofloxacin, and amoxicillin is not recommended as a first-line agent unless the isolate is proven to be susceptible.

^O Although tetracyclines are not recommended for pregnant women, their use may be indicated for life-threatening illness. Adverse effects on developing teeth and bones are dose-related; therefore, doxycycline might be used for a short time (7-14 days) before 6 months of gestation.

Anthrax meningitis can be treated using the inhalational anthrax guidelines; however, IV treatment with a fluoroquinolone plus 1-2 antimicrobials with good central nervous system (CNS) penetration

and activity against *B. anthracis* (i.e., rifampin, vancomycin, penicillin, ampicillin, meropenem) is recommended. The addition of corticosteroids may help manage cerebral edema.²³

Mass casualty setting: Use of oral antibiotics may be necessary if the number of patients exceeds the medical care capacity for individual medical management. If pharmaceutical resources permit, therapy with at least two agents is recommended over monotherapy.

Prophylaxis of Persons Exposed but Without Symptoms

Postexposure prophylaxis (PEP) is the administration of antibiotics, with or without vaccine, after suspected exposure to anthrax has occurred but before symptoms are present. (If symptoms are present, see section on treatment, above). In general, PEP is recommended for persons exposed to an air space or package contaminated with *B. anthracis*. Unvaccinated laboratory workers exposed to *B. anthracis* cultures should also receive PEP.¹ As there is no known person to person transmission of inhalational anthrax, prophylaxis should not be offered to contacts of cases, unless also exposed to the original source.¹

Postexposure prophylaxis of potential inhalational anthrax consists of oral administration of either ciprofloxacin or doxycycline. Therapy should be continued for 60 days. Patients treated for exposure should be informed of the importance of completing the full course of antibiotic prophylaxis regardless of the absence of symptoms.^{1, 22, 24} The Food and Drug Administration (FDA) has also approved levofloxacin and penicillin G procaine for PEP of inhalational anthrax.²⁵ And levofloxacin was approved recently for children older than 6 months.²⁶ Because of concerns about use of doxycycline or ciprofloxacin in children and about doxycycline use in pregnant women, the CDC has indicated that for prophylaxis, therapy can be switched to amoxicillin in these groups if the isolate is determined to be susceptible. Amoxicillin may also be considered for patients allergic to both ciprofloxacin and doxycycline.^{1, 22, 24}

The Advisory Committee on Immunization Practices recommends the use of combined antimicrobial prophylaxis and vaccine [Biothrax (formerly Anthrax vaccine absorbed, AVA)]. Biothrax is not licensed for this use by the FDA, and would need to be given under an Investigational New Drug (IND) application. The recommended regimen is three vaccine doses (given at 0, 2, and 4 weeks after exposure) and at least a 30-day course of antimicrobial therapy. The CDC does not recommend vaccination in pregnant women given lack of data.²⁷

Following the 2001 attacks, exposed persons were given the option of (1) 60 days of antibiotic prophylaxis; (2) 100 days of antibiotic prophylaxis, and (3) 100 days of antibiotic prophylaxis, plus anthrax vaccine (under IND protocol).²⁸

Anthrax Vaccine

The anthrax vaccine Biothrax (formerly Anthrax vaccine absorbed, AVA) is available but only in limited supply that is controlled by federal authorities. It is an inactivated cell-free filtrate of an avirulent strain of *B. anthracis*. Local reactions and mild systemic reactions are common. Severe allergic reactions are rare (<1 per 100,000).^{1, 27}

The anthrax vaccine is licensed for pre-exposure use to prevent cutaneous anthrax in healthy, nonpregnant adults 18-65 years of age who have a high likelihood of coming into contact with anthrax, including certain laboratory workers and animal processing workers. AVA is not currently licensed for postexposure use and must be given in this context under an FDA investigational drug protocol. The CDC may recommend its use for PEP under some circumstances. Research is underway on new anthrax vaccines.^{1, 27}

Developmental Anthrax Therapeutics

Additional therapeutic candidates for treatment and prophylaxis of anthrax are currently under development. The Department of Health and Human Services announced plans to purchase the antibody-based therapeutic candidates immune globulin (AIG) and ABthrax™ (raxibacumab) for the strategic national stockpile. These therapeutic approaches use antibodies to neutralize anthrax toxin. Neither AIG nor ABthrax™ is FDA approved, but either may be authorized for use as an investigational new drug in an emergency. Studies are still in progress to determine efficacy of these therapeutics in anthrax treatment and prophylaxis.⁶

COMPLICATIONS AND ADMISSION CRITERIA

Without early antibiotic treatment, inhalational anthrax progresses to pneumonitis marked by severe respiratory distress and cyanosis, and is often accompanied by pleural effusion. Patients with anthrax pneumonitis are particularly likely to develop septicemia and septic shock due to hematogenous dissemination of the bacteria. Sepsis may also develop as a complication of cutaneous anthrax or gastrointestinal anthrax. Anthrax meningitis may occur as a consequence of hematogenous dissemination.

Patients with suspected or confirmed inhalational, gastrointestinal, or meningeal anthrax, as well as those with cutaneous anthrax who exhibit head or neck lesions, extensive edema, or systemic signs of illness, require admission for intravenous antibiotic therapy and supportive care.

INFECTION CONTROL

These recommendations are current as of this document date. SFDPH will provide periodic updates as needed and situational guidance in response to events (www.sfdcdp.org).

Clinicians should notify local public health authorities, their institution's infection control professional, and their laboratory of any suspected anthrax cases. Public health authorities may conduct epidemiologic investigations and implement disease control interventions to protect the public. Both HICPAC (Hospital Infection Control Practices Advisory Committee) of the CDC and the Working Group for Civilian Biodefense recommend **Standard Precautions** for anthrax patients in a hospital setting without the need for isolation. Person to person transmission has only rarely been reported for patients with cutaneous anthrax and **Standard Precautions** are considered adequate. Routine laboratory procedures should be carried out under Biosafety Level 2 (BSL-2) conditions.^{1, 29}

Decontamination

Contaminated surfaces can be disinfected with commercially available bleach or a 1:10 dilution of household bleach and water. All persons exposed to an aerosol containing *B. anthracis* should be instructed to wash body surfaces and clothing with soap and water.¹

PEARLS AND PITFALLS

- The initial (prodromal) phase of inhalational anthrax resembles an influenza-like syndrome and can be difficult to distinguish from seasonal respiratory illnesses. Nasal congestion and rhinorrhea, however, are common features of seasonal influenza-like syndromes and are unusual with pulmonary anthrax.
- The classic radiographic findings of inhalational anthrax – CXR showing a widened mediastinum (due to hilar lymphadenopathy) and pulmonary effusion – although not unique to anthrax, should nonetheless prompt a high level of clinical suspicion.
- The necrotic, edematous, eschar-covered skin lesion of cutaneous anthrax is usually painless, which is an important differentiating feature from a brown recluse spider bite.

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