

# County of Santa Clara

Public Health Department

3003 Moorpark Avenue  
San Jose, California 95128



Martin Fenstersheib, M.D., M.P.H.  
Health Officer

**DATE:** October 22, 2001

**TO:** All Santa Clara County Physicians

**FROM:** Martin Fenstersheib, MD, MPH  
Health Officer

Sara H. Cody, MD  
Assistant Health Officer

**RE: Alleged Anthrax Exposure: Guidelines for Physicians**

To date, there have been no reported cases of anthrax or documented exposures to anthrax in California. However, the events on the East Coast have caused considerable anxiety and concern among patients and health professionals alike across the country, including Santa Clara County.

These guidelines are based on guidance given by the CDC, the California Dept of Health Services, and the "Consensus Statement on Anthrax as a Biologic Weapon: Medical and Public Health Management" (JAMA 1999, Vol 281:1735-45, <http://jama.ama-assn.org/>). We have modified these guidelines in an effort to make them more user friendly. Although they are not exhaustive, these guidelines should help with the majority of patient presentations.

This document will guide the provider through performance of a risk assessment for each patient, medical management, indications for laboratory testing, and indications for prophylactic antibiotics.

## **I. Risk Assessment**

### **Has your patient had an exposure to anthrax?**

**YES.** At this point, very few patients meet the criteria for definite exposure to anthrax. Exposure refers exclusively to persons with exposure to documented anthrax, either:

1. exposure to an item/substance that has been confirmed to contain anthrax, OR
2. exposure to the same item(s)/environment as another person who has tested positive for anthrax carriage or has culture confirmed clinical disease.

Physicians evaluating patients potentially exposed to anthrax at the American Media Inc. building in Boca Raton, FL, the NBC studio (30 Rockefeller Plaza) in New York City, or the Hart Senate Building in Washington, DC, should call the Santa Clara County Public Health Officer on call for further instruction.

**NO.** The vast majority of patients fall into this category and can be reassured. We strongly discourage stockpiling of antibiotics “just in case”.

**UNCERTAIN.** If the patient doesn’t clearly fall into either the YES or NO category above, assess the risk of exposure to anthrax by considering: (1) the **credibility** of the threat (probability that substance is anthrax), (2) the **route** of exposure (probability that illness would result from exposure), and (3) **symptoms** (probability that signs and symptoms represent anthrax infection).

1. Credibility of the threat – the FBI, local law enforcement, fire departments, and hazardous materials teams have primary responsibility for determining the credibility of the threat. Any suspicious package, at home or at work, should be reported to local law enforcement who will involve the FBI and others as appropriate.

An exposure to a substance may be higher risk if:

- There is a threatening message with the powder or substance.
- The substance is brown or sandy-brown rather than stark white. Of note, the positive NBC letter is reported to have had brownish sand-like material in it.
- A suspicious letter or package is involved (see Appendix on suspicious packages).

Situations that may be less worrisome for true anthrax/biological agent exposure include:

- A white powder is found without a note, where one might expect someone to have spilled sugar, flour, etc.
- A white powder comes in an envelope with expected mail that is easy to trace to the sending source.

If the patient reports that the FBI has opened an investigation and taken the substance/item, the credibility of the threat is assumed to be high. However, often times the FBI does not open an investigation but significant uncertainty remains for the patient and clinician as to whether the substance/item might have contained anthrax. In these cases, getting the substance tested can be extremely valuable. The Santa Clara County Public Health Laboratory (SCCPHL) will test items evaluated and submitted by law enforcement (fire, police, or HAZMAT). *The SCCPHL will not test items submitted directly by citizens.*

2. Route of exposure – the clinician should determine whether the “exposure” might result in inhalational or cutaneous anthrax were it to be anthrax spores.

- inhalational anthrax – generally requires a large dose of invisibly fine powder – particles 1-5 microns in size, the size necessary to get into the alveoli. It is technologically very difficult to get anthrax into a form where it can be inhaled. Re-aerosolization of particles on clothing and on surfaces into particles of this size is nearly impossible. Thus, visible settled powders and letters or boxes that are opened and contain powders are usually not serious threats for inhalational anthrax. Thus, the immediate risk to people “exposed” in these situations is small. Inhalational anthrax

would be of concern if: a) a person got a face full of fine powder with heavy contamination of eyes, nose and throat; b) there was a real concern of aerosolization based on warning that an air handling system is contaminated or warning that a biological agent was released in a public space.

- cutaneous anthrax – appears to require lower doses and is the most plausible form of anthrax that could be caused by letters and packages that did not have obvious aerosolizing devices – all one needs is spores rubbed into the skin or cuts in the skin. Given its characteristic clinical picture and very good prognosis when recognized and treated, potential exposures can readily be managed by observation and treatment as clinically needed.

3. Signs and symptoms – assess whether the patient has signs and symptoms compatible with anthrax infection:

- ***Inhalational anthrax:*** A brief prodrome resembling a viral respiratory illness followed by development of hypoxia and dyspnea, with radiographic evidence of mediastinal widening. Initial symptoms include sore throat, mild fever, muscle aches and malaise. These may progress to respiratory failure and shock. Meningitis frequently develops. This is the most lethal form of anthrax and results from inspiration of 8,000-40,000 spores of *B. anthracis*. The incubation of inhalational anthrax among humans is reported to range between 1 and 7 days but may be as long as 60 days. Host factors, dose of exposure and chemoprophylaxis may play a role. Case fatality rate is very high.
- ***Cutaneous anthrax:*** A skin lesion evolving from a papule, through a vesicular stage, to a depressed black eschar. This is the most common naturally occurring type of infection (>95%) and usually occurs after skin contact with contaminated meat, wool, hides, or leather from infected animals. Incubation period ranges from 1-12 days. Skin infection begins as a small papule, progresses to a vesicle in 1-2 days followed by a necrotic ulcer. The lesion is usually painless, but patients also may have fever, malaise, headache and regional lymphadenopathy. The case fatality rate for cutaneous anthrax is 20% without, and less than 1% with, antibiotic treatment.
- ***Gastrointestinal anthrax:*** Severe abdominal distress followed by fever and signs of septicemia. This form of anthrax usually follows the consumption of raw or undercooked contaminated meat and usually has an incubation period of 1-7 days. An oropharyngeal and an abdominal form of the disease have also been described. Involvement of the pharynx is usually characterized by lesions at the base of the tongue, sore throat, dysphagia, fever, and regional lymphadenopathy. Lower bowel inflammation usually causes nausea, loss of appetite, vomiting and fever, followed by abdominal pain, vomiting blood, and bloody diarrhea. The case-fatality rate is estimated to be 25-60%. The effect of early antibiotic treatment on that case-fatality rate is not defined.

## **II. Medical Management**

### Definite exposure to known anthrax

Prescribe 60 days of antibiotic prophylaxis (see table below), educate patient about signs and symptoms of anthrax infection, and notify the Public Health Department (408-885-4214 during business hours; 408-299-2501 after hours).

### No exposure to anthrax

Reassure patient. We do not recommend collecting a nasal swab or blood for a serologic test to try to confirm that there is no evidence of exposure to anthrax.

### Uncertain exposure to anthrax

*High credibility threat, inhalational exposure to powdery substance, no symptoms:*

If the FBI has evaluated a suspicious package and deemed a threat is present, AND the patient had real potential for inhalational exposure (e.g., got a face and nose full of powder), consider starting prophylactic antibiotics (see table below) and continuing them until exposure has been ruled out through testing of the substance. Notify the Public Health Department (408-885-4214 during business hours; 408-299-2501 after hours).

*High credibility threat, inhalational exposure to powdery substance, flu-like symptoms present:*

In a scenario similar to the one above where the patient presents with symptoms that are compatible with early inhalational anthrax infection, draw blood cultures, obtain chest x-ray, start antibiotics, and alert Public Health Department (408-885-4214 during business hours; 408-299-2501 after hours).

*High credibility threat, cutaneous exposure, no symptoms:*

If the situation suggests real potential for cutaneous exposure (e.g., direct hand contact with brownish powder AND FBI determines presence of a threat), provide reassurance and counseling about the signs and symptoms of cutaneous anthrax and wait to start prophylactic antibiotics until culture of the powder is complete. If no powder is available for testing, watch for signs and symptoms. Nasal swab testing is not recommended.

*Low credibility threat, inhalational or cutaneous exposure, no symptoms:*

If the only potential exposure to a powder/suspicious substance is cutaneous (the usual situation with finding powder on a surface, opening a letter with powder in it), provide advice on what to look for (red spot → papule → vesicle → black center over several days to a week), reassure them that cutaneous anthrax can be readily diagnosed and easily treated. An inhalational exposure is somewhat more problematic since there are no tests to determine whether a person has been exposed. We recommend testing of the substance. Please have patient call law enforcement to do a threat assessment. The Santa Clara County Public Health

Laboratory will accept specimens from law enforcement, but not from worried individuals. We do not recommend collecting a nasal swab or blood for serology, nor do we recommend prescribing antibiotic prophylaxis.

### III. Laboratory Tests

#### Nasal swabs

CDC does not recommend the use of nasal swab testing on a routine basis to determine whether a person has been exposed to *B. anthracis* or as a diagnostic tool that would be relied upon to guide prophylaxis and treatment. Their use in recent investigations by CDC has been for epidemiologic purposes only, as an adjunct to an environmental investigation where there is a known exposure event, to help determine the extent of exposure. The sensitivity, specificity, and positive/negative predictive value of nasal swab cultures are unknown. In particular, the sensitivity of this method for detecting exposure to *B. anthracis* spores is unknown.

#### Serologic testing

CDC does not recommend the use of serologic testing on a routine basis to determine whether a person has been exposed to *B. anthracis* or as a diagnostic tool to guide decision about prophylaxis and treatment. As described above for nasal swab testing, the use of serologic tests in recent investigations by CDC has been for epidemiologic purposes only where there is a known exposure to *B. anthracis*. Again, the sensitivity, specificity, and positive/negative predictive value of serologic tests for *B. anthracis* are unknown.

#### Laboratory diagnosis of anthrax infection in patients with compatible symptoms

- Inhalational anthrax: blood gram stain and culture, CSF gram stain and culture (if meningeal signs are present); chest X-ray
- Gastrointestinal anthrax: blood culture
- Cutaneous anthrax: vesicular fluid and blood culture

Evaluation of possible anthrax infection for individuals not connected with the incidents in Florida, New York or Washington, D. C. should be performed through standard laboratory tests, following the Laboratory Response Network (LRN) Level A Clinical Guidelines for rule-out and presumptive testing <http://www.bt.cdc.gov> (follow the link for Resources: Agents/Diseases – *Bacillus anthracis*).

#### a. Presumptive identification criteria (level A LRN laboratory)

1. From clinical samples, such as blood, CSF, or skin lesion (vesicular fluid or eschar) material: encapsulated Gram-positive rods
2. From growth on sheep blood agar: large Gram-positive rods

3. Non-motile
4. Non-hemolytic on sheep blood agar

Additional LRN criteria for confirmation of *B. anthracis* are available through level B laboratories and involve:

- b. Confirmatory criteria for identification of *B. anthracis* (level B LRN laboratory)
  1. Capsule production (visualization of capsule), and
  2. Lysis by gamma-phage, or
  3. Direct fluorescent antibody assays (DFA)

Rapid screening assays, such as nucleic acid signatures and antigen detection, which can be performed directly on clinical specimens and environmental samples, are being made available for restricted use in LRN B and C level laboratories.

The Santa Clara County Public Health Laboratory is currently a Level A public health laboratory. Contact our laboratory (during business hours: 408-885-4247; after hours 408-299-2501) to facilitate specimen submission to a level B or C laboratory.

**IV. Prophylactic use of antibiotics**

Antibiotic prophylaxis should be limited to those who have a confirmed exposure to *B. anthracis* or who have had a strongly suspected exposure as described above (FBI assessment that threat is present and route of exposure is likely to be inhalational, with gross amounts of powder on the face/nose). Indiscriminate use of ciprofloxacin and other antibiotics can contribute to antimicrobial resistance and lessen the effectiveness of these agents against many infections. Inappropriate stockpiling of ciprofloxacin may threaten the supply of this antibiotic should it be urgently required.

If post-exposure prophylaxis is required following a confirmed or strongly suspected exposure to *B. anthracis*, the following regimens have been recommended by the CDC for use of doxycycline or ciprofloxacin:

	Initial therapy	Duration
Adults, including pregnant women and immuno-compromised persons	Ciprofloxacin 500 mg po BID  OR  Doxycycline 100 mg po BID	60 days (if only suspected but not confirmed exposure, may stop antibiotics if testing of substance rules out exposure to <i>B. anthracis</i> )

Children	Ciprofloxacin 15-20 mg/kg po Q 12 hrs (not to exceed 1 gram/day)  OR  Doxycycline  >8 yrs and >45 kg: 100 mg po BID  >8 yrs and ≤45 kg: 2.2 mg/kg po BID  ≤8 yrs: 2.2 mg/kg po BID	60 days (if only suspected but not confirmed exposure, may stop antibiotics if testing of substance rules out exposure to <i>B. anthracis</i> )
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- If susceptibility testing allows, therapy should be changed to oral amoxicillin (if no penicillin allergy) for post-exposure prophylaxis to continue therapy out to 60 days.
- Although tetracyclines are not recommended during pregnancy, 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 course of therapy (7-14 days) prior to the 6<sup>th</sup> month of gestation.
- Use of tetracyclines and fluoroquinolones in children has potential adverse effects. These risks must be weighed carefully against the risk for developing life-threatening disease. If a release of *B. anthracis* is confirmed, children should be treated initially with ciprofloxacin or doxycycline as prophylaxis, but therapy should be changed to oral amoxicillin 40 mg/kg of body mass per day divided every 8 hours (not to exceed 500 mg TID) as soon as penicillin susceptibility of the organism has been confirmed.

## APPENDIX: HOW TO IDENTIFY SUSPICIOUS PACKAGES AND LETTERS

Some characteristics of suspicious packages and letters include the following:

- Excessive postage
- Handwritten or poorly typed addresses
- Incorrect titles
- Title, but no name
- Misspellings of common words
- Oily stains, discolorations or odor
- No return address
- Excessive weight
- Lopsided or uneven envelope
- Protruding wires or aluminum foil
- Excessive security material such as masking tape, string, etc.
- Visual distractions
- Ticking sound
- Marked with restrictive endorsements, such as “Personal” or “Confidential”
- Shows a city or state in the postmark that does not match the return address

Primary Author: Santa Clara County Health Department

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