

October 16, 2001

TO: City and County Health Departments, Emergency Medicine Directors,  
Infection Control Practitioners, Infectious Disease Physicians, Laboratory  
Directors and Others on the OSDH Public Health Alert System

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Oklahoma State Department of Health

SUBJECT: PUBLIC HEALTH ALERT: BIOTERRORISM

Infection Control Practitioners: Please distribute this document to the Emergency  
Department and medical staff.

Recent events indicate that anthrax is being used in acts of terrorism. To date, contaminated letters delivered through the mail have been the apparent means of dissemination. Media coverage of these events has caused a great deal of public fear that has resulted in the need for the health-care community to be knowledgeable about this threat so that they can respond appropriately. The enclosed guidelines are intended to provide important information to health-care professionals to assist them in addressing issues related to bioterrorism (BT). Other information will be disseminated as it becomes available. Please share this information with all appropriate medical, nursing, laboratory and pharmacy staff in your facility.

#### **Summary of Recommendations:**

- At present, there is no evidence of human cases of anthrax in Oklahoma. Also no anthrax contaminated packages or letters have been identified. However, health professionals should remain alert for possible BT activity.
- Immediately report any confirmed or suspected cases of anthrax or other potential BT agents (including plague, smallpox, tularemia, brucellosis), and any unusual disease manifestations or clusters of disease to the **Oklahoma State Department of Health (OSDH), Communicable Disease Division, 405/271-4060 (24 hours/day, 7 days/week.)**
- The routine prescribing of prophylactic antibiotics in the absence of evidence that a BT event has occurred in Oklahoma is strongly discouraged.
- Nasal cultures for anthrax are primarily for epidemiological purposes and should not be used in the evaluation of asymptomatic patients or patients with no confirmed exposure to anthrax.
- Serological testing for anthrax is a developmental test at the CDC. At present it is used for epidemiological purposes and is not helpful for evaluating asymptomatic patients or patients with no confirmed exposure to anthrax.
- The risk of transmitting anthrax through a contaminated letter or package is extremely low. Testing of suspicious substances can be performed by the OSDH laboratory. Persons who receive threatening letters or packages should contact local law enforcement for investigation and transport to the OSDH lab.

# Oklahoma State Department of Health

## Public Health Guidelines for Bioterrorism

(These recommendations are modified from CDC Recommendations of October 14, 2001)

### I. Responding to anthrax or other biological agent threats

Detailed recommendations for responding to anthrax mail threats can be found in the document “Recommendations to Prevent the Transmission of Biological Agents Through Letters or Packages Delivered in the Mail”. In general, when a person receives a threatening letter or package, or opens a letter or package in which a suspicious substance spills out, they should contact their local law enforcement agency or dial 911. Whenever possible, the law enforcement agency will respond to the incident and make arrangements to transport the package to the OSDH Lab for testing. The response to these incidents may vary from county to county and Health Department administrators are encouraged to coordinate these efforts with local police and fire departments. Persons who open a letter or package that contains a substance thought to possibly be anthrax do not need to be routinely given prophylactic antibiotics in the absence of laboratory documentation that the substance is indeed anthrax, or other evidence to suggest that a BT event might have occurred.

### II. Recommendations for persons possibly exposed to anthrax

#### A. Asymptomatic patient WITHOUT known exposure

- Reassure the patient about the rarity of infection without known exposure.
- It's important for people to know that there is no screening test available for the detection of anthrax infection in an asymptomatic person. Nasopharyngeal swabs and blood serum tests should not be used for diagnosis or screening; they are generally used as an epidemiologic tool or to assist in confirming the diagnosis in a person with symptoms compatible with anthrax.

#### B. Asymptomatic patient WITH known exposure

- Conduct an individual risk assessment with public health officials to determine if post-exposure prophylaxis is necessary. Currently, there are no screening tests available for the detection of anthrax infection in an asymptomatic person.
- Decontaminating the patient and their clothing is not routinely recommended. However, persons who may have come in contact with a suspicious substance should be advised to wash hands immediately, shower as soon as possible, and wash clothes with soap and hot water as soon as possible.
- **Post-exposure Prophylaxis (PEP) Recommendations** : Antibiotics should only be used in situations in which there is evidence to suggest that a BT event may have occurred and that the patient might have been exposed. The routine prescribing of antibiotics without credible evidence of an exposure is strongly discouraged. Anthrax is not spread from person to person ; PEP is therefore not recommended for family members and other personal contacts of exposed persons unless they were similarly exposed.

	Initial therapy	Duration
Adults (including pregnant woman <sup>1,2</sup> and immunocompromised)	Ciprofloxacin 500 mg po BID <b>Or</b> Doxycycline 100 mg po BID	60 days
Children <sup>1,3</sup>	Ciprofloxacin 15-20 mg/kg po Q12 hrs <sup>4</sup> <b>Or</b> Doxycycline <sup>5</sup> : >8 yrs and >45 kg: 100 mg po BID >8 yrs and = 45 kg: 2.2 mg/kg po BID = 8 yrs: same as >8 yrs and = 45 kg	60 days

1. If susceptibility testing allows, therapy should be changed to oral amoxicillin for post-exposure prophylaxis to continue therapy out to 60 days. In Florida, susceptibility testing determined that the isolate was penicillin susceptible, and therefore amoxicillin was indicated as a first-line agent.
2. Although tetracyclines are not recommended during pregnancy, their use may be indicated for life-threatening illness. Adverse affects 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. Please consult physician after the 6<sup>th</sup> month of gestation for recommendations.
3. Use of tetracyclines and fluoroquinolones in children has 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 three times daily) as soon as penicillin susceptibility of the organism has been confirmed.
4. Ciprofloxacin dose should not exceed 1 gram/day in children.
5. In 1991, the American Academy of Pediatrics amended their recommendation to allow treatment of young children with tetracyclines for serious infections, such as, Rocky Mountain Spotted Fever, for which doxycycline may be indicated. Doxycycline is preferred for its twice-a-day dosing and low incidence of gastrointestinal side effects.

### C. Hospitalized Patients with Symptoms Compatible with Anthrax

- Notify public health officials so they can begin an epidemiologic investigation.
- Confirm the diagnosis by obtaining the appropriate laboratory specimens based on the clinical form of anthrax that is suspected (inhalational, gastrointestinal, or cutaneous).
  - Inhalational anthrax: nasal swab, blood, CSF, and/or sputum
  - Gastrointestinal anthrax: vomitus, feces, and/or blood
  - Cutaneous anthrax: vesicular fluid and/or blood

## III. Signs and Symptoms of Anthrax Infection

For a detailed review of anthrax, refer to: Ingelsby TV, et al. Anthrax as a biological weapon: Medical and public health management, JAMA 1999;281:1735-1745 (available online at <http://jama.ama-assn.org>).

***Inhalational (pulmonary) anthrax:*** A brief prodrome resembling a viral respiratory illness followed by development of hypoxia and dyspnea, with radiographic evidence of mediastinal widening. This is the most lethal form of anthrax and results from inspiration of 8,000-40,000 spores of *B. anthracis*. The incubation period of inhalational anthrax is unclear, but it is reported to range between 1 and 7 days possibly ranging up to 42 days. Initial symptoms include sore throat, mild fever, muscle aches and malaise. These may progress to respiratory failure and shock. Meningitis frequently develops. Physical findings are usually nonspecific. The chest x-ray may reveal a widened mediastinum. Diagnostic modalities include gram stain of blood, and culturing of blood, CSF and sputum. Nasopharyngeal culture can be used in conjunction with other cultures but should not be used alone in the evaluation of symptomatic patients. Detection of *B. anthracis* by gram stain of blood or on blood culture may not be diagnostic until late in the course of illness. Therapy includes high dose penicillin, ciprofloxacin or doxycycline. Case-fatality is estimated to be at least 75%, even with all possible supportive care including appropriate antibiotics. Though estimates of the impact of the delay in postexposure prophylaxis or treatment on survival can only be approximated, it has been suggested that for each day of delay in initiating postexposure prophylaxis the case-fatality rate increases by 5 to 10%. Pulmonary anthrax is not spread person-to-person.

***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 is considered to have an incubation period of 1-7 days. An oropharyngeal and an abdominal form of the disease have been described in this category. 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. Diagnostic modalities include gram stain of blood and culture of vomitus, stool and blood. The case-fatality is estimated to be 25-60%, and the effect of early antibiotic treatment on that case-fatality is not defined.

***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. Diagnosis should be attempted by gram stain and culture of fluid from the lesion and blood. The case fatality for cutaneous anthrax is 20% without and 1% with antibiotic treatment.

**Any suspected case of anthrax should be immediately reported to the Communicable Disease Division of the Oklahoma State Department of Health at (405) 271-4060, 24 hours/day, 7 days/week.**

**Any previously healthy patient with the following clinical presentations should be immediately reported to OSDH.**

- **A severe, unexplained febrile illness or death,**
- **Sepsis or respiratory failure with a widened mediastinum,**
- **Sepsis with gram-positive rods or a *Bacillus* species identified in the blood or CSF.**

Clinical laboratories should take care not to regard all isolates of *Bacillus species* as contaminants, especially if isolated from blood or CSF, or in patients with multiple positive cultures. OSDH recommends that all sterile site *Bacillus* isolates be further evaluated, and if non-motile or non-hemolytic, or if the clinical syndrome is suggestive of anthrax, the isolates should be immediately referred to the OSDH Public Health Lab (405/271-5070, or after hours 405/271-4060).

**IV. Other Issues Related to Anthrax:** Recent events have created a great deal of public fear and the subsequent need for information on issues related to this threat. The following provides information for some of the frequently asked questions.

**Antibiotics:** Antibiotics may be indicated to protect persons from developing disease in situations in which there is evidence that a BT event occurred. However, the routine prescribing and stockpiling of antibiotics in the absence of a BT event is strongly discouraged. Potential problems with such a practice include adverse drug reactions, persons taking the drugs inappropriately, enhancing the development of antibiotic resistant organisms, and the use of expired medications. A major concern with this practice is the potential for depleting local supplies of antibiotics that would not be available for routine or emergency use.

**Anthrax vaccine:** The vaccine is currently only available to military personnel deployed to areas of the world where there is increased risk for exposure to anthrax and other BT agents. The vaccine is not available to the public and there is no plan at present for routine vaccination of the general public.

**Gas masks:** The use of gas masks to protect against biological agents is not recommended. Contrary to previous terrorist events involving explosions or crashes, the release of anthrax or other BT agents will likely go unnoticed and people will not know that they are being exposed to anthrax at the time it is occurring. People would therefore have to wear the mask at all times to protect against an unobserved event.

**Nasal swabs:** Following the recent death of a Florida man, healthy coworkers in the same building as the case patient were tested with nasal cultures to determine if there was evidence of a more widespread exposure. However, nasal cultures have no role in the evaluation of persons in the absence of evidence of a BT event. They are generally only used for epidemiologic purposes or in conjunction with other diagnostic tests (culture of blood, CSF, or sputum) in persons with symptoms compatible with anthrax.

**Serology:** Serological testing for anthrax is a developmental test at the CDC and is not routinely available. It is currently being used to aid in the epidemiological investigations but at present is not helpful for establishing diagnosis during acute illness.

**How is Oklahoma responding to the threat of Bioterrorism?** A system for surveillance and control of infectious diseases has been established in Oklahoma for several decades. That system is coordinated at the state level by the Communicable Disease Division of the Oklahoma State Department of Health, and functions at the local level through city and county health departments. The Infectious Disease Reporting System provides the information required to identify and monitor infectious diseases in the state. Important partners in the effort to quickly identify and intervene in disease outbreaks include Infection Control Practitioners in hospitals, microbiology laboratories, the emergency response system, Poison Control Center, and physicians and other health professionals. This long-established system provides an excellent foundation for responding to BT and was expanded in 1999 through federal grants to meet specific BT-related responsibilities. In particular, funds have been used to improve our laboratory capabilities to quickly identify BT agents and also to hire a full time BT coordinator (Robert Petrone, PhD, 405/271-4060).

**V. General References:** For more detailed information concerning potential BT agents, please consult the following references or websites:

- American College of Physicians: <http://www.acponline.org/bioterr/>
- American Society of Microbiology: <http://www.asmtusa.org/pesrc/bioprep.htm>
- Association for Infection Control Practitioners: <http://www.apic.org/bioterror/>
- CDC Bioterrorism Preparedness and Response: <http://www.bt.cdc.gov>.
- Infectious Disease Society of America: <http://www.idsociety.org>
- Johns Hopkins Center for Civilian Biodefense: <http://www.hopkins-biodefense.org>  
The Johns Hopkins Center for Civilian Biodefense has written consensus guidelines on the medical and public health management of the primary bioterrorist agents, including smallpox, anthrax, botulism, plague and tularemia. These guidelines were published in the Journal of the American Medical Association and archived copies are available at <http://jama.ama-assn.org>.
- US Army Medical Research Institute of Infectious Diseases: <http://www.usamriid.army.mil/education/bluebook.html>

## **VI. Anthrax Information for Laboratory Personnel**

Clinical lab personnel will most likely be the first ones to perform preliminary testing on clinical specimens from patients who may have been intentionally exposed to the organism, and will play a critical role in facilitating rapid identification of *B. anthracis*. These guidelines provide background information and guidance to clinical laboratory personnel in recognizing *Bacillus anthracis* in a clinical specimen. Laboratory confirmation of *B. anthracis* should be performed at the State Public Health Laboratory.

**Any suspected isolate of *B. anthracis* must be reported to the OSDH Laboratory IMMEDIATELY (405/271-5070, or 405/271-4060 after hours).**

## HANDLING LABORATORY SPECIMENS (possible *B. anthracis*)

- Risk to lab personnel from handling clinical lab specimens with *B. anthracis* is low, but it is important to minimize possible exposures to personnel as well as prevent contamination of the lab. Standard lab practices are sufficient. Perform lab tests in an annually certified Class II Biological Safety Cabinet; if that is not possible, then use standard lab protective eyewear and a mask.
- If exposure to contaminated sharps occurs:
  - Follow standard reporting procedures for sharps exposures
  - Thoroughly irrigate site with soap and water and apply a disinfectant solution such as a 0.5% hypochlorite solution. **DO NOT SCRUB AREA.**
  - Promptly begin prophylaxis for cutaneous anthrax
  - Recommended treatment for cutaneous exposure: prophylaxis with Ciprofloxacin 500 mg by mouth twice a day for 7-10 days or Doxycycline 100 mg by mouth twice a day for 7-10 days.
  - Notify the OSDH Public Health Laboratory.

## ROLE OF THE CLINICAL LABORATORY

- Perform laboratory tests for presumptive identification of *B. anthracis* on clinical specimens
- Raise your index of suspicion for *B. anthracis* when the clinical picture (provided by the clinician) involves a rapidly progressive respiratory illness of unknown cause in a previously healthy person
- Refer any suspected isolates **IMMEDIATELY** to the OSDH Public Health Lab.

## PRESUMPTIVE IDENTIFICATION OF *Bacillus anthracis*

- **Direct smears from clinical specimens**
  - Encapsulated broad rods in short chains, 2-4 cells. India Ink will demonstrate capsule (Gram stain will not)
  - *B. anthracis* will not usually be present in clinical specimens until late in course of the disease
- **Smears from sheep blood agar or other routine nutrient medium**
  - Non-encapsulated broad rods in long chains
  - Encapsulated bacilli will only grow in nutrient agar supplemented with 0.8% sodium bicarbonate in the presence of 5% CO<sub>2</sub> (Note: this procedure is performed in Level B laboratories)

## Gram stain morphology of *B. anthracis*

- Broad, gram-positive rod: 1-1.5 x 3-5 μ
- Oval, central to subterminal spores: 1 x 1.5 μ with no significant swelling of cell
- Spores usually **NOT** present in clinical specimens unless exposed to atmospheric O<sub>2</sub>

### Colony Characteristics of *B. anthracis*

- ***Bacillus anthracis* can be isolated primarily from blood, sputum, CSF, vesicular fluid or eschar, and stool (if gastrointestinal anthrax).**
- After incubation on a blood agar plate for 15-24 hours at 35-37° C, well isolated colonies are 2-5 mm in diameter; heavily inoculated areas may show growth in 6-8 hours
- Gray-white, flat or slightly convex colonies are irregularly round, with edges that slightly undulate, and have “ground glass” appearance
- Often have comma-shaped protrusions from colony edge (“Medusa head” colonies)
- Tenacious consistency (when teased with a loop, the growth will stand up like a beaten egg white)
- Non-hemolytic (weak hemolysis may be observed under areas of confluent growth in aging cultures and should NOT be confused with real  $\beta$ -hemolysis)
- Will not grow on MacConkey agar
- Non-motile

### Presumptive Identification key for *Bacillus anthracis*

- Non-hemolytic
- Non-motile
- Encapsulated (requires India ink to visualize the capsule)
- Gram-positive, sporeforming rod

### If *B. anthracis* is suspected

- The health care provider, local law enforcement, and the local and State DOH should be notified immediately
- Do not perform further tests once you have reason to suspect *B. anthracis*. The specimen should be transported to the OSDH Lab as directed (see Packaging and Transporting Protocol below)
- Level B laboratories (OSDH Lab) will perform the following presumptive and confirmatory tests:
  - lysis by gamma phage
  - capsule detection (by DFA)
  - detection of cell-wall polysaccharide antigen by DFA

### DECONTAMINATION

- Effective sporicidal decontamination solutions
- Commercially-available bleach, 0.5% hypochlorite (a 1:10 dilution of household bleach)
- Rinse off the concentrated bleach to avoid its caustic effects

#### Surfaces and non-sterilizable equipment

- Work surfaces should be wiped before and after use with a sporicidal decontamination solution
- Routinely clean non-sterilizable equipment with a decontamination solution

#### Contaminated instruments (pipettes, needles, loops, micro slides)

- Soak in a decontamination solution until autoclaving

#### Accidental spills of material known or suspected to be contaminated with *B. anthracis*

- For contamination involving fresh clinical samples:
  - Flood with a decontamination solution
  - Soak five minutes before cleaning up
- For contamination involving lab samples, such as culture plates or blood cultures, or spills occurring in areas that are below room temperature:
  - Gently cover spill, then liberally apply decontamination solution
  - Soak for one hour before cleaning up
  - Any materials soiled during the clean-up must be autoclaved or incinerated

#### DISPOSAL

- Incinerate or steam sterilize cultures, infected material, and suspect material

#### PACKAGING and TRANSPORTING PROTOCOL

Packaging and labeling specimens is the same as for any infectious substance

- If the specimen is a dry powder or paper material, place it in a plastic zip-lock bag, and place biohazard label.
- If the specimen is a clinical specimen, place biohazard label on the specimen receptacle, wrap the receptacle with an absorbent material.
- Place the bag or specimen receptacle into a leak proof container with a tight cover that is labeled “biohazard.”
- Place this container into a second leak proof container with a tight cover that is labeled “biohazard.” The size of the second container should be no larger than a one-gallon paint can.
- For a clinical specimen, an ice pack (not ice) should be placed in the second container to keep the specimen cold
- If the specimen is not a clinical specimen, but is paper or powder, the ice pack should be omitted
- Place the second container into a third leak proof container with a tight cover that is labeled “biohazard.” The third container should be no larger than a five-gallon paint can.
- Both containers should meet state and federal regulations for transport of hazardous material, and be properly labeled.

### Transporting specimens to the OSDH Lab

- Will be coordinated with the OSDH Lab at [405/271-5070 or 405/271-4060 after hours].
- Local law enforcement or FBI personnel may be utilized to transport specimens if bioterrorism is suspected.
- In cases where the specimen is shipped by commercial carrier, ship according to State and Federal shipping regulations.

### REFERENCES FOR LABORATORY GUIDELINES

- Laboratory Protocols for bioterrorism response laboratories for the identification of *Bacillus anthracis*. CDC BT public web site: [www.bt.cdc.gov](http://www.bt.cdc.gov)
- Inglesby TV, Henderson DA, Barlett JG, Ascher MS, et al. Anthrax as a biological weapon: Medical and public health management (consensus statement). *JAMA*, May 12, 1999;281(18):1735-1745.
- No authors listed. Biological warfare and terrorism: the military and public health response. U.S. Army, Public Health Training Network, Centers for Disease Control, Food and Drug Administration, Satellite broadcast, September 21-23, 1999.

### HELPFUL WEBSITES

- Biosafety in the Microbiology Lab [www.cdc.gov/od/ohs](http://www.cdc.gov/od/ohs)
- Guideline for Isolation Precautions [www.cdc.gov/ncidod/hip](http://www.cdc.gov/ncidod/hip)
- Public Health Image Library [www.phil.cdc.gov](http://www.phil.cdc.gov)
- CDC Division of Laboratory Systems (DLS) [www.phppo.cdc.gov/dls/default.asp](http://www.phppo.cdc.gov/dls/default.asp)
- World Health Organization (WHO): Guidelines for the Surveillance and Control of Anthrax in Humans and Animals [www.who.int/emc-documents/zoonoses/whoemczdi986c.html](http://www.who.int/emc-documents/zoonoses/whoemczdi986c.html)