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CDC HEALTH UPDATE

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Revised CDC Guidelines for State Health Departments To State Health Officers, State Epidemiologists and State Laboratory Directors

I. Advice to the Public

How To Handle Anthrax and Other Biological Agent Threats

Many facilities in communities around the country have received anthrax threat letters. Most were empty envelopes; some have contained powdery substances. The purpose of these guidelines is to recommend procedures for handling such incidents.

DO NOT PANIC

1. Anthrax organisms can cause infection in the skin, gastrointestinal system, or the lungs. To do, so the organism must be rubbed into abraded skin, swallowed, or inhaled as a fine, aerosolized mist. Disease can be prevented after exposure to the anthrax spores by early treatment with the appropriate antibiotics. Anthrax is not spread from one person to another person.

2. For anthrax to be effective as a covert agent, it must be aerosolized into very small particles. This is difficult to do, and requires a great deal of technical skill and special equipment. If these small particles are inhaled, life-threatening lung infection can occur, but prompt recognition and treatment are effective.

Suspicious Letter or Package

1. Do not shake or empty the contents of any suspicious envelope or package; DO NOT try to clean up powders or fluids..

2. PLACE the envelope or package in a plastic bag or some other type of container to

prevent leakage of contents.

3. If you do not have any container, then COVER the envelope or package with anything

(e.g., clothing, paper, trash can, etc.) and do not remove this cover.

4. Then LEAVE the room and CLOSE the door, or section off the area to prevent others

from entering (i.e., keep others away).

5. WASH your hands with **soap and water** to prevent spreading any powder to your face or skin.

6. What to do next:

- If you are at **HOME**, then report the incident to local police.
- If you are at WORK, then report the incident to local police, **and** notify your building security official or an available supervisor.

7. If possible, LIST all people who were in the room or area when this suspicious letter or package was recognized. Give this list to both the local public health authorities and law enforcement officials for follow-up investigations and advice.

8. Remove heavily contaminated clothing and place in a plastic bag that can be sealed; give the bag to law enforcement personnel.

9. Shower with soap and water as soon as possible. Do not use bleach or disinfectant on your skin.

II. Advice to State and Local Health Officials

A. Asymptomatic patient WITHOUT known exposure

- Provide reassurance to the patient about the rarity of infection without known exposure.
- Recommend the patient see a health care provider for further concerns and/or diagnostic tests.
- Discourage use of nasal swabs for diagnosis of exposure. (Nasal swabs and blood serum tests are used as an epidemiological tool to characterize an outbreak when there is a known biologic agent.)

B. Asymptomatic patient WITH potential exposure

- Conduct an individual risk assessment and refer to a health care provider if post-exposure prophylaxis is necessary.
- Decontaminating the patient, other than by washing with soap and water, is not routinely recommended.

Post-exposure Prophylaxis (PEP) Recommendations

	Initial therapy	Duration
Adults (including pregnant women [1][2] and immmunocompromised)	Ciprofloxacin 500 mg po BID **Or**	60 days

	Doxycycline 100 mg po BID	
Children [1,3]	Ciprofloxacin 15-20 mg/kg po Q12 hrs[4] **Or** Doxycycline[5]: >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

C. Patients with symptoms compatible with anthrax

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: blood, CSF (if meningeal signs are present); chest X-ray

- Gastrointestinal anthrax: blood

- Cutaneous anthrax: vesicular fluid and blood

Evaluation of possible anthrax infection for individuals not connected with the AMI incident in Florida should be performed through standard laboratory tests, following the Laboratory Response Network (LRN [6]) 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 level B laboratory criteria for confirmation of *B. anthracis* are available through State Public Health 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.

III. Signs and Symptoms of 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. This, the most lethal, form of anthrax results from inspiration of 8,000-40,000 spores of *B. anthracis*. The incubation of inhalational anthrax among humans is unclear, but it is reported to range between 1 and 7 days possibly ranging up to 60 days. Host factors, dose of exposure and chemoprophylaxis may play a role. Initial symptoms include sore throat, mild fever, muscle aches and malaise. These may progress to respiratory failure and shock. Meningitis frequently develops. Case-fatality estimates for inhalational anthrax are based on incomplete information regarding exposed populations and infected populations in the few case series and studies that have been published. However, case-fatality is extremely high, even with all possible supportive care including appropriate antibiotics. Records of industrially acquired inhalational anthrax in the United Kingdom before antibiotics were available reveal that 97% of cases were fatal. With antibiotic treatment the fatality rate is estimated to be at least 75%. Estimates of the impact of the delay in post-exposure prophylaxis or treatment on survival are not known.

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. The case-fatality rate is estimated to be 25-60%, the effect of early antibiotic treatment on that case-fatality rate 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. The case fatality rate for cutaneous anthrax is 20% without, and less than 1% with, antibiotic treatment.

IV. Advice to Laboratory Personnel

These guidelines provide background information and guidance to clinical laboratory personnel in recognizing *Bacillus anthracis* in a clinical specimen. They are NOT intended to provide training for laboratory identification of *B. anthracis*. 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*. 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 State Public Health Laboratory IMMEDIATELY. The State Public Health Laboratory is available for consultation or testing 24 hours per day and can be reached through the Department of Health Communicable Disease Epidemiology 24-hour emergency number. Following an appropriate consultation with the State Public Health Lab regarding a suspected isolate of *B. anthracis*, communication should then be established with the local FBI field office for possible law enforcement involvement.

A. 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:

- Wear gloves and protective gowns when handling clinical specimens
- Wash immediately with soap and water if there is direct contact with a clinical or lab specimen
- Avoid splashing or creating aerosols
- 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
- Blood cultures should be maintained in a closed system (blood culture bottles)
- Keep culture plates covered at all times; minimize exposure when extracting specimens for testing
- Work on a smooth surface that can be cleaned easily and wipe with bleach regularly

If lab or clinical specimen material is spilled or splashed onto lab personnel:

- Remove outer clothing carefully while still in the lab and place in a labeled, plastic bag
- Remove rest of clothing in the locker room and place in a labeled, plastic bag
- Shower thoroughly with soap and water in the locker room
- Inform the supervisor and physician

If exposure to contaminated sharps occurs:

- Follow standard reporting procedures for sharps exposures
- Thoroughly irrigate site with soap and 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 14 days or Doxycycline 100 mg by mouth twice a day for 14 days.

- Notify the State Department of Health (SDOH) and the State Public Health Laboratory (SPHL)

B. Role of the clinical laboratory

Perform laboratory tests for to rule out 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 one is unable to rule out IMMEDIATELY to the SDOH and SPHL

C. Presumptive identification of *Bacillus anthracis*

Direct smears from clinical specimens

- Encapsulated broad rods in short chains, 2-4 cells. Gram stain can demonstrate clear zones (capsule) around rods. An India ink stain should be used to further visualize the capsule microscopically.

- *B. anthracis* will not usually be present in clinical specimens until late in the course of the disease

Smears from sheep blood agar or other routine nutrient medium

- Non-encapsulated broad rods in long chains

- When grown on nutrient agar in presence of 5% CO_2 or other basal media supplemented with 0.8% sodium bicarbonate, virulent strains will yield heavily encapsulated rods (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_2

Colonial 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 β-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, spore-forming 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 DOH as directed (see Packaging and Transporting Protocol)
- Level B laboratories (State DOH) will perform the following presumptive and confirmatory tests:

  -lysis by gamma phage

  -capsule detection (by DFA)

  -detection of cell-wall polysaccharide antigen by DFA

D. Decontamination

- Effective sporicidal decontamination solutions approved for hospital use
- Commercially-available bleach, 0.5% hypochlorite (a 1:10 dilution of household bleach); may be corrosive to some surfaces
- 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 is performed

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

E. Disposal

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

F. 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 (see diagram)
- If the specimen is a clinical specimen, place biohazard label on the specimen receptacle, wrap the receptacle with an absorbent material (see diagram)
- 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 DOH Public Health Lab

- Will be coordinated with the DOH Public Health Lab at [state telephone number]
- Local 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

G. Helpful web sites

- Biosafety in the Microbiology Lab www.cdc.gov/od/ohs
- Guideline for Isolation Precautions www.cdc.gov/ncidod/hip
- Public Health Image Library phil.cdc.gov
- World Health Organization (WHO): Guidelines for the Surveillance and Control of Anthrax in Humans and Animals
  www.who.int/emc-documents/zoonoses/whoemczdi986c.html

H. References for laboratory guidelines

- Laboratory protocols for clinical Laboratories for the identification of *Bacillus anthracis*. CDC BT public web site: 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.

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[1]

If susceptibility testing ity, as in the recent *B. anthracis* exposures in Florida, therapy should be changed to oral amoxicillin for post-exposure prophylaxis to continue for 60 days.

[2]

Although tetracyclines are not recomindicates susceptibilmended 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 6th month of gestation. Consult physician after the 6th 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 80 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.

[6]

Laboratory Response Network for Bioterrorism (LRN) is a collaborative partnership and multilevel system designed to link state and local public health laboratories with advanced capacity clinical, military, veterinary, agricultural, water and food-testing laboratories. The LRN operates as a network of laboratories (laboratory levels designated A: hospital laboratories, B: state health laboratories, C: CDC laboratory, D: CDC and USAMRIID) with progressively stringent levels of safety, containment and technical proficiency necessary to perform the essential rule-out, rule-in, and referral functions required for agent identification. Network access provides all public health laboratories with the means to accept and transfer specimens to appropriate facilities where definitive testing can be undertaken. This facilitates early detection and **suspect-level** identification at the local clinical laboratory level, which is subsequently supported by more advanced capacity for rapid **presumptive and confirmatory-level testing** at state and large metropolitan public health laboratories. Further definitive characterization or highly specialized testing is provided by CDC, which serves as the national public health reference laboratory for major threat agents. The LRN consists of over 100 core and advanced capacity public health laboratories. In order to maintain network continuity, the respective State Public Health Laboratory Directors serve as the designated notification hub for maintaining operational integrity at the local level as well as communicating with CDC and FBI as appropriate.

Issues regarding the clinical use of threat agent assays: All of the biodetection assays and reagents utilized in the LRN, are intended for use in public health surveillance and the unique need related to the public health emergency, civilian biodefense and national security interests. These reagents are neither manufactured for commercial distribution nor provided for use in research purposes. An individual biodetection assay (and associated reagents) used in the standardized testing

algorithm within the LRN should not be used to support a clinical diagnosis nor initiate a medical intervention without confirmation of the laboratory-based identification by another medically established diagnostic product or procedure.

The Centers for Disease Control and Prevention (CDC) protects people's health and safety by preventing and controlling diseases and injuries; enhances health decisions by providing credible information on critical health issues; and promotes healthy living through strong partnerships with local, national and international organizations.

DEPARTMENT OF HEALTH AND HUMAN SERVICES