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Anthrax Surveillance Protocol

Anthrax may result from a naturally occurring, unintentional exposure such as from infected animals or animal products; or from an intentional exposure such as from a bioterrorism (BT) event. This protocol applies when a clinical case of cutaneous, gastrointestinal, injection or inhalational anthrax is highly suspected or confirmed.

Provider Responsibilities

1) Report confirmed or suspected cases of anthrax to the local health department immediately by phone 24/7/365; do not wait for laboratory confirmation. Anticipate the need to collaborate with public health on:
   a) Confirmation of the clinical diagnosis. Anticipate the urgent need to share medical records and laboratory and radiological data to assist with confirmation of the diagnosis. Radiographs are critical for confirmation of inhalation anthrax. Pictures of skin lesions are extremely helpful in the process of confirmation of cutaneous anthrax.
   b) Laboratory confirmation of the diagnosis. Laboratory testing should begin at the hospital laboratory. If results are suspicious for anthrax, confirmatory testing must occur through the Office of Laboratory Services (304-558-3530). The health department may also request tissue blocks and other pathological specimens, if available and appropriate.
   c) Investigation of the source of infection. Health officials will need to investigate urgently to identify the source of infection. This investigation will usually begin with interviews of the patient, family and close friends about all activities and travel during the incubation period.

Laboratory Responsibilities

1) Report confirmed or suspect cases of anthrax to the local health department immediately.

2) Fax a laboratory report or a completed 'yellow card' to the local health department.

3) Consult with the Office of Laboratory Services (304-558-3530) urgently regarding any requests for testing or confirmation of anthrax in a clinical or environmental sample. Refer suspect isolates to Office of Laboratory Services for confirmation and further characterization.

Local Health Responsibilities

1) Prior to the occurrence of an anthrax case
   a) Protect employee health:
      i) Educate employees:
         (1) Anthrax is NOT transmitted from a person who has the disease. Standard precautions should be used with persons diagnosed with anthrax.
         (2) Anthrax CAN be transmitted by direct contact with or inhalation of spores. Untrained unprotected workers should NOT enter an area known or suspected to be contaminated

with anthrax spores or come into direct contact with items or equipment contaminated with spores until the area has been decontaminated.

ii) Assemble and train outbreak response teams. The best training or 'drill' for anthrax response is routine outbreak investigation. ALL the epidemiological skills required for response to anthrax -- development of a case definition; case-finding; patient and family interviews; hypothesis formulation and testing – can be practiced during routine outbreak investigation.

iii) Educate health care providers and the public in the recognition and diagnosis of anthrax.

iv) Educate providers and laboratories to report anthrax infections to the local health department in the patient's county of residence immediately.

2) If a suspected case of anthrax is reported, the LHD should contact the Division of Infectious Disease Epidemiology (DIDE) immediately (do not wait for lab confirmation). The local health department should anticipate the need to collaborate with DIDE, other state and local jurisdictions and Federal public health officials and law enforcement.

3) Steps in investigation

a) Confirm cases:

i) For each suspected case, immediately obtain complete clinical and laboratory history. Review the WVEDSS Anthrax Investigation Form, complete any missing data, and determine whether a case is clinically or laboratory confirmed (See 'Case Definition').

ii) Assure that appropriate laboratory specimens are obtained on each suspected case (see Laboratory Notes). Specimens of blood or vesicular fluid (for cutaneous anthrax cases) are to be sent to the local hospital laboratory (Sentinel lab) for preliminary confirmation of *Bacillus anthracis*. If results are suspicious, the specimens should be sent to the WV Office of Laboratory Services (OLS) (Reference lab) for confirmation. Specimens should be packaged and shipped to OLS according to the OLS laboratory protocol.

b) Incident Triage – critical:

i) Evaluate the possibility of laboratory artifact: Are the history, clinical picture and laboratory results all consistent with anthrax?

ii) Determine if the case may have experienced natural exposure to anthrax during the incubation period, including:

(1) Exposure to a) infected livestock; b) to wool, hides, leather or other leather products from infected animals, or c) ingestion of infected animals.

(2) Obtain a travel history to determine if the case traveled to an enzootic area during the incubation period.

(3) Determine if the index case has used injection drugs.

iii) If a plausible source is identified on the initial interview, begin active surveillance to identify other cases exposed to the same source. Consider expanded active surveillance to evaluate other potential sources of infection, as indicated.

c) Outbreak investigation: Since anthrax does not occur naturally in West Virginia, a single case is defined as an outbreak. Outbreak investigation requires collaboration with experienced

epidemiologists, environmentalists and laboratorians. See the DIDE outbreak protocol. Some of the basic steps are identified here:

i) Case Finding:
   (1) Begin enhanced passive surveillance: Using the standard anthrax case definition, immediately begin enhanced passive surveillance as needed with health care providers and laboratories in the county. Educate health care providers and the public in the recognition and diagnosis of anthrax.
   (2) Conduct active surveillance: Be prepared to expand active surveillance throughout the region, e.g., be prepared to contact providers and laboratories searching for additional cases, and review/abstract patient records.
   (3) Confirm new cases: Receive and screen reports of suspected cases, and confirm new cases.
ii) Case investigation: Complete and submit the WVEDSS form
iii) Collaborate with DIDE on the case/outbreak investigation.

4) Identify exposed populations:
   a) Definition of an exposed individual: An exposed individual will be a person who shared or possibly shared airspace that was contaminated by *B. anthracis*, had direct contact with contaminated material such as spores or other environmental exposures as part of a BT event, touched an infected animal, processed animal hides or wool from an endemic area, injected potentially contaminated illicit drugs, or ingested contaminated food or water.
   b) Develop a line listing of all persons possibly exposed. Consult DIDE about appropriate information to capture on the line list.

5) Surveillance of exposed population:
   a) Contact and referral of exposed: **Assure that all exposed individuals are contacted within 24 hours** and refer them for post exposure prophylaxis (PEP) and anthrax vaccine (See Treatment section.). For large populations, incident command should alert the public about the location of clinical centers for treatment or PEP through media announcements.
   b) Surveillance of exposed individuals: Conduct regular surveillance of all exposed individuals for the appropriate incubation period. For respiratory exposure, the incubation period may be up to 100 days.
   c) Document surveillance activities on a line list. Consult with DIDE on line list development.

6) Prevention and Control:
   a) Environmental exposures: After the source has been identified, remove people from any environment confirmed or suspected to be contaminated with anthrax spores until decontamination is achieved.
   b) Post exposure prophylaxis: Because of the short incubation period, and the high mortality, PEP must begin before the investigation is complete. Consult with DIDE on recommendations. In consultation with CDC, DIDE will recommend to the State Health Commissioner that PEP should be offered to:

i) Groups of persons in which 2 or more persons have culture-confirmed anthrax (and therefore common-source exposure is likely or plausible). PEP should be offered until inhalational exposure is confirmed or ruled out or for 60 days.
ii) Groups of persons in which 1 person has culture-confirmed anthrax and an associated environmental source is also culture positive. PEP should be offered until inhalational exposure is confirmed or ruled out or for 60 days.
iii) Groups of persons undergoing investigation for probable exposure (e.g., environmental sampling). PEP should be offered for 5-10 days pending laboratory results and a final recommendation.

7) Treatment of Cases: In consultation with CDC, DIDE will recommend to the State Health Commissioner that cases should be treated according to current guidelines (See Treatment Section.)

Division of Infectious Disease Epidemiology Responsibilities

1) Prior to the report of a case of anthrax:
   a) Train DIDE response staff in occupational health issues surrounding anthrax case investigation
   b) Maintain capacity to respond rapidly to consultation, outbreak investigation and field investigation by routine response to infectious disease outbreaks and, regular training and education through attendance at conferences and literature review. Maintain skilled and experienced epidemiology workforce. Maintain updated protocols, information sheets, investigation forms and website.
2) Notify CDC urgently of a confirmed or suspected case or outbreak.
3) During an outbreak:
   a) Support the local health department(s) as needed, including leadership of field investigation.
   b) Brief the chain of command within BPH.
   c) Make recommendations for:
      1) Initiating incident command. A single case of intentionally disseminated anthrax will result in a recommendation to open incident command.
      2) Offering vaccination and prophylaxis to targeted populations
      3) Appropriate messages for public and providers
   d) Develop outbreak case definition as needed, based on the CDC/CSTE definition and incorporating elements of person, place and time. In the event of a large exposure, a loose definition (e.g., a person with fever (>38.5C) and cough or dyspnea) may be suitable for initial case-finding. The case definition should evolve as more information (e.g., exposures/risk factors) is obtained.
   e) Develop expanded investigation forms and line lists to support investigation activities
      1) Develop a line list of cases: Develop a line listing of all confirmed and suspect cases. Record information on:
         (1) Case ID number (use this number to link to other databases),
         (2) Name,

(3) Age, date of birth,
(4) Location (hospital, clinic, home),
(5) Date of onset of symptoms,
(6) Classification of case (pending, ruled out, suspected, probably, and confirmed)
(7) Type of case (cutaneous, inhalational , gastrointestinal, oropharyngeal, meningeal),
(8) Laboratory (date collected, specimen source, specimen type, results),
(9) Status of clinical information (complete or incomplete),
10) Status of exposure information (complete or incomplete),
11) Treatment,
12) Outcome and date.

Use the line listing to make work assignments to complete missing information.

e) Develop and maintain a data base of pertinent clinical and exposure data for hypothesis testing, as follows:
   1) In collaboration with local health departments / CDC, interview a representative sample of cases and obtain a complete risk factor and exposure history, including travel and activities during the cases' exposure period (during the incubation period, before onset of symptoms). Exposure period / incubation period for inhalational anthrax may be up to 100 days.
   2) If a possible source is suspected, continue the interview with the same sample of cases. Obtain more detailed information, including the type, location, duration of exposure, and other details to characterize the possible exposure source.
   3) Perform epidemiological, laboratory and environmental studies to test / refine / confirm hypotheses.
   4) Analyze and report data on numbers of cases and epidemiological findings. Share with incident command and decision-makers.

f) Develop a line listing of all persons possibly exposed. Items on the line list might include:
   1) Case ID number (use this number to link to other databases),
   2) Name,
   3) Age, date of birth,
   4) Location (hospital, clinic, home),
   5) Symptomatic? If yes, record date and time of onset of symptoms and enter into the case line list. Assign follow-up,
   6) Classification of case (pending, ruled out, suspected, clinically confirmed, and laboratory confirmed),
   7) Date / time contacted
   8) Date / time interview completed
   9) Date / time antibiotic prophylaxis started.
   10) Name of antibiotic and dose and date started.
   11) Date first dose of anthrax vaccine. (Use WVSIIS to record ALL doses / site of injection / lot number, etc. of anthrax vaccine.)
   12) Follow up date and status (well, referred for evaluation, case, no information)

   Use the line list to organize the work of the team assigned to follow up exposed persons.

g) Collaborate with OLS to confirm suspected cases and publish antimicrobial susceptibility data.
   1) Refine treatment and prophylaxis recommendations based on susceptibility data.

Disease Prevention Objectives

Prevent disease in high risk populations through:
- Education of professionals and the public to avoid exposure to any identified risk.

Disease Control Objectives

Prevent unnecessary illness and death through rapid identification of populations exposed to anthrax so appropriate treatment or post exposure prophylaxis can quickly be administered.

Surveillance Objectives

Rapidly detect and confirm a case or outbreak of anthrax if it occurs in WV.

Public Health Significance

In the U.S., the incidence of naturally acquired anthrax is extremely low. A handful of naturally occurring cases have been reported from the United States in the last decade: inhalational and gastrointestinal cases related to drum-making from contaminated animal hides or exposure to animal products and dust.

In the fall of 2001, however; 11 cases of inhalational anthrax and 11 cases of cutaneous anthrax were linked to *B. anthracis* sent through the mail. Letters were mailed to media targets and the United States Senate. In general, media targets were more likely to develop cutaneous disease. Letters processed through high-speed sorters at the Hamilton and Brentwood postal facilities, likely resulting in aerosolization of *B anthracis* spores resulted in inhalational disease in postal workers. Epidemiologists used multiple tools to address this crisis, including:

- Case finding through active surveillance and enhanced passive surveillance;
- Case and key informant interviews;
- Environmental sampling;
- Antimicrobial susceptibility testing and molecular analysis of *B anthracis* isolates; and
- Antimicrobial prophylaxis and vaccination of exposed persons.

It is likely that prompt initiation of antimicrobial prophylaxis prevented illness in postal workers and senate staff. Clearly, the prompt response of investigators is important to controlling the extent of an outbreak due to intentional dissemination of *B anthracis* spores.

Within the last decade, a new form of anthrax – injectional anthrax – has been reported among injection drug users in Europe. It is thought that contaminated heroin is the source.

Clinical Description

Anthrax presents as four distinct clinical syndromes in humans: cutaneous, inhalational, gastrointestinal and injectional.

Cutaneous: The cutaneous form occurs most frequently on the hands, neck, and forearms of persons working with infected livestock or contaminated wool, hides, leather, or hair. Spores enter a cut or abrasion on the skin. Within 3-5 days, a pruritic papule (raised itchy bump) is identified. This progresses over a few days to a fluid-filled vesicle, and then a painless ulcer (usually 1-3 cm in diameter) with a characteristic black necrotic (dying) area in the center. There is surrounding edema and there may be swelling of regional lymph nodes. The lesion typically dries and forms a coal-black eschar (scab) surrounded by edema (swelling). This local infection can occasionally disseminate into lymph nodes and blood stream causing a fatal systemic infection. Untreated, mortality from cutaneous anthrax is around 20%.

Inhalational: The first stage of illness is characterized by non-specific symptoms: fever, cough, headache, vomiting, chills, weakness or malaise, abdominal pain, and chest pain. This initial phase lasts approximately 4 days. In the second stage, symptoms progress abruptly with fever, dyspnea, diaphoresis, and shock. In advanced disease, hypotension and cyanosis progress rapidly to death. Chest X-ray may show a widened mediastinum consistent with lymphadenopathy, pulmonary infiltrates, and effusions. Hemorrhagic meningitis and gastrointestinal involvement may also occur due to hematological dissemination of *B anthracis*. In the first ten 2001 BT cases, all had abnormalities on chest X-ray: widened mediastinum was present in 7 cases, pleural effusions in 8 cases, and infiltrates in 6 cases. The case fatality rate was around 50% with intensive therapy.

Gastrointestinal: Anthrax may follow the consumption of contaminated meat or ingestion of spores. Upper gastrointestinal disease ("oral-pharyngeal form") results in oral or esophageal ulcers and leads to the development of regional lymphadenopathy, edema and sepsis. The lower gastrointestinal disease form presents with nausea, loss of appetite, vomiting, and fever followed by abdominal pain, vomiting of blood, and severe diarrhea. Several days after presentation, ascites (fluid in the abdominal cavity) may develop and peritoneal fluid may be culture-positive for *B anthracis.* Radiological studies may demonstrate ascites, thickening of the intestinal wall and enlarged mesenteric lymph nodes. Mortality is high and occurs in association with hemorrhage, fluid and electrolyte imbalance, intestinal perforation, sepsis and/or shock.

Injectional: This form of anthrax was recently described for the first time in Europe in heroin injection users. No cases of injectional anthrax have been identified in the United States. While the presentation may sometimes mimic cutaneous anthrax with eschar formation and surrounding edema, clinical presentation may be similar to other skin infections associated with injection drug use, and the diagnosis may be initially missed. Injectional anthrax may be associated with subcutaneous

abscess formation and extensive soft tissue involvement requiring extensive surgical debridement. From soft tissue, B anthracis may disseminate to the bloodstream and other organ sites and result in death.

Bacillus anthracis produces toxins and other virulence factors after germination inside the host: lethal toxin (LT), edema toxin (ET) and proteases. LT promotes shock by disruption of endothelial cells, resulting in progressive hypotension, hemoconcentration and increased lactic acid. ET promotes substantial extravasation of fluid into soft tissues as well as increases in urine output and hyponatremia, suggesting renal tubular dysfunction. Proteases result in tissue damage. Finally, the *B anthracis* cell wall causes inflammation and hemodynamic and organ dysfunction. Patients and animals dying with anthrax have very high bacterial loads. When the bacteria breaks down, the resultant inflammation may also contribute to the development of shock.

LT forms when lethal factor joins with protective antigen (PA). Similarly, ET forms when edema factor combines with PA. Scientists have now developed antibodies to PA as a possible adjunctive treatment for humans infected with anthrax.

Etiologic Agent

Bacillus anthracis, the causative agent of anthrax, is an aerobic, gram-positive spore-forming, nonmotile rod. The spores are the usual infective form**.** The spores are environmentally stable, resistant to extremes of temperature, humidity and ultraviolet light. They can survive extended periods of time in the environment without nutrients. When introduced into a human or animal host, they rapidly germinate leading to disease.

Reservoir

Anthrax is primarily a zoonotic disease of herbivores, with cattle, sheep, goats, and horses being the usual animal hosts, but other animals may be infected. These animals become infected while grazing due to exposure to spores in contaminated soil. Presumably, infected animals die rapidly enabling the carcass to further contaminate the soil, thereby perpetuating the cycle. Anthrax is enzootic in sub-Saharan Africa, Asia, and some parts of southern Europe and Australia. Parts of the Western United States have cases in livestock with rare spillover into humans.

Mode of Transmission

Humans generally contract the disease by handling contaminated hair, wool, hides, flesh, blood, or excreta of infected animals; by contact with contaminated soil; or by contact with contaminated manufactured products of animal origin. Infection is introduced by: 1) skin contact via scratches, abrasions or wounds; 2) inhalation of spores, 3) ingestion of insufficiently cooked infected meat or spores; or 4) injection of contaminated material (e.g. drugs).

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With intentional exposure, as in a bioterrorist release, breathing in the spores or contact with an opening in the skin (cuts, scratches, abrasions, etc) have been the most likely routes of entry into the body.

Injectional anthrax is thought to be related to unintentional contamination of heroin during manufacture or smuggling.

Incubation Period

The incubation period depends on the route of exposure.

Cutaneous: 1-12 days
Gastrointestinal and oropharyngeal: 1-6 days
Inhalational: usually 1-6 days; up to 100 days in non-human primates
Injectional: 1-10 days, based on limited data

Infectious Period

Person-to-person transmission has not been documented. Use standard precautions with anthrax patients.

Outbreak Recognition

One case of anthrax constitutes an outbreak.

An outbreak due to intentional dissemination of anthrax spores might present initially as large numbers of previously healthy patients with influenza-like illness; followed by sudden progression to shock and multi-organ failure after a few days illness. Most patients would have abnormal chest radiographs, including many with a widened mediastinum.

Case Definition

Cutaneous Anthrax:
An acute illness, or post-mortem examination revealing a painless skin lesion developing over 2 to 6 days from a papular through a vesicular stage into a depressed black eschar with surrounding edema. Fever, malaise and lymphadenopathy may accompany the lesion.

Inhalation Anthrax:
An acute illness, or post-mortem examination revealing a prodrome resembling a viral respiratory illness, followed by hypoxia, dyspnea or acute respiratory distress with resulting cyanosis and shock. Radiological evidence of mediastinal widening or pleural effusion is common.

Gastrointestinal Anthrax:
An acute illness, or post-mortem examination revealing severe abdominal pain and tenderness, nausea, vomiting, hematemesis, bloody diarrhea, anorexia, fever, abdominal swelling and septicemia.

Oropharyngeal Anthrax:
An acute illness, or post-mortem examination revealing a painless mucosal lesion in the oral cavity or oropharynx, with cervical adenopathy, edema, pharyngitis, fever, and possibly septicemia.

Meningeal Anthrax:
An acute illness, or post-mortem examination revealing fever, convulsions, coma, or meningeal signs. Signs of another form will likely be evident as this syndrome is usually secondary to the above syndromes.

Case Classification

Suspected
An illness suggestive of one of the known anthrax clinical forms. No definitive, presumptive, or suggestive laboratory evidence of *B. anthracis*, or epidemiologic evidence relating it to anthrax.

Probable
A clinically compatible illness that does not meet the confirmed case definition, but with one of the following:

- Epidemiological link to a documented anthrax environmental exposure;
- Evidence of *B. anthracis* DNA (for example, by LRN-validated polymerase chain reaction) in clinical specimens collected from a normally sterile site (such as blood or cerebrospinal fluid [CSF]) or lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal);
- Positive result on testing of clinical serum specimens using the Quick ELISA Anthrax-PA kit;
- Detection of Lethal Factor (LF) in clinical serum specimens by LF mass spectrometry
- Positive result on testing of culture from clinical specimens with the RedLine Alert test.

Confirmed
A clinically compatible illness with one of the following:

- Culture and identification of *B. anthracis* from clinical specimens by the Laboratory Response Network (LRN);
- Demonstration of *B. anthracis* antigens in tissues by immunohistochemical staining using both *B. anthracis* cell wall and capsule monoclonal antibodies;

- Evidence of a four-fold rise in antibodies to protective antigen between acute and convalescent sera or a fourfold change in antibodies to protective antigen in paired convalescent sera using Centers for Disease Control and Prevention (CDC) quantitative anti-PA IgG ELISA testing;
- Documented anthrax environmental exposure AND evidence of *B. anthracis* DNA (for example, by LRN-validated polymerase chain reaction) in clinical specimens collected from a normally sterile site (such as blood or CSF) or lesion of other affected tissue (skin, pulmonary, reticuloendothelial, or gastrointestinal).

Laboratory Notes

The Office of Laboratory Services can test a wide variety of clinical and environmental specimens by PCR and conventional methods. Extensive guidance on specimen collection for diagnosis of anthrax is available at: http://www.cdc.gov/anthrax/labs/recommended_specimen.html Clinical laboratories should consult the Office of Laboratory Services (304-558-3530) about specimen collection and confirmatory testing.

Preventive Interventions

1) Sixty days of oral antibiotics and three doses of anthrax vaccine are recommended for persons exposed to anthrax. Since anthrax is highly lethal, prophylaxis must begin as soon as possible.

2) Personal protective equipment (PPE): Proper PPE must be employed by all personnel will enter an area contaminated with *B anthracis* spores. Untrained and unprotected personnel should NOT enter a contaminated zone until decontamination is complete.

3) Infection Control Procedures: Standard precautions are recommended for patient care.

4) In the event of a naturally occurring case of anthrax, remove people from the source of infected livestock, wool, hide, or leather products, etc.

5) Decontamination of the environment is technically difficult and should be undertaken only with expert guidance. Depending on the situation, a mixture of technologies may be required. See Emerg Infect Disease, 2003; vol 9: 623-7 for a discussion.

6) Management of deceased persons or animals with anthrax:
   a) Cremation is recommended. Embalming may be associated with special risks.
   b) If autopsy is performed, all instruments should be autoclaved or incinerated. Disinfection should be completed with a sporucidal agent.

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Treatment

A complete guide to treatment is beyond the scope of this protocol. Expert consultation is recommended, as well as review of: http://www.cdc.gov/anthrax/medicalcare/index.html This website has recommendations for adults, pregnant women and children. Important elements of treatment are:

- Prompt antimicrobial therapy to be adjusted when antimicrobial susceptibility results are available:
  - Systemic anthrax with suspected anthrax meningitis or when meningitis cannot be excluded: 3 drug treatment (see recommendations)
  - Systemic anthrax and anthrax meningitis has been excluded: 2 drug treatment
  - Cutaneous anthrax with no systemic disease: single oral agent
- For patients with systemic illness, in addition to antimicrobial therapy:
  - Careful monitoring in hospital with attention to airway and hemodynamic status as these patients can deteriorate rapidly
  - Evacuate pleural effusions and ascites. This appears to offer a survival advantage
  - Use of monoclonal antibodies or anthrax immune globulin against protective antigen confers a survival advantage by suppressing the action of toxins released by *B anthracis.*
  - Use of systemic steroids for patients with cutaneous involvement of the head or neck or patients with meningitis.
- Patients who were exposed to spores should receive long-term antibiotic therapy similar to prophylactic regimens to suppress *B anthracis* released from spores
- Patients exposed to spores should receive 3 doses of anthrax vaccine; at diagnosis and 2 and 4 weeks later.

Surveillance Indicators

See outbreak protocol.

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