

Plague

Surveillance Protocol

Plague may occur from an unintentional exposure to infected rodents and their fleas or through an intentional exposure such as a bioterrorism (BT) event. When necessary this protocol addresses unintentional and intentional exposures separately; otherwise the protocol applies to both situations. This protocol applies if a case of plague is highly suspected and does not apply to non-specific pulmonary, gastrointestinal, or rash illnesses.

Provider Responsibilities

- 1) Report suspect or confirmed cases of plague immediately by phone to the local health department where the patient is a resident. Complete the provider (yellow) section of the WVEDSS form and forward to the local health department.
- 2) Notify the infection control practitioner immediately for hospitalized patients. Assure that the case-patient is appropriately isolated using standard and droplet precautions.
- 3) Assure that the laboratory forwards any isolates of *Yersinia pestis* to the Office of Laboratory Services for confirmation. The Office of Laboratory Services is available at (304)-558-3530 or on the web at: <http://www.wvdhhr.org/labservices/index.cfm>
- 4) Plan to collaborate with public health officials to identify close contacts of patients with pneumonic plague (unprotected face-to-face exposure within 3 feet of the case-patient), including health care workers.

Laboratory Responsibilities

- 1) Report suspect or confirmed *Yersinia pestis* immediately to:
 - a) The physician;
 - b) The infection control practitioner; and
 - c) The local health department.
 - 2) Reports to the health department should include: Name, full address, date of birth, specimen source, test performed, test result and normal value. Fax a laboratory report or a completed 'yellow card' to the local health department.
 - 3) Forward the suspect isolate to the Office of Laboratory Services. For information, contact OLS by phone at (304)-558-3530. Information is also available on the web at: <http://www.wvdhhr.org/labservices/index.cfm>
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Public Health Action

The state and LHDs should do the following:

- 1) Prior to the occurrence of a case of plague
 - a) Protect employee health
 - i) Identify high risk employees: Identify high risk employees who will be involved in the response to a bioterrorism (BT) event or may have direct contact to plague cases. High risk individuals may include state and local epidemiologic response team members and support workers whose duties may require face-to-face contact with patients with pneumonic plague (e.g., interviewers).
 - ii) Educate high risk employees: Educate high risk employees about plague from a BT event, including respiratory droplet precautions and isolation of cases (See Preventive Interventions section).
 - iii) Personal Protective Equipment (PPE): Educate employees on the use of proper PPE AND provide appropriate PPE to employees for use during an outbreak, and ensure fit testing for employees for respirator use.
 - b) Assemble a BT epidemiologic response team: Identify staff for a BT epidemiologic response team that can adequately respond to a large outbreak by conducting surveillance and epidemiologic investigations response after a BT event.
 - i) Identify surge capacity for BT epidemiological response team.
 - ii) Train BT epidemiologic response team: Periodically train and pre-drill individuals on the team in their respective responsibilities during an outbreak.
 - c) Educate health care providers and the public in the recognition and diagnosis of plague.
 - d) Educate veterinarians to report confirmed or suspected cases of plague in animals to the West Virginia Department of Agriculture.
- 2) When a plague case is reported
 - a) Report the case to the Infectious Disease Epidemiology Program (IDEP) immediately (do not wait for lab confirmation to contact IDEP). Anticipate the need to collaborate with state and Federal public health officials, and public health officials in other state and local jurisdictions.
 - b) Isolation of case: For pneumonic plague, assure the case is appropriately isolated (standard and respiratory droplet precautions).

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- c) Confirm cases:
 - i) For each suspected case, immediately obtain a complete clinical and laboratory history. Review the provider section of the *WVEDSS Plague Investigation Form*, and obtain any missing clinical or laboratory information 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 sputum, blood, and lymph node aspirates/biopsy are to be sent to the local hospital laboratory (Sentinel lab) for preliminary confirmation of plague. If results are suspicious, the specimens will be sent to the WV Office of Laboratory Services (OLS) (Reference lab) for confirmation. Specimens will be packaged and shipped to OLS according to the OLS laboratory protocol.

- d) Confirmation of an intentional or unintentional exposure and notification
 - i) **Immediately determine whether the case was due to an unintentional, non-BT exposure.**
 - (1) Check for natural exposure to plague within 7 days prior to onset of symptoms including:
 - (a) contact with a case of pneumonic plague or travel to a plague endemic area, or
 - (b) contact with infected cats, prairie dogs, or rodents, or their fleas
 - (2) If a clear source is identified, initiate active surveillance to identify other persons exposed to the same source.
 - (3) If no clear source is identified on initial interview, begin active surveillance to identify other cases.

- e) **Notify IDEP immediately if a case is clinically or laboratory confirmed or if a BT event is suspected.** IDEP will notify the State Epidemiologist who will notify the State Health Commissioner. The WVBPH shall coordinate the response with other federal, state and local agencies according to the notification procedure in the WV Public Health Threat Preparedness Surveillance and Epidemiologic Response Plan.
 - i) Activate the BT response team: Activate staff on BT epidemiologic response team and review their responsibilities in the investigation.
 - ii) Protect employee health:
 - (1) Identify all high risk employees (See Section A.1).
 - (2) Assure protection of employee health following procedures in the Preventive Interventions Section.

- f) Case Finding and Case Ascertainment:
 - i) Develop a working case definition: Develop a working case definition for the outbreak investigation. After an outbreak has been identified, a working case definition may be considered as follows: 1) a person with fever (>38.5C) or cough (suspect case), 2) a suspected or probable case that meets the clinical case definition while laboratory

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confirmation of plague is pending; or 3) a confirmed case of plague (See Case Definition Section). The case definition should evolve as more information (e.g., exposures/risk factors) is obtained.

- ii) Begin enhanced passive surveillance: Immediately begin enhanced passive surveillance as needed with health care providers and laboratories in the county.
 - iii) Educate veterinarians to report confirmed or suspected cases of veterinary plague to the West Virginia Department of Agriculture.
 - iv) Prepare for active surveillance: If necessary, alert the regional epidemiologist and be prepared to expand active surveillance throughout the region, e.g., be prepared to interview providers and patients, and review/abstract patient records.
 - v) Confirm new cases: Receive and screen reports of suspected cases, and confirm new cases.
 - vi) Develop a line list of cases: Develop a line listing of all suspect, probable, and laboratory confirmed cases using a *Case Line List Form*. Record information on:
 - (1) Case ID number (use this ID number to link the line list with other data sets),
 - (2) Name, age, date of birth,
 - (3) Location (hospital, clinic, home),
 - (4) Time of onset of symptoms,
 - (5) Classification of case (pending, ruled out, suspected, clinically confirmed, and laboratory confirmed),
 - (6) Lab confirmation status (confirmed, negative, pending),
 - (7) Status of clinical information (complete or incomplete), and
 - (8) Status of exposure information (complete or incomplete).
 - (9) Status of contact tracing (complete or incomplete)
 - vii) Complete missing data by contacting providers for further information and/or assuring that appropriate laboratory specimens are submitted for confirmation.
 - viii) Use this master line list to manage work assignments!
- g) Contact tracing (for pneumonic plague only):
- i) Identify contacts. Interview all suspected, probable, and confirmed cases of pneumonic plague and identify all persons who had direct contact with the case since the case's onset of symptoms (henceforth referred to as a case-contact). Use forms 2B and 2D for contact tracing.
 - (1) Direct contacts: Direct contacts are defined as any person who has had face-to-face contact (within 2 meters) with a suspected, probable, or confirmed case of plague during the infectious period (See Infectious Period Section).
 - ii) Locate case contacts: Record locating information for each case-contact on form 2D. Use work and school telephone numbers, telephone directories, voting lists, neighborhood interviews, site visits, hangouts, etc., to trace case-contacts when locating information is unknown or incomplete. If case-contacts cannot be found through these mechanisms, other sources for notification, such as media announcements, may have to be considered.

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- iii) Begin post-exposure prophylaxis: Refer contacts for initiation of post-exposure prophylaxis.
 - iv) Begin surveillance of contacts: Place contacts under daily surveillance and document clinical status daily using form 2E.
 - v) Refer symptomatic contacts to medical evaluation. Contact the health care provider in advance so that infection control measures can be applied immediately on arrival of the case-contact.
- h) Exposure assessment: Consult IDEP. The basic steps are outlined here:
- i) Interview a representative sample of 8-10 cases and obtain a complete risk factor and exposure history including travel and activities during the case's exposure period (1-7 days before symptom onset).
 - ii) If a possible BT event or intentional exposure location/source is suspected, continue the interview with the same sample of cases. Determine more detailed information, including the type, location and specific areas, duration, relative amount, and method of dissemination of exposure for the possible BT event.
 - iii) For large outbreaks a case-control or cohort study may be needed. Consult IDEP.
 - iv) Conduct further epidemiological, laboratory or environmental assessment to confirm findings from the case-control / cohort study.
- i) Identify exposed population:
- i) Definition of an exposed individual: An exposed individual will be a person who shared or possibly shared airspace that was contaminated by *Y. pestis*, had direct contact with or inhaled contaminated material such as powder or other environmental exposures as part of a BT event, or shared airspace with an infected animal (e.g., with pneumonic plague), or was bitten by infected fleas from an infected animal.
 - ii) Develop a line listing of all persons possibly exposed using the *Exposed Individual Line Listing Form*. Record each person's exposure risk based upon proximity to exposure.
- j) Prevention and Control:
- i) After the source has been identified, remove people from any possible or confirmed contaminated environment until the environment is deemed safe.
 - ii) Post exposure prophylaxis (PEP): Because of the short incubation period, and the high mortality, PEP must begin before the investigation is complete. See Treatment Section for PEP guidelines. Consider offering PEP to:
 - (1) Groups of persons in which 2 or more persons have culture-confirmed plague (and therefore common-source exposure is likely or plausible). PEP should be offered for up to 7 days (See Treatment Section.)
 - (2) Groups of persons in which 1 person has culture-confirmed plague and there is a common environmental exposure which was confirmed positive for *Y. pestis*. PEP should be offered for up to 7 days.
 - (3) Groups of persons in which multiple persons meet the suspect case definition and have

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onset of illness within 3 days.

(4) PEP should be offered for up to 7 days pending culture results, epidemiological and environmental investigation and a final recommendation.

k) Surveillance of exposed population:

- i) Interview exposed individuals: **Assure that all exposed individuals are interviewed within 24 hours** and refer them to a clinical center for post exposure prophylaxis (PEP), as necessary (See Treatment Section).
- ii) Surveillance of exposed: Conduct daily interviews for 7 days after last exposure and determine whether exposed individuals develop fever (>101F) or cough. Refer symptomatic persons to a clinical center for isolation and treatment.
- iii) If an exposed individual does not have signs/symptoms of plague by the end of 7 days, then discontinue surveillance. Interview all exposed individuals to verify they have no symptoms at 7 days, and if so, indicate status of exposed individual as *Aclosed@* on *Exposed Individual Line Listing Form*.
- iv) If exposed individual develops fever (>38.5 C or 101F) or cough then assure referral for parenteral therapy (See Treatment Section) after cultures are obtained, and assure implementation of appropriate infection control and preventive interventions (See Preventive Intervention Section). Enter status of this person as a case and move person to *Case Line List Form*. Begin contact tracing for this new case.

3) Based on epidemiological, environmental and laboratory evaluation, IDEP will recommend treatment and prophylaxis guidelines to the State Health Commissioner who will communicate recommendations to incident command. Recommendations will be made available as soon as a case is suspected or confirmed. Recommendations will be revised as new information (antibiotic susceptibilities, nature of the exposure(s)/risk factors, characterization of the population at risk) evolves.

Disease Control Objectives

Prevent unnecessary illness and death through 1) rapid identification of populations exposed to plague so appropriate treatment or post exposure prophylaxis can quickly be administered and 2) adherence to infection control isolation and barrier guidelines via standard and droplet precautions.

Disease Prevention Objectives

Prevent disease in high risk populations through:

1. Education of health care workers regarding the use of droplet precautions when dealing with pneumonic plague up to 48 hours following institution of appropriate antibiotic therapy.
 2. Education of public to contact the West Virginia Department of Agriculture for the proper disposal of infected animals.
 3. Education of workers that may be exposed to infected animals in proper hygiene and
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personnel protective measures.

Surveillance Objectives

To rapidly detect and confirm a case of plague when it occurs in WV.

Public Health Significance

In the United States, 10-15 fifteen people each year are diagnosed with plague in the United States and approximately 14% (1 out of 7) of the cases of plague are fatal. Fatalities are associated with delays in diagnosis and treatment. Cases in the United States are mainly sporadic cases in rural areas associated with rats and rat fleas. Seventeen cases of pneumonic plague from 1972 to 1994 were acquired from household cats. There has never been a case of plague reported in West Virginia.

In the U.S., 390 cases were reported from 1947-1996, 84% of which were bubonic, 13% septicemic, and 2% pneumonic. Concomitant case fatality rates were 14%, 22%, and 57%, respectively (JAMA, 283(10), May 3, 2000).

Because of the terrorist events of 2001 associated with anthrax, and because large quantities of plague may have been weaponized, a bioterrorist event in which *Y. Pestis* is aerosolized cannot be ruled out. In 1970, the World Health Organization reported that in a worst-case scenario, if 50 mg of *Y. Pestis* was released as an aerosol over a city of 5 million people, pneumonic plague could occur in as many as 150,000 persons, 36,000 of whom would be expected to die.

Clinical Description

There are five individual forms of plague. Common systemic symptoms include headache, fever, cough, chills and progressive weakness. Accurate diagnosis of plague may be delayed by the presence of gastrointestinal symptoms (nausea, vomiting, diarrhea and abdominal pain), or absence of the classic bubo.

1. **Pneumonic Plague:** The clinical symptoms of this form of plague involving the lungs include a cough, fever, difficulty breathing and hemoptysis (bloody sputum). Patients with pneumonic plague will require substantial advanced medical supportive care in addition to antimicrobial therapy. Complications of this gram-negative sepsis include adult respiratory distress syndrome, disseminated intravascular coagulation, shock, and multiorgan failure.

- a. Plague following a BT attack:

Pneumonic plague is the most likely form of plague following a bioterrorist event. The pathogenesis and clinical manifestations of plague following a BT attack would be notably

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different than naturally occurring plague. Inhaled aerosolized *Y. Pestis* would cause primary pneumonic plague. The time from exposure to aerosolized plague bacilli until development of first symptoms in humans and nonhuman primates has been found to be 1 to 6 days and most often, 2 to 4 days. The first sign of illness would be expected to be fever with cough and dyspnea, sometimes with the production of bloody, watery, or less commonly, purulent sputum. Prominent gastrointestinal symptoms, including nausea, vomiting, abdominal pain, and diarrhea, might be present.

The ensuing clinical findings of primary pneumonic plague are similar to those of any severe rapidly progressive pneumonia and are quite similar to those of secondary pneumonic plague (which may develop following onset of bubonic or primary septicemic plague). Clinicopathological features may help to distinguish primary from secondary pneumonic plague. In contrast to secondary pneumonic plague, primary pneumonic plague would include absence of buboes (except, rarely, cervical buboes) and, on pathological examination, pulmonary disease with areas of profound lobular exudation and bacillary aggregation. Chest radiographs are variable, but bilateral infiltrates or consolidation are common.

Laboratory studies may reveal leukocytosis with toxic granulations, coagulation abnormalities, aminotransferase elevations, azotemia, and other evidence of multiorgan failure. All are nonspecific findings associated with sepsis and systemic inflammatory response syndrome.

The time from respiratory failure to death in humans is reported to have been between 2 to 6 days in epidemics during the preantibiotic era, with a mean of 2 to 4 days.

2. Bubonic Plague: is the most common form of naturally occurring plague. Patients have acute onset of fever and painful swollen lymph nodes (also known as buboes). The inguinal lymph nodes are most commonly involved, but the axillary or cervical lymph nodes may also be affected.
3. Septicemic Plague: Clinical symptoms include low blood pressure, acute respiratory problems and bleeding into the skin and other organs. This usually results from a complication of bubonic or pneumonic plague. When septicemic plague occurs alone, buboes do not develop.
4. Pharyngeal Plague: clinically this would appear to be a viral or streptococcal pharyngitis, but the cervical lymphadenopathy associated with this would be much more painful and severe.
5. Meningeal Plague: this is the most rare form of plague. Plague meningitis follows the hematogenous seeding of bacilli into the meninges and is associated with symptoms of fever, headache, and meningismus.

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Etiologic Agent

Yersinia pestis is a non-motile, gram-negative bacillus sometimes coccobacillus.

Reservoir

Plague is a zoonotic disease associated with rodents (mainly ground squirrels) and fleas. Rabbits, hares, wild carnivores, prairie dogs and domestic cats may also serve as a source of infection.

Mode of Transmission

Primary pneumonic plague is transmitted through airborne droplets from an infected human or animal (especially household cats) with respiratory plague or from aerosol exposure in the laboratory setting.

The most common source of a human exposure to bubonic plague is through the bite of an infected flea. This form of plague may also be transmitted less commonly through the direct contact or handling of infected tissues and fluids from animals (i.e. a bite or scratch from a household cat).

Septicemic plague may be transmitted by handling infectious materials, may be transmitted through the bite of an infected flea or more commonly as a complication of bubonic or pneumonic plague.

Neither bubonic plague nor septicemic plague spreads directly from person to person. A small percentage of patients with bubonic or septicemic plague develop secondary pneumonic plague and can then spread the disease by respiratory droplets. Persons containing the disease by this route develop primary pneumonic plague.

Pharyngeal plague is a rare form of plague that may follow inhalation or ingestion of the plague bacilli.

Meningeal plague may occur as a complication of inadequately treated septicemic or bubonic plague. A high mortality is associated with this form of plague.

A bioterrorist event would most likely occur through aerosolization of the plague bacillus.

Incubation Period

Signs and symptoms may develop from 2-8 days after being bitten by a flea, but can be a few days more in individuals that have been previously immunized. The incubation period for primary plague pneumonia is 1-4 days. An airborne exposure (i.e., from a BT event) would likely cause symptoms in 1-6 days. Contacts are considered to be at risk for development of pneumonic plague for up to 7 days after exposure to a case with pneumonic plague.

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Infectious Period

A person is infectious from onset of cough until 48 hours after treatment with antibiotics and signs of clinical improvement.

Outbreak Recognition

Outbreak recognition and investigation requires timely and complete epidemiological investigation paired with a timely and thorough laboratory investigation. As West Virginia has never reported a case of plague, one case is defined as an outbreak.

Case Definition

Clinical Description

Plague is transmitted by humans, fleas, or direct exposure to infected tissues via respiratory droplets; the disease is characterized by fever, cough, chills, headache, malaise, prostration, and leukocytosis that manifests in one or more of the following principal clinical forms:

1. Regional lymphadenitis (bubonic plague)
2. Septicemia without an evident bubo (septicemic plague)
3. Plague pneumonia, resulting from hematogenous spread in bubonic or septicemic cases (secondary pneumonic plague) or inhalation of infectious droplets (primary pneumonic plague)
4. Pharyngitis and cervical lymphadenitis resulting from exposure to larger infectious droplets or ingestion of infected tissues (pharyngeal plague)

Laboratory criteria for diagnosis

Presumptive

1. Elevated serum antibody titer(s) to *Yersinia pestis* fraction 1 (F1) antigen (without documented fourfold or greater change) in a patient with no history of plague vaccination or
2. Detection of F1 antigen in a clinical specimen by fluorescent assay.

Confirmatory

1. Isolation of *Y. pestis* from a clinical specimen or
2. Fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen.

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Case classification:

Suspected: a clinically compatible case without presumptive or confirmatory laboratory results.

Probable: a clinically compatible case with presumptive laboratory results.

Confirmed: a clinically compatible case with confirmatory laboratory results.

Laboratory Notes

Specimens

The following clinical specimens may be collected for testing for *Y. pestis*: sputum, lymph node biopsy, or blood.

Laboratory resources

Environmental samples should be sent to OLS for testing (Reference lab). Clinical specimens should be sent to hospitals or sentinel labs for rule-out or presumptive testing for *Y. Pestis*. If Sentinel lab tests indicate suspicious findings consistent with *Y. pestis* isolates should be sent to OLS for confirmation.

Preventive Interventions

The available evidence indicates that person-to-person transmission of pneumonic plague occurs via respiratory droplets. Droplet transmission-occurs when droplets containing microorganisms generated from the infected person, primarily during coughing, sneezing, and talking and during the performance of certain procedures, such as suctioning and bronchoscopy, are propelled a short distance and deposited on the host conjunctivae, nasal mucosa, and/or mouth. Because these relatively large droplets do not remain suspended in the air, special air handling and ventilation are not required to prevent droplet transmission; droplet transmission should not be confused with airborne transmission via droplet nuclei, which are much smaller.

The following preventions are recommended:

1. Environmental exposure precautions: Proper PPE including clothing and respirator use must be employed by all personnel who are exposed to *Y. pestis* by entering an environmentally contaminated exposure zone in a BT event.
2. Infection control procedures: Standard and respiratory droplet precautions are recommended for all personnel who have face-to-face contact with suspected, probable, or confirmed cases of plague or close contacts of patients, and for handling bodies of deceased patients. Recommendations for infection control against transmission of *Y. Pestis* are as follows (JAMA, May 8, 2002, 287:2391-2405):

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- c. Close contacts: Staff who have close contact with cases should practice standard and respiratory droplet precautions (surgical mask, gown, gloves, and eye protection). Employees and individuals coming into close contact with suspected or confirmed plague patients who have had less than 48 hours of antimicrobial therapy should wear surgical masks. Unnecessary close contact within the first 48 hours of therapy should be avoided.
 - d. Isolation of patients and close contacts:
 - (1) Patients: Patients should remain isolated during the first 48 hours of antibiotic therapy and until clinical improvement occurs. If isolation is impossible due to a large number of patients, patients may be cohorted while undergoing antibiotic therapy. Patients being transported should also wear surgical masks.
 - (2) Close contacts: Previous public health guidelines have advised strict isolation for all close contacts of plague patients who refuse prophylaxis. In modern times, pneumonic plague has not spread widely or rapidly within a community, and thus, isolation of close contacts refusing prophylaxis is not recommended. Instead close contacts should be put under surveillance for development of fever or cough during 7 days post exposure and treated immediately.
 - c. Housekeeping: Hospital rooms of patients should receive terminal cleaning in a manner consistent with standard precautions and clothing and linens contaminated with body fluids should be disinfected.
 - d. Laboratories: Laboratories should observe biosafety level 2 conditions. Activities with a high potential for aerosol or droplet production (centrifuging, grinding, vigorous shaking, animal studies) require biosafety level 3 conditions.
 - e. Deceased patients: Bodies of deceased patients should be handled with standard and droplet precautions:
 - (1) Contact with remains should be limited to trained personnel.
 - (2) Safety precautions for transporting corpses for burial should be the same as those for transporting ill patients.
 - (3) Aerosol-generating procedures such as bone saws associated with surgery or postmortem examination which are associated with special risks of transmission are not recommended. If such procedures are necessary, then high efficiency particulate air filtered masks and negative pressure rooms should be used.
6. Prophylaxis: Prophylaxis of all exposed individuals and contacts of pneumonic plague cases is
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recommended. In addition, treatment of all cases is recommended (See Treatment Section). In the U.S., there is no vaccine currently available for primary pneumonic plague. A U.S. licensed formaldehyde-killed whole bacilli vaccine was discontinued by manufacturers in 1999 and was effective in preventing bubonic plague.

7. **Environmental exposures:** Remove people from the environment (e.g., contaminated by a BT event) until the environment is deemed safe. There is no evidence that residual *Y. pestis* bacilli pose an environmental threat to the population following dissemination of a primary aerosol such as in a BT event. There is no spore forming life cycle similar to *Bacillus anthracis*. *Y. pestis* is very sensitive to sunlight and heating and does not survive long outside the host. There is some evidence that the bacterium may survive in the soil for some time, but there is no evidence to suggest an environmental risk to humans and thus no need for environmental decontamination. In a WHO analysis, a plague aerosol was estimated to be infectious for only 1 hour.
8. For naturally occurring incidents, remove people from exposure to infected cats, rodents, or their fleas.

Treatment

Treatment and post exposure prophylaxis recommendations are based on JAMA, 283(17), May 3,2000. Recommendations for use of antimicrobials following a deliberate release of plague are made on the basis of limited knowledge: a few published trials on treating human plague and a limited number of animal studies. A further complication is the possibility that a large number of people will need treatment.

In a contained casualty setting, where a modest number of people require treatment, parenteral antibiotic therapy is recommended. Preferred parenteral forms of the antimicrobials streptomycin or gentamicin are recommended. In a mass casualty setting, intravenous or intramuscular therapy may not be possible, so oral therapy, preferably with doxycycline (or tetracycline) or ciprofloxacin, should be administered.

Patients with pneumonic plague will require substantial advanced medical supportive care. Complications of gram-negative sepsis would be expected, including adult respiratory distress syndrome, disseminated intravascular coagulation, shock, and multiorgan failure.

Refer to the 'Working Group Recommendation for Treatment of Patients With Pneumonic Plague in the Contained and Mass Casualty Settings and for Postexposure Prophylaxis' for detailed treatment and prophylaxis recommendations (medication and dose): <http://jama.ama-assn.org/cgi/reprint/283/17/2281> (Table 2, below)

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Table 2. Working Group Recommendations for Treatment of Patients With Pneumonic Plague in the Contained and Mass Casualty Settings and for Postexposure Prophylaxis*

Patient Category	Recommended Therapy
Contained Casualty Setting	
Adults	Preferred choices
	Streptomycin, 1 g IM twice daily
	Gentamicin, 5 mg/kg IM or IV once daily or 2 mg/kg loading dose followed by 1.7 mg/kg IM or IV 3 times daily†
	Alternative choices
	Doxycycline, 100 mg IV twice daily or 200 mg IV once daily
Ciprofloxacin, 400 mg IV twice daily‡	
Chloramphenicol, 25 mg/kg IV 4 times daily§	
Children	Preferred choices
	Streptomycin, 15 mg/kg IM twice daily (maximum daily dose, 2 g)
	Gentamicin, 2.5 mg/kg IM or IV 3 times daily†
	Alternative choices
	Doxycycline, If ≥45 kg, give adult dosage
	If <45 kg, give 2.2 mg/kg IV twice daily (maximum, 200 mg/d)
Ciprofloxacin, 15 mg/kg IV twice daily‡	
Chloramphenicol, 25 mg/kg IV 4 times daily§	
Pregnant women¶	Preferred choice
	Gentamicin, 5 mg/kg IM or IV once daily or 2 mg/kg loading dose followed by 1.7 mg/kg IM or IV 3 times daily†
	Alternative choices
	Doxycycline, 100 mg IV twice daily or 200 mg IV once daily
Ciprofloxacin, 400 mg IV twice daily‡	
Mass Casualty Setting and Postexposure Prophylaxis#	
Adults	Preferred choices
	Doxycycline, 100 mg orally twice daily††
	Ciprofloxacin, 500 mg orally twice daily‡
	Alternative choice
Chloramphenicol, 25 mg/kg orally 4 times daily§**	
Children	Preferred choice
	Doxycycline,†† If ≥45 kg, give adult dosage
	If <45 kg, then give 2.2 mg/kg orally twice daily
	Ciprofloxacin, 20 mg/kg orally twice daily
	Alternative choices
Chloramphenicol, 25 mg/kg orally 4 times daily§**	
Pregnant women¶	Preferred choices
	Doxycycline, 100 mg orally twice daily††
	Ciprofloxacin, 500 mg orally twice daily
	Alternative choices
Chloramphenicol, 25 mg/kg orally 4 times daily§**	

*These are consensus recommendations of the Working Group on Civilian Biodefense and are not necessarily approved by the Food and Drug Administration. See "Therapy" section for explanations. One antimicrobial agent should be selected. Therapy should be continued for 10 days. Oral therapy should be substituted when patient's condition improves. IM indicates intramuscularly; IV, intravenously.

†Aminoglycosides must be adjusted according to renal function. Evidence suggests that gentamicin, 5 mg/kg IM or IV once daily, would be efficacious in children, although this is not yet widely accepted in clinical practice. Neonates up to 1 week of age and premature infants should receive gentamicin, 2.5 mg/kg IV twice daily.

‡Other fluoroquinolones can be substituted at doses appropriate for age. Ciprofloxacin dosage should not exceed 1 g/d in children.

§Concentration should be maintained between 5 and 20 µg/mL. Concentrations greater than 25 µg/mL can cause reversible bone marrow suppression.^{25,62}

||Refer to "Management of Special Groups" for details. In children, ciprofloxacin dose should not exceed 1 g/d, chloramphenicol should not exceed 4 g/d. Children younger than 2 years should not receive chloramphenicol.

¶Refer to "Management of Special Groups" for details and for discussion of breastfeeding women. In neonates, gentamicin loading dose of 4 mg/kg should be given initially.⁶³

#Duration of treatment of plague in mass casualty setting is 10 days. Duration of postexposure prophylaxis to prevent plague infection is 7 days.

**Children younger than 2 years should not receive chloramphenicol. Oral formulation available only outside the United States.

††Tetracycline could be substituted for doxycycline.

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Additional treatment and prophylaxis notes:

- Management of breastfeeding women: Treat the mother and infant with the same antibiotic based on what is safe and effective for the baby. In the contained casualty setting, gentamicin is recommended. In the mass casualty setting, doxycycline is recommended. Fluoroquinolones are the recommended alternative.
- Once plague is confirmed or strongly suspected in a particular area, anyone in that area with fever (of 38.5 C or higher) or cough should immediately be treated with antimicrobials for presumptive pneumonic plague. Delaying therapy until tests confirm plague will greatly decrease the person's chance of survival.
- Doxycycline is the first-choice antibiotic for postexposure prophylaxis; other recommended antibiotics are included in the guidelines referenced above.
- Asymptomatic persons who have had household, hospital, or other close contact (2 meters or less) with persons with untreated pneumonic plague should receive postexposure prophylaxis for 7 days and be monitored for fever and cough. Tetracycline, doxycycline, sulfonamides, and chloramphenicol have been recommended for these individuals. On the basis of mice studies, fluoroquinolones might also be protective.
- Persons refusing prophylaxis should be closely monitored for the development of fever or cough for the first 7 days after exposure and should be treated immediately if either occur.
- Clinical deterioration of patients despite early presumptive therapy could indicate antimicrobial resistance and should be promptly evaluated.
- Special measures should be taken for treatment or prophylaxis of those unaware of the outbreak or those requiring special assistance, such as persons who are homeless or who have cognitive disorders.

Surveillance Indicators

1. Time between suspicion of plague and first report to public health.
2. Proportion of investigations with complete risk factor and exposure data collection.
3. Time between suspicion of plague and completion of clinical history.
4. Time between suspicion of plague and completion of risk factor and exposure data collection for BT event.
5. Time from suspicion of plague and identification of source of exposure in a BT event.

Plague

Surveillance Protocol

References

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