

Plague

Summary

Plague is a flea-transmitted bacterial infection of rodents caused by *Yersinia pestis*. Fleas incidentally transmit the infection to humans and other susceptible mammalian hosts. Humans may also contract the disease from direct contact with an infected animal. The most common clinical form is acute regional lymphadenitis, called bubonic plague. Less common clinical forms include septicemic, pneumonic, and meningial plague. Pneumonic plague can be spread from person to person via airborne transmission, potentially leading to epidemics of primary pneumonic plague. Plague is subject to the International Health Regulations and immediately reportable to the Health Department and the World Health Organization. Plague is treatable with antibiotics, but has a high fatality rate with inadequate or delayed treatment. Plague preventive measures include: isolation of pneumonic plague patients; prophylactic treatment of pneumonic case contacts; avoiding contact with rodents and their fleas; reducing rodent harborage around the home; using flea control on pets; and preventing pets from hunting.

Agent

- Plague is caused by *Yersinia pestis*, a gram-negative, bi-polar staining, non-motile, non-spore forming coccobacillus.

Transmission

- Reservoir: Wild rodents (especially ground squirrels) are the natural vertebrate reservoir of plague. Lagomorphs (rabbits and hares), wild carnivores, and domestic cats may also be a source of infection to humans.
- Vector: In New Mexico, the rock squirrel flea, *Oropsylla montana*, is the most important vector of plague for humans. Many more flea species are involved in the transmission of sylvatic (wildlife) plague.
- Mode of Transmission: Most humans acquire plague through the bites of infected fleas. Fleas can be carried into the home by pet dogs and cats, and may be abundant in woodpiles or burrows where peridomestic rodents such as rock squirrels (*Spermophilus variegatus*) have succumbed to plague infection. Plague may also be transmitted by 1) direct contact with tissues and fluids of infected rodents, rabbits or carnivores, including domestic cats and dogs; 2) bites or scratches from an infected domestic cat; 3) inhalation of respiratory droplets from a person or domestic cat with plague pneumonia or pharyngitis; 4) ingestion of raw or undercooked meat from an infected animal; and 5) rarely the mishandling of plague cultures by laboratory workers.
- Period of Communicability: Uncomplicated bubonic plague is not contagious and patients do not place their family, other social contacts or attendants at

risk. Household members, however, may be at risk of exposure to the same zoonotic source as the index case. Draining buboes of plague patients should be considered infectious up to 48 hours after start of effective therapy. Pneumonic plague is transmitted by respiratory droplet; person-to-person or cat-to-person transmission can occur from a plague pneumonia source when there is close (i.e., less than 2 meters) direct contact with the infected patient. Patients with pneumonic plague are infectious until 48 hours of appropriate antimicrobial therapy has been given AND there is evidence of clinical improvement (however, no person-to-person spread of pneumonic plague has occurred in the United States since 1924; five cases of primary pneumonic plague acquired from domestic cats have been reported in the interval 1977 – 1998).

Clinical Disease

- **Incubation period:** For bubonic plague, the incubation period is 2 to 8 days. For primary pneumonic plague, the incubation period is 1 to 6 days.
- **Illness:** The common symptoms of plague include fever, severe malaise, weakness, headache, chills, myalgia and sometimes gastrointestinal symptoms. Specific forms of plague include:
 - a. **Bubonic:** This is the most common form of plague. Patients experience pain in the affected regional lymph node (called a bubo) that drains the site of the flea bite. The infected node may not be palpably enlarged during early stages. The three most common bubo locations, in descending order, are femoral/inguinal, axillary, and cervical. A femoral or inguinal bubo is likely to appear in those persons who are bitten on the leg by an infectious flea, whereas those who contract plague as a result of handling an infected animal are likely to develop an axillary bubo. Progression of signs and symptoms is usually rapid with the affected buboes becoming excruciatingly tender and painful. In some instances, usually with delayed treatment, the infection causes destruction of the lymph node with subsequent bacteremia. Untreated bubonic plague has a case fatality rate of 50-60%.
 - b. **Septicemic:** Septicemic plague is a progressive, overwhelming bloodstream infection that can result from untreated bubonic plague (i.e., secondary septicemic plague), but may also occur without prior lymphadenopathy (i.e., primary septicemic plague). Primary septicemic plague is especially dangerous due to difficulty of rapid diagnosis in the absence of a bubo. Gastrointestinal signs and symptoms are prominent in primary septicemic plague, including nausea, vomiting, abdominal pain, and diarrhea. Dissemination of *Y. pestis* to other organ systems via the bloodstream can result in secondary pneumonic plague, meningitis, endophthalmitis, multiple lymphadenitis, and hepatic or splenic abscesses. Plague endotoxin can produce septic shock, disseminated intravascular coagulation (DIC), multiple organ failure, coma, and death.

- c. Pneumonic: Hematogenous spread of plague bacilli to the lungs can result in secondary pneumonic plague. Entry of the plague bacillus via the respiratory tract may result in primary plague pneumonia, the most fulminating and fatal form of plague. Pneumonic plague patients are likely to have cough, chest pain, dyspnea and hemoptysis. Segmental pneumonitis may progress to bronchopneumonia and then to bilateral lung involvement. Pulmonary complications may include localized areas of necrosis and cavitation, pleurisy with effusion, and adult respiratory distress syndrome. Untreated pneumonic plague is almost always fatal.
- d. Other syndromes:
- Asymptomatic or subclinical infections with plague are rare to nonexistent.
 - Plague meningitis is a rare complication and typically occurs more than one week following inadequately treated bubonic plague. This form of plague is characterized by fever, headache, stiff neck, delirium, confusion, obtundation or coma. It is more common in patients with axillary buboes. Meningeal plague may be a primary manifestation (i.e., without prior lymphadenitis).
 - Plague pharyngitis may resemble tonsillitis. Anterior cervical lymph nodes are usually inflamed. Contamination of the oropharynx with *Y. pestis*-infected material is presumed to follow inhalation or ingestion of plague bacilli.
 - Plague should be considered in any patient who presents with fever and acute lymphadenitis and resides in a known plague area. Plague has been found in animals or fleas throughout New Mexico; 81% of human cases in New Mexico have occurred in seven northern counties: Bernalillo, McKinley, Rio Arriba, San Miguel, Sandoval, Santa Fe, and Taos. Other risk factors that increase the likelihood of plague include: onset in May-October; residence in a rural or semi-rural area; hunting cats in the household; presence of insect bites; handling sick or dead animals; fleas on pets; history of hunting or trapping.

Laboratory Diagnosis

- A positive fluorescent antibody stain for the presence of *Y. pestis* in direct smears or cultures of a bubo aspirate, sputum, cerebrospinal fluid, or blood provides rapid, presumptive evidence of *Y. pestis* infection.
- A single positive serologic test result ($\geq 1:10$ for total antibody) by passive hemagglutination assay or enzyme immunoassay in an unimmunized patient who has not previously had plague also provides presumptive evidence of infection. A 4-fold difference in total antibody titer between two serum specimens obtained three to four weeks apart provides serologic confirmation.
- Diagnosis of plague usually is confirmed by culture of *Y. pestis* from blood, bubo aspirate, or other clinical specimen. Samples should be submitted to the

New Mexico Department of Health Scientific Laboratory Division (SLD) for microbiological confirmation. At SLD, contact the General Microbiology section (505-841-2541) or the Virology section (505-841-2535) for questions about specimen submission.

Treatment

- Prompt diagnosis and treatment are critical for reducing the high fatality rate of plague. When human plague is suspected on clinical and epidemiological grounds, appropriate specimens for diagnosis should be obtained immediately, and the patient should be started on specific antimicrobial therapy pending laboratory confirmation.
- Treatment of disease: It is important for physicians with suspected cases to discuss the case with the on-call infectious disease physician at University Hospital in Albuquerque (1-888-UNM-PALS) to assist in diagnosis and treatment decisions. Streptomycin is effective against *Y. pestis* and is considered the drug of choice for treatment of plague, particularly the pneumonic form. However, streptomycin has limited availability. A recent retrospective study demonstrated that gentamicin alone, or in combination with tetracycline, was as efficacious as streptomycin for treating human plague. Chloramphenicol penetrates tissues well and may be an option for treating plague meningitis, endophthalmitis, myocarditis, and pleuritis. Tetracycline is effective for uncomplicated plague; tetracycline and doxycycline are usually given for prophylactic treatment of plague contacts. Tetracycline or doxycycline should not be given to pregnant women or children ≤ 8 years old unless benefits outweigh risks of dental staining. For children, trimethoprim-sulfamethoxazole may also be an option for prophylaxis.
- Prophylactic Therapy: Persons in close contact (i.e., less than 2 meters) with a human or feline case of pneumonic plague or with draining buboes (humans or animals), or persons likely to have been exposed to *Y. pestis* through flea bites or direct contact with a plague-infected animal, or persons exposed to plague in a laboratory accident, should receive antibiotic preventive therapy if exposure occurred within the previous week. Contacts should be instructed to measure their temperature twice a day for seven days and see a physician immediately if fever greater than 100 °F develops. Contact the Epidemiology and Response Division at 505-827-0006 regarding specific recommendations for plague prophylaxis.
- Supportive Therapy: Most patients are febrile with constitutional signs and symptoms, including nausea and vomiting. Hypotension and dehydration are common. Patients should be aggressively monitored and clinicians should be prepared for possible septic shock, multiple organ failure, adult respiratory distress syndrome, and disseminated intravascular coagulopathy. Buboes occasionally require incision and draining.

Surveillance

- Case Definition:
 - Confirmed* – a clinically compatible case with confirmatory laboratory results (isolation of *Y. pestis* from a clinical specimen; fourfold or greater change in serum antibody titer to *Y. pestis* F1 antigen).
 - Probable* – a clinically compatible case with presumptive laboratory results (elevated serum antibody titer(s) to *Y. pestis* F1 antigen, without a fourfold or greater change, in a patient with no history of plague vaccination; detection of F1 antigen in a clinical specimen by fluorescent assay).
 - Suspected* - a clinically compatible case without presumptive or confirmatory laboratory results; or gram-negative and/or bipolar-staining coccobacilli are seen on a smear taken from affected tissues.
- Reporting: **Report all suspected or confirmed cases of plague immediately to the Epidemiology and Response Division (ERD) at 505-827-0006.** Information needed includes: patient's name, age, sex, race, ethnicity, home address, home phone number, occupation and health care provider. The Epidemiology and Response Division will complete a plague case report form.
- Case Investigation: Complete the CDC Plague Surveillance Report form and mail to the Epidemiology and Response Division, P.O. Box 26110, Santa Fe, New Mexico 87501-6110, or fax to 505-827-0013. Investigation information should also be entered in NM-EDSS per established procedures.

Control Measures

1. Case management
 - 1.1. Isolation: For bubonic, septicemic, and pneumonic plague, droplet isolation is required until 48 hours of appropriate antibiotic therapy have been given and there has been a favorable clinical response (i.e., defervescence).
 - 1.2. Prophylaxis: Not applicable.
2. Contact management
 - 2.1. Isolation: None required.
 - 2.2. Prophylaxis (see Treatment section also):
 - Asymptomatic persons having household or other close contact (i.e., less than 2 meters) with persons or animals with untreated pneumonic plague should receive postexposure antibiotic prophylaxis for 7 days. Additionally, contacts should measure their temperature twice a day for seven days and see a physician immediately if fever greater than 100 °F develops.
 - Close contacts of persons or animals with draining buboes may also need postexposure prophylaxis. Consult with the Epidemiology and Response Division for further recommendations.

- Close contacts of persons or animals with nondraining buboes should measure their temperature twice a day for seven days and see a physician immediately if fever greater than 100 °F develops.
3. Prevention
- 3.1. Immunization: Manufacture of U.S.-licensed inactivated whole cell *Y. pestis* vaccine was discontinued in 1999 and is no longer available.
- 3.2. Surveillance of rodent and flea populations: The Department of Health Zoonoses team conducts a field investigation of every confirmed case of plague to assess the likely source of infection and potential risk to others in that environment. Routine surveillance of rodents and fleas is conducted in known plague enzootic areas. Report rodent die-offs (e.g., a previously active prairie dog colony that has suddenly disappeared) to the Epidemiology and Response Division. Within Bernalillo County, report rodent die-offs to the Albuquerque Environmental Health Department's Bio-Disease Management Program (505-873-6613).
- 3.3. Control of rodents and fleas: Interdictive flea control may be carried out on a limited basis where the risk of flea transmission to humans is high, such as during a plague epizootic in a housing area. Rodent control on a limited basis should only be done after effective flea control is accomplished. Sylvatic plague defies most control measures because the wild rodent reservoirs are so widespread and diverse.
- 3.4. Public education: Educate the public about risk factors, preventive measures, and signs and symptoms of plague.
- Control fleas on pets and prevent pets from roaming.
 - Avoid contact with dead and sick animals or rodent nests or burrows.
 - Reduce rodent harborage around the home, such as junk piles and abandoned vehicles.
 - Stack woodpiles at least 12 inches above the ground and 100 feet from the house.
 - Rodent-proof houses and outbuildings.
 - Wear rubber gloves when handling wild game.
 - Keep cats indoors or hunting cats outdoors. Immediately take to the vet any pet (especially a cat but also a dog) that hunts and has signs of fever and lethargy.

References

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