# 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 meningeal plague. Pneumonic plague can be spread from person to person via airborne transmission, potentially leading to epidemics of primary pneumonic plague. Plague is immediately reportable to the New Mexico Department of Health. Plague is treatable with antibiotics, but has a high fatality rate with inadequate or delayed treatment. Plague preventive measures include: droplet isolation of plague patients; prophylactic treatment of pneumonic case contacts and those with exposures to animals with plague; 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, domestic cats, and domestic dogs, 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 though other infected flea species can also transmit plague to 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 peri-domestic 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 care givers 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 droplets. Person to person or cat-to-

person transmission can occur from a pneumonic plague source when there is close (less than two meters) direct contact with an infected coughing 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, although in 2014 there was one documented case of a possible human-to-human transmission in Colorado where the case also had direct contact with an infected dog. Five cases of primary pneumonic plague acquired from domestic cats were reported in the interval 1977 – 1998.

## Clinical Disease

**Incubation period:**

For bubonic plague, the incubation period is 2-8 days. For primary pneumonic plague, the incubation period is 1-6 days.

**Illness:**

The common signs and symptoms of plague include fever, severe malaise, weakness, headache, chills, myalgia and sometimes gastrointestinal symptoms. Specific forms of plague include:

1. **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%.
2. **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.
3. **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 acute respiratory distress syndrome. Untreated pneumonic plague is almost always fatal.

4. **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. The majority of human cases in New Mexico have occurred in seven northern counties: Bernalillo, McKinley, Rio Arriba, San Miguel, Sandoval, Santa Fe, and Taos. Other factors that increase the likelihood of plague include: illness onset in May-October; residence in a rural or semi-rural area; household cats that hunt; presence of insect bites; handling sick or dead animals; fleas on pets; and, a history of hunting or trapping.

## Laboratory Diagnosis

*Confirmatory*

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

Diagnosis of plague usually is confirmed by culture of *Y. pestis* from blood, bubo aspirate, or other clinical specimens. Samples should be submitted to the New Mexico Department of Health Scientific Laboratory Division (SLD) for confirmation. At SLD, contact the General Microbiology section (505-383-9128 or 505-383-9127) for questions about specimen submission.

*Presumptive*

- 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
- Detection of F1 antigen in a clinical specimen by fluorescent assay

## 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 an infectious disease specialist 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 and can be ototoxic and/or nephrotoxic. Gentamicin in standard doses for age given intramuscularly or intravenously appears to be an equally effective alternative to streptomycin. Chloramphenicol penetrates tissues well and may be an option for treating plague meningitis, endophthalmitis, myocarditis, and pleuritis, though in rare instances it can cause aplastic anemia. Fluoroquinolones also have been found to be effective in treating plague in animal and in vitro studies but currently only levofloxacin is approved by the US Food and Drug Administration for both treatment of plague and prophylaxis after exposure to plague. Tetracyclines are 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 $\leq$ 8 years old unless benefits outweigh risks of dental staining. For children, trimethoprim-sulfamethoxazole may also be an option for prophylaxis. Trimethoprim-sulfamethoxazole should not be considered a first-line treatment option when treating bubonic plague and should not be used as monotherapy to treat pneumonic or septicemic plague, because some studies have shown higher treatment failure rates and delayed treatment responses.
- Prophylactic Therapy: Persons in close contact (i.e., less than two 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 ERD 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 hospitalized and aggressively monitored, and clinicians should be prepared for possible septic shock, multiple organ failure, acute 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.

*Probable* – a clinically compatible case with presumptive laboratory results.

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

Reporting:

Report all suspected, probable 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 87502-6110, 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 precautions are 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 (also see treatment section):

   2.2.a Asymptomatic persons having household or other close contact (i.e., less than two meters) with persons or animals with untreated pneumonic plague should receive post-exposure antibiotic prophylaxis for seven 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.

   2.2.b Close contacts of persons or animals with draining buboes may also need post-exposure prophylaxis. Consult with ERD for further recommendations.

   2.2.c 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 US 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 in New Mexico to assess the likely source of infection and potential risk to others in that environment. Report rodent die-offs (e.g., a previously active prairie dog colony that has suddenly disappeared) to ERD. Within Bernalillo County, report rodent die-offs to the Albuquerque Environmental Health Department's Urban Biology Division (505-452-5300).

   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.

3.4.a Control fleas on pets and prevent pets from roaming.

3.4.b Avoid contact with dead and sick animals or rodent nests or burrows.

3.4.c Reduce rodent harborage around the home, such as junk piles and abandoned vehicles.

3.4.d Stack woodpiles at least 24 inches above the ground and 100 feet from the house.

3.4.e Rodent-proof houses and outbuildings.

3.4.f Wear rubber gloves when handling wild game.

3.4.g Keep cats indoors or hunting cats outdoors. Immediately take to veterinarian any pet (especially a cat but also a dog) that hunts and has signs of fever and lethargy.

## References

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See Plague Fact Sheets (English) (Spanish).