

STATE OF COLORADO

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Dedicated to protecting and improving the health and environment of the people of Colorado

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Colorado Department
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RECOMMENDATIONS FOR THE MANAGEMENT, DIAGNOSIS AND TREATMENT OF SUSPECTED FELINE PLAGUE CASES

HISTORY: Feline plague is a serious, life-threatening disease caused by infection with the bacteria *Yersinia pestis*. Plague is enzootic throughout Colorado, sustained in a rodent-flea transmission cycle involving numerous wild rodent species. Cats are highly susceptible to infection. In enzootic areas plague should be considered in the differential diagnosis of any cat presenting with fever of unknown origin. A plague-infected cat will generally have a history of roaming freely in a rural or semi-rural enzootic area, or be a known hunter.

TRANSMISSION: Although the most common route of infection is via consumption of infected rodents, cats may also be infected by flea bites. Transmission from cats to humans has occurred by mechanical transportation of infected fleas into a home environment, bites, scratches, contact with infectious tissues and fluids and via aerosol droplet spread. The incubation period is 2-5 days.

CLINICAL PRESENTATION: Cats can present with 3 clinical manifestations of plague: bubonic, septicemic and pneumonic. The "bubonic" form of plague is the mostly commonly observed, affecting 53% of cats with plague in a New Mexico clinical survey (Eidson, 1991). Cats with bubonic plague usually present with fever, lethargy, anorexia and regional lymphadenopathy (bubos). Among cats with the bubonic form, 75% had unilateral or bilateral submandibular and/or retropharyngeal lymphadenitis. Abscessed lymph nodes may be clinically indistinguishable from abscesses due to other causes, e.g. bite wounds. Fever ($>39.2^{\circ}\text{C}$, $>102.6^{\circ}\text{F}$) is a consistent finding, although moribund cats may be hypothermic. Oral lesions are often present.

In the New Mexico survey, 8% of affected cats were septicemic, and in another 29%, the form of illness was unknown but presumed to be septicemic. Cats with primary septicemic plague will have no obviously enlarged lymph nodes, but will present with fever, lethargy, and anorexia, progressing to overt signs of Gram-negative bacterial sepsis, including vomiting, diarrhea, tachycardia, prolonged capillary refill time, cold extremities, pale mucous membranes, disseminated intravascular coagulopathy (DIC), multi-organ failure and acute respiratory distress syndrome (ARDS).

Of particular concern for cat owners and veterinary clinical staff is the pneumonic form of feline plague which poses a potential for respiratory droplet spread to humans. Pneumonic plague may develop secondary to bubonic or septicemic plague and is characterized by fever, dyspnea, oral/nasal discharge and coughing or sneezing. Pneumonic involvement was present in 10% of infected cats in the New Mexico study. In all suspected plague cases, auscultation of the chest and thoracic x-rays should be done to assess pulmonary involvement. Typical radiographic findings include changes suggestive of diffuse interstitial pneumonia or coalescing areas of necrosis forming an abscess

CASE MANAGEMENT: Suspected cases should be hospitalized and placed in strict isolation. An appropriate insecticide should be used to treat the animal for fleas and the owner should be counseled to flea-treat other companion animals. Attending staff should use standard barrier precautions including gloves, masks and gowns while examining and treating suspect animals. Surgical masks may not provide protection from respiratory droplet exposure via inhalation and a well-fitted N-95 rated mask is recommended for pneumonic cases.

Y. pestis is very sensitive to light and drying and respiratory droplets do not remain suspended so special air handling systems are not required to prevent spread. Respiratory isolation should continue until thoracic x-rays have ruled-out pneumonia or until the completion of 48 hours of antibiotic therapy. Bubo exudates, respiratory secretions, blood and sputum should be considered infectious and any materials used during treatment should be disinfected, autoclaved, or incinerated.

Because of the risk of disease transmission to cat owners, cats should remain hospitalized until afebrile or a negative test result for plague is obtained. All suspected or confirmed feline plague cases **must be reported immediately** to the local or state health department.

DIAGNOSIS: Confirmation of feline plague is obtained by isolation of the causative agent, *Yersinia pestis*, a gram-negative, aerobic, bi-polar staining rod, from blood, bubo aspirates or tissue specimens, or by a four-fold rise in plague antibody titers on paired acute and convalescent serum, collected two weeks apart. A presumptive diagnosis can be based on a single elevated antibody titer or on a positive fluorescent antibody (FA) stain of a lymph node aspirate or tissue impression smear in a clinically compatible case. The WBC count is generally elevated with a marked neutrophilia.

DIAGNOSTIC SPECIMENS: Appropriate diagnostic specimens and procedures for submitting them are listed below **in order of preference**. Collection of specimens should be done using protective equipment including masks, gloves and gowns and procedures to prevent human exposure. Samples should be collected prior to initiation of antimicrobial therapy; however, samples should still be taken and submitted for testing even if antibiotics have been given. Specimens should be shipped for same-day or overnight delivery at ambient temperatures to the state public health laboratory. **Due to state budget cuts, CDPHE lab has had to institute charges for diagnostic feline samples. Samples may be routed to the Centers for Disease Control lab at no cost. Call the contact numbers listed below for information on current testing costs and options.**

1) **Bubo aspirates:** Abscess exudate or pus from an enlarged lymph node or abscess should be collected via fine-needle aspiration and placed in a sterile specimen tube without preservatives, such as a 5ml red-top blood tube. If insufficient material can be aspirated, a small amount of physiological (i.e. non-bacteriostatic) saline can be injected into the affected node and re-aspirated. Small quantities of exudate or pus can also be collected on a sterile swab and placed in a bacterial transport medium or used to make fluorescent antibody (FA) impression smears. The FA test is the most sensitive and specific test that can be done rapidly.

2) **Tissue samples:** Fresh tissues (lymph node, liver, spleen, lung) from biopsy or post-mortem exam should be kept moist with sterile, non-bacteriostatic saline solution (i.e. a wet cotton ball in the collection tube with the tissue sample). If transit time will exceed 24 hours the specimens can be **frozen**. DO NOT use formalin or other preservatives. The whole carcass can also be submitted.

3) **Blood cultures:** In septicemic animals, *Y. pestis* can be isolated from blood on standard blood,

chocolate, or MacConkey's agars. Blood should be collected in a tube with anti-coagulant (purple-top EDTA collection tube) and plated or placed in liquid culture media as quickly after collection as possible. Gram-stain studies on a blood smear can also be performed.

4) Impression smears for FA exam: When growing in a host animal or incubated in culture at 38° C, *Y. pestis* produces an F1 antigen that can be detected with a FA test. Bubo aspirate, lymph node, liver, spleen or lung tissue and sputum (in pneumonic cases) are acceptable specimens for FA testing. For aspirates and sputum use a swab to make a thin smear on a clean glass slide. For tissue samples, slice the specimen with a scalpel to expose a fresh surface and gently touch the slides to the tissue. Slides should be allowed to air dry, then fixed with absolute methanol for five minutes or gently heat-fixed. Two slides should be prepared for each sample. Additional slides can be prepared for examination with gram, Giemsa's or Wayson's stains.

5) Serum specimens: Cats develop humoral antibodies following plague infection, usually detectable within 10-14 days of challenge. Thus, early in the course of disease, results of serologic tests are often negative because animals have not yet seroconverted. In suspect animals, paired sera should be collected during the acute illness and approximately 2 to 3 weeks after illness onset. Serum should be separated from the clot to prevent contamination due to cellular lysis.

SPECIMEN SHIPMENT: The Colorado Department of Public Health and Environment should be notified of any suspected feline plague case and details on the specimens being sent. Specimens must be securely packaged with enough absorbent material to prevent any spills or leakage. If you do not have a laboratory requisition form #272 call 303-692-2700 during regular business to have a form faxed to you to include with the shipment.

To establish an account with CDPHE Laboratory, call 303-692-3094. An account with a unique Customer ID number will be set up for your clinic. CDPHE Lab customers with established accounts can call 303-692-3074 to order a supply of pre-printed requisition form #272 for submitting plague or rabies specimens.

Ship specimens to: Colorado Department of Public Health & Environment; Laboratory Services Division 8100 Lowry Blvd; Denver, CO 80230-6928.

TREATMENT: Antimicrobial treatment is recommended for 10-21 days, or until 3 days after the patient has become afebrile and recovered clinically. Clinical response is generally rapid, except in moribund cases, and animals are considered non-infectious following 48 hours of antibiotic therapy. Patients receiving parenteral antibiotics may be switched to oral therapy upon clinical improvement. Penicillin analogs are not efficacious.

Recommended Antibiotic Protocols for Feline Plague Cases

Antibiotic	Dosage	Action
Gentamicin*	2-3 mg/kg tid, IM or SQ	Bactericidal
Enrofloxacin*	5 mg/kg, IM or SQ, daily	Bactericidal
Doxycycline	10 mg/kg, PO, daily	Bacteriostatic
Tetracycline	22 mg/kg tid, PO	Bacteriostatic
Chloramphenicol	50 mg/kg bid, PO	Bacteriostatic

*Injectable antibiotics may be preferred during the acute stage of infection to avoid contact with oral cavity secretions and reduce the risk of bites.

CONSIDERATIONS FOR DOGS AND OTHER SPECIES: Dogs are frequently infected with *Y. pestis*, but highly resistant to plague, thus most infections are asymptomatic. Transient fever and anorexia of short duration (<72 hours) may be noted, accompanied rarely by lymphadenitis. Antibiotic therapy is usually not indicated except in severely ill animals. Dogs cannot directly transmit plague to humans, however, numerous human cases have resulted from the transport of infected fleas or rodent/rabbit carcasses into the residential environment. Flea treatment should be done. Domestic livestock have rarely been identified as infected with *Y. pestis*. Clinical plague has been reported in wildlife species including felids (bobcat, lynx), deer and antelope. Wild canids (coyote, fox) are generally resistant to illness. Diagnostic specimens are the same, however, the lack of enlarged lymph nodes and short duration of bacteremia, usually limits testing to the demonstration of plague antibody titers.

CONSIDERATIONS FOR VETERINARY STAFF AND OWNERS: Every case of cat plague represents a potential risk for human exposure and illness. Acquiring primary pneumonic plague from cats is a particular risk for veterinarians, their assistants and pet owners. The usual incubation period for bubonic plague in humans is 2 to 6 days. The incubation period for primary pneumonic plague is considerably shorter, only 1 to 3 days. Most fatalities are a result of a delay in appropriate antimicrobial therapy.

Veterinary clinic personnel and owners should be advised of these risks. In the event of known exposure (bite, scratch, fluid contact) to *Y. pestis* or the abrupt onset of a febrile illness, medical attention must be obtained immediately. The local or state health department should be notified of any potential exposures to an infected cat and can assist with evaluating the risk of transmission. Persons potentially exposed will either be recommended to start antibiotic prophylaxis or to initiate a 7 day active fever watch, depending on the type and timing of the exposure to the infected animal.

Animal owners in plague endemic areas should be advised to confine pets and to apply a flea control product such as a spray or powder at least weekly to pets which go outside. This is especially important during the most common periods of plague transmission (March through October). Clients should be warned that pets should not share sleeping areas with family members. Reports of rapid die-offs of rodents or rabbits should be forwarded to the local health department.

CONSULTATION: The Colorado Department of Public Health and Environment is available for consultation, laboratory support or to report a suspect case. The telephone number is (303) 692-2700 during normal business hours and (303) 370-9395 for holiday, weekend and after-hour emergencies. To set up a laboratory account or order pre-printed lab requisition #272 forms call 303-692-3074.

Suggested References

1. Orloski KA, Lathrop, SL. Plague: A Veterinary Perspective. JAVMA, 222, (4): 444-448, 2003.
2. Gasper PW, Barnes AM, Quan TJ, et al. Plague (*Yersinia pestis*) in Cats: Description of Experimentally Induced Disease. J Med Entmol 30(1):20-26, 1993.
3. Eidson M, Thilsted JP, Rollag OJ. Clinical, clinicopathologic, and pathologic features of plague in cats: 119 cases. J Am Vet Med Assoc 199(9):1191-1197, 1991.
4. Rosser WW. Bubonic plague. J Am Vet Med Assoc 191(4):406-409, 1987.
5. Gage KL, Dennis DT, Orloski KA, Ettestad P, Brown TL, Reynolds PJ, Pape WJ, Fritz CL, Carter LG., and Stein JD. Cases of human plague associated with exposure to infected domestic cats. Clin. Infect. Dis. 30:893-900. 2000.