

STATE OF COLORADO

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RECOMMENDATIONS FOR THE MANAGEMENT, DIAGNOSIS AND TREATMENT OF SUSPECTED VETERINARY PLAGUE CASES

HISTORY: Plague is a serious, life-threatening disease caused by infection with the bacterium *Yersinia pestis*. Plague is endemic throughout Colorado, sustained in a rodent-flea transmission cycle involving numerous wild rodent species. Cats are highly susceptible to infection. Dogs are more resistant but can develop clinical illness that may become severe. Plague-infected domestic pets generally have a history of roaming freely in rural or semi-rural areas or are known hunters.

TRANSMISSION: Although the most common route of infection is by consumption of infected rodents, pets may also be infected by flea bites. Transmission from pets to humans has occurred by transportation of infected fleas into the home, by cat bites and scratches, by aerosol droplet spread, and by contact with infectious tissues and fluids. The incubation period is normally 1-7 days. Plague should be considered as a differential diagnosis in pets that present with a fever of unknown origin and have a history of contact with prairie dogs or other rodents in endemic areas. Flea treatment should be done upon first suspicion of plague.

CLINICAL PRESENTATION IN CATS: Cats can present with three clinical manifestations of plague: bubonic, septicemic and pneumonic. The "bubonic" form of plague is most commonly observed. Cats with bubonic plague usually present with fever, lethargy, anorexia and regional lymphadenopathy (buboes). 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.

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, with 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. **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.

CONSIDERATIONS FOR DOGS: Dogs can be infected with *Y. pestis* and show symptoms. Transient fever and anorexia of short duration (<72 hours) may be noted, accompanied rarely by lymphadenitis. Severe disease including respiratory involvement is possible (but rare) and can result in a fatal illness.

CONSIDERATIONS FOR OTHER SPECIES Domestic livestock have rarely been reported 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 but are frequently found to be seropositive in plague endemic areas. Diagnostic specimens are the same as with cats and dogs, however, the lack of enlarged lymph nodes and short duration of bacteremia usually limits testing to the demonstration of plague antibody titers.

CASE MANAGEMENT: Suspected cases with respiratory involvement (e.g. coughing, sneezing, or pulmonary radiographic changes) or which are producing any discharge (e.g. draining abscess) should be hospitalized and placed in strict isolation until plague has been ruled-out or 48 hours of antibiotic therapy has been completed. A flea control product should be used to treat the animal for fleas and owners should be counseled to also flea-treat other companion animals. Attending staff should use standard barrier and droplet precautions, which include gloves, gowns, masks and eye protection (or face shield) while examining and treating suspect animals.

Yersinia pestis is very sensitive to light and drying, and respiratory droplets do not remain suspended. Therefore, 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.

All suspected or confirmed plague cases **must be reported immediately** to the local or state health department.

DIAGNOSIS: Confirmation of veterinary plague is obtained by isolation of the causative agent, *Y. 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. The WBC count is generally elevated with a marked neutrophilia. The CDPHE laboratory can conduct PCR testing on the appropriate specimens.

DIAGNOSTIC SPECIMENS: Appropriate diagnostic specimens and procedures for submitting them are listed below **in order of preference**. Specimen collection should be done using appropriate personal protective equipment. 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 to the state public health laboratory. Samples which cannot be tested by the state health department lab, such as serum samples, may be routed by our lab to the CDC's laboratory at no cost. Call the contact numbers listed below for information on current testing costs and options. Samples may also be submitted to CSU for fee-based testing. *Note: All specimens being tested for plague should also be tested for tularemia. Tests for both diseases can be done using the same samples.

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 is aspirated, a small amount of physiological (i.e. non-bacteriostatic) saline can be injected into the affected node and re-aspirated. Small quantities of exudates or pus can be collected on a sterile swab and placed in bacterial transport medium for PCR testing.

2) **Whole blood:** Blood should be collected in a tube with anti-coagulant (purple-top EDTA collection tube) and may be submitted for PCR testing, smear and gram stain, or culture (see below).

3) **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. ***Please contact CDPHE Molecular Science lab (303-692-3286) before submitting specimens from sites other than those listed above.**

4) **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. If plates or liquid culture media are not available, blood in an EDTA tube can be submitted to the lab for culture.

5) **Serum specimens*:** Humoral antibodies develop 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. ***Serum specimens must be submitted to the CDC for testing, and a report of results may not be available for several weeks**

SPECIMEN SHIPMENT: The Colorado Department of Public Health and Environment should be notified of any suspected 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 hours to have a form faxed to you for inclusion with the shipment.

An **account** may be established with the state health department laboratory by phone or online.

- **Phone:** Call 303-692-3485. An account with a unique Customer ID number will be set up for your clinic, and if needed, the lab will fax you a laboratory requisition form #272. CDPHE Lab customers with established accounts can call 303-692-3485 to order a supply of pre-printed requisition form #272 for submitting plague or tularemia specimens.
- **Online:** Go to <http://tinyurl.com/CDPHE-Lab>. In the bottom center of the webpage you will find the "Customer Resources" box. Click the "Order from the Lab" link in the box. In the middle of that page click on "Public Health Testing Supply Order Form", scroll down slightly to "Customer Information" and fill in the appropriate blanks.

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. Parenteral treatment is preferable for the first 48 hours to prevent human exposure during dosing of oral antibiotics. Patients receiving parenteral antibiotics may be switched to oral therapy after 48 hours. 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 VETERINARY STAFF AND OWNERS: Every case of veterinary plague represents a potential risk for human exposure and illness. Acquiring primary pneumonic plague from symptomatic pets is a particular risk for veterinarians, their assistants and pet owners. The usual incubation period for plague in humans is one to six days. Most fatalities result from 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 pet and can assist with evaluating the risk of transmission. Persons potentially exposed will either be recommended to start antibiotic prophylaxis or to initiate a seven-day active fever watch, depending on the type and timing of the exposure to the infected animal.

Animal owners in plague endemic areas are advised to keep pets from roaming, to maintain pets on a veterinarian-recommended flea control program, and to ensure any sick pet is examined promptly by a veterinarian. This is especially important during the most common periods of plague transmission (March through October). Clients should be warned that sick 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.

Suggested References

1. Orloski KA, Lathrop, SL. Plague: A Veterinary Perspective. JAVMA, 222, (4): 444-448, 2003.
2. 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.
3. 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.
4. Nichols MC, Ettestad PJ, VinHatton ES, Melman SD, Onischuk L, Pierce EA, and Aragon AS. Yersinia pestis infection in dogs: 62 cases (2003-2011). J Am Vet Med Assoc 244(10):1176-1180, 2014.