A Quick Guide to Management of Suspected Veterinary Cases of Plague

NOTE: Specimens MUST be sent to Colorado State University's Veterinary Diagnostic Lab for Testing

Reporting & Consults:

The Colorado Department of Public Health and Environment (CDPHE) is available for consultation, laboratory support or to report a suspect case: call (303) 692-2700 during normal business hours.
Call (303) 370-9395 for holiday, weekend and after-hour emergencies.

Clinical Presentations:

Cats:

- Fever (>102.6°F, >39.2°C), lethargy, anorexia; AND one of the following syndromes
    - Bubonic: lymphadenopathy (abscessed lymph nodes can be indistinguishable from abscesses due to other causes)-may be unilateral, bilateral or regional
    - Septicemic: febrile illness progressing to sepsis; lymph nodes may not be enlarged
    - Pneumonic: dyspnea, oral/nasal discharge, coughing/sneezing; radiographic changes consistent with diffuse interstitial pneumonia or abscess and is often hemorrhagic later in the disease course

Dogs:

- Clinical disease in dogs is rare but has previously been laboratory confirmed in 2 dogs in Colorado.
    - Most infected dogs will be asymptomatic or have a mild disease that goes unnoticed.
- The 2 dogs with confirmed plague presented with:
    - Fever, malaise, lobar pneumonia, and hemoptysis.
    - Unfortunately both dogs were euthanized due to poor prognosis.

Management:

- Pneumonic cases or any case with a draining abscess:
    - Hospitalize and strictly isolate patient until plague is ruled out or 72 hours of appropriate antibiotic therapy is complete
- All cases:
    - Apply flea control product for patient and other contact animals including all housemates
    - Use barrier and droplet precautions (gloves, gowns, mask, eye protection) for staff caring for patient
    - Consider bubo exudates, respiratory secretions, blood, and sputum highly infectious

Diagnosis: (note: all specimens being tested for plague should also be tested for Tularemia

see Tularemia guidance here)

- Preferred specimen types: bubo aspirates, tissue, or isolate from culture of whole blood
- Specimen collections:
    - Bubo/lymph node aspirates: fine-needle aspiration in sterile specimen tube without preservatives
    - Whole blood: collect in purple-top EDTA collection tube
- Serology will be negative for the first week of illness
- Specimens should be sent to Colorado State University's Veterinary Diagnostic Laboratory here: CSU VDL
- Do NOT send specimens to CDPHE's state public health laboratory unless you get approval from the zoonoses department at 303-692-2700. If you do not get prior approval, the specimens will NOT be tested.

Treatment
Start treatment as soon as specimens are collected, do not wait on test results (delays in treatment or using the wrong antibiotic can result in patient death).

• IV fluoroquinolone for a minimum of 72 hours, followed by PO for remainder of course
  ○ Enrofloxacin at 5 mg/kg total daily dose: Feline
  ■ Higher dose may be considered for canine patients
  ■ Safety information available at: www.drugs.com/pro/baytril.html
  ○ If patient seriously ill consider using IV gentamicin
  ■ www.drugs.com/vet/gentocin-injectable-solution-100-mg-ml-can.html
• Additional antibiotic coverage for other pathogens may be considered by the treating veterinarian while waiting on test results.
• Public Health should be contacted immediately to conduct staff risk assessments

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

Report all suspected or confirmed plague cases to the Colorado Department of Public Health and Environment. A laboratory diagnosis is not required to report a suspect case.

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 exposure to rodents or being in prairie dog colonies 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). The abscessed lymph nodes are frequently the submandibular lymph nodes. Abscessed lymph nodes may be clinically indistinguishable from abscesses due to other causes, e.g. bite wounds. Fever (>39.2°C, >102.6°F) is a consistent finding although moribund cats may be hypothermic. Oral lesions are often present.

Cats with septicemic plague may 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 radiographs 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.

CLINICAL PRESENTATION FOR DOGS: While dogs are normally resistant to infection with *Y. pestis*, on rare occasions dogs can be infected 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. There have been at least two dogs in Colorado that died from plague. Both of these dogs presented with fever, malaise, and lobar pneumonia that progressed to hemoptysis within 24 hours.

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, hemoptysis, 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 72 hours of appropriate antibiotic therapy (suggested choices, dose and duration in table below) has been completed. A species specific, veterinarian-approved flea control product should be used to treat the animal for fleas. Owners should be counseled to also treat their other companion animals for fleas. 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.

Y. 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. However, respiratory isolation should continue until thoracic radiographs have ruled out pneumonia or until the completion of 72 hours of appropriate 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.

DIAGNOSIS: The preferred confirmatory test for veterinary plague is culture isolation of the causative agent, *Y. pestis*, from blood, bubo aspirates or tissue specimens. A four-fold rise in plague antibody titers on paired acute and convalescent serum collected three to four weeks apart is also confirmatory, however a presumptive diagnosis can be based on a single elevated antibody titer of 1:32 or greater. The WBC count is generally elevated with a marked neutrophilia. The pneumonic form may show evidence of pneumonic lesions on thoracic radiographs.

The Colorado State University Veterinary Diagnostic Laboratory (link here) is the preferred laboratory for plague and Tularemia testing for animals and is a fee-for-service laboratory. Additionally, CSU is the preferred laboratory for all animal specimens in cases where diseases other than plague or tularemia need to be ruled out. CSU can also perform full necropsies.

Samples should NOT be sent to the CDPHE public health laboratory without prior approval from a veterinary epidemiologist. The CDPHE laboratory CANNOT perform necropsies or diagnostics other than plague and tularemia testing.

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 CSU laboratory. Samples which cannot be tested by the state department lab, such as serum samples, may be routed by the lab to the CDC's laboratory at no cost. Call the contact number listed below for information on current testing costs and options.

Prior antibiotic therapy with an appropriate antibiotic (see table below) should be discussed with the laboratory before sending specimens since treatment with any antibiotic therapy, including cephalosporins, penicillins and fluoroquinolones, may also affect *Y. pestis* PCR/culture test results causing a false negative result.

1) **Bubo/lymph node aspirates:** Abscess exudate or pus from an enlarged lymph node should be collected via fine-needle aspiration and placed in a sterile specimen tube without preservatives, such as a 5 ml 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 exudate 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 to CSU Veterinary Diagnostic Laboratory.

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 3 to 4 weeks after illness onset. Serum should be separated from the clot to prevent contamination due to cell lysis.

Note: All specimens being tested for plague should also be tested for Tularemia. Tests for both diseases can be done using the same samples.

SPECIMEN SHIPMENT:

The Colorado Department of Public Health and Environment should be notified of any suspected plague cases and details on the specimens being sent for testing.

Specimens should be sent to Colorado State University's Veterinary Diagnostic Laboratory. See website for guidance on fees and to set up an account. Specimens must be securely packaged with enough absorbent material to prevent any spills or leakage.

ANY PLAGUE SUSPECT SHOULD ALSO BE TESTED FOR TULAREMIA (see Tularemia guidance document on our website here.

Prior antibiotic therapy with an appropriate antibiotic (see table below) should be discussed with the CSU's laboratory before sending specimens since treatment with any antibiotic therapy, including cephalosporins, penicillins and fluoroquinolones, may also affect *Y. pestis* PCR/culture test results causing a false negative result. Specimens must be securely packaged with enough absorbent material to prevent any spills or leakage.

TREATMENT: Do not delay treatment while waiting for diagnostic results. Antimicrobial treatment is recommended for 10-21 days, or until 3 days after the patient is afebrile and has recovered clinically. Clinical response is generally rapid, except in moribund cases, and animals are generally considered non-infectious following 72 hours of antibiotic therapy, however the duration of infectivity in cats is not completely known. Parenteral treatment is preferable for the first 72 hours to prevent human exposure during dosing of oral antibiotics. Patients receiving parenteral antibiotics may be switched to oral therapy after 72 hours. **Penicillin analogs are not efficacious and should not be used to treat suspect plague cases.**

Antimicrobial Therapy for Plague (adapted from Greene 2013)

Drug	Dose [a]	Route	Duration (days)
Enrofloxacin	5mg/kg daily	PO	10
Gentamicin [b] Drug of choice for seriously ill dogs and cats	Dogs: 6-8 mg/kg q 24 hours Cats: 6-8 mg/kg q 24 hours	SC, IM, IV	21

Doxycycline [c,d]	Dogs: 5-10 mg/kg q 12 hours Cats: 50-100mg/cat q 12 hours	PO	21
Trimethoprim-sulfonamide	Dogs: 15 mg/kg q 12 hours Cats: 15 mg/kg q 12 hours	PO, IV, IM	21
Chloramphenicol [d]	Dogs: 50 mg/kg q 8 hours Cat:s 50 mg/kg[e] q 12 hours	PO PO, SC	21 21

IM= intramuscular; IV= intravenous; PO=by mouth; SC= subcutaneous

[a]Dose per administration at specified interval
[b]Use in caution with dogs and cats with renal failure and monitor renal function during use.
[c]Do not break or crush tablets because they are irritating to the esophagus. In cats, this is a total dose to administer, not a mg/kg dose.
[d]Relapses can occur with bacteriostatic drugs such as doxycycline or chloramphenicol.
[e]Myelosuppression is possible at this dose. Monitoring complete blood cell counts is advised.

Owners should be advised to wear gloves when administering Chloramphenicol to their companion animals. *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 1 to 6 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 after handling a patient with plague, medical attention must be obtained immediately. The Colorado Department of Public Health and Environment 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 7-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 and tick 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 die-offs of rodents or rabbits, especially prairie dogs, should be forwarded to the local public health agency.

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 (ask for the zoonoses department) during normal business hours and (303) 370-9395 for holiday, weekend and after-hour emergencies.

References

Centers for Disease Control, https://www.cdc.gov/plague/healthcare/veterinarians.html

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(303) 692-2700
https://www.colorado.gov/pacific/cdphe/animal-related-diseases
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