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

Updated: June 2016

*Report all suspect or confirmed Tularemia cases to local or state health departments. A laboratory diagnosis is **not** required to report a suspect case.*

BACKGROUND:

Tularemia is a serious disease caused by infection with the Gram negative bacterium *Francisella tularensis*. Tularemia is endemic throughout the United States, including Colorado. It circulates in lagomorphs (rabbits and hares) and rodents such as mice, voles, muskrats, ground squirrels and beavers. It is most commonly transmitted among these animals by tick bite. Cats are highly susceptible to infection and often develop a severe, even fatal illness. Dogs are more resistant but can develop clinical illness that may become severe. Tularemia infected domestic pets generally have a history of roaming and hunting.

TRANSMISSION:

The infective dose of this bacterium is very small, and it can persist for long periods in water, soil, and in carcasses under the right environmental conditions. Although the most common route of infection is by consumption of infected rabbits or rodents, pets may also be infected by ticks and biting flies, by inhaling the bacteria, or through exposure to contaminated water or soil.

The incubation period is normally 1-10 days but may be longer. Consider tularemia (and plague) as a differential diagnosis in pets that present with acute fever, with or without lymphadenopathy, and a history of contact with rabbits or rodents. The most common transmission route from infected pets to humans is by bite, resulting most commonly in ulceroglandular or typhoidal (septic) forms of tularemia. Human-to-human transmission has not been reported.

CLINICAL PRESENTATION IN CATS:

Cats are highly susceptible to tularemia and are at increased risk due to predatory behavior. They present with a range of symptoms including anorexia, lethargy, sudden fever, lymphadenopathy, cough, diarrhea, vomiting and presence of abscesses, pustules and oral ulcers. Mild illness may progress to sepsis and rapid death.

Symptoms depend on the route of bacteria entry into the body, which is typically ingestion of infected prey animals. If the cat presents with a cough, perform chest auscultation and thoracic x-rays to assess pulmonary involvement since pneumonic tularemia can occur and be fatal. Since animals with pneumonic forms of tularemia and plague can present with identical symptoms, veterinarians and clients should use isolation precautions until plague is ruled out (refer to Case Management section).

CONSIDERATIONS FOR DOGS:

Dogs can develop clinical illness, but less commonly than cats. Elevated titers are common in dogs, suggesting that exposure to *F. tularensis* is common, but actual illness

may often be mild or inapparent. Symptomatic dogs may demonstrate fever, anorexia, mucopurulent ocular and nasal discharge or lymphadenopathy. Puppies may be more susceptible than older animals.

CONSIDERATIONS FOR OTHER SPECIES:

Infected rabbits may be lethargic or non-responsive, huddle together or die suddenly. Domestic rabbits (*Oryctolagus cuniculus*) are generally considered to be resistant to tularemia. Of livestock, sheep are most commonly affected. They are highly susceptible and may become severely ill. Sheep outbreaks are associated with severe tick infestations. Horses may also develop severe illness, whereas cattle are resistant and rarely develop symptoms. Pigs, fish, amphibians, hamsters and birds can also be infected.

CASE MANAGEMENT:

Suspect 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 until 48 hours of antibiotic therapy has been completed. Treat suspect tularemia or plague cases with a flea and tick control product as soon as possible. Counsel owners to treat all other companion animals as well. Attending staff should use standard barrier and droplet precautions, which include gloves, gowns, masks and eye protection (or a face shield) while examining and treating suspect animals or performing necropsies.

Consider lymph node exudates, tissues, respiratory secretions, blood, sputum and body fluids infectious, and any materials used during treatment should be disinfected, autoclaved or incinerated.

DIAGNOSIS:

Tularemia can be confirmed by culture isolation of the causative agent, a gram-negative, aerobic, coccobacillus from blood, lymph node aspirates or tissue specimens. It is important to note *F. tularensis* will not grow on conventional laboratory media, and colonies may take 2 to 4 days to appear. Unlike *Y. pestis*, *F. tularensis* is rarely detected on Gram-stained smears. CSU laboratories can culture these specimens.

Samples such as swabs of affected areas (i.e. ulcers), lesion biopsies, lymph node aspirates or blood can also be evaluated by PCR or direct fluorescent assay (DFA). The CSU lab and CDPHE laboratory can conduct PCR testing on the appropriate specimens.

Antibody may not be detectable until the second or third week of illness, so a false negative may be reported if serum is collected too early during illness. Tube agglutination assays or enzyme-linked immunosorbent assays (ELISAs) are commonly used to diagnose tularemia. A four-fold titer increase between paired acute and convalescent sera collected at least two weeks apart is confirmatory. A presumptive diagnosis can be based on a single elevated antibody titer of ≥1:160. Antibody assays are available from commercial laboratories.

DIAGNOSTIC SPECIMENS:

Recommended diagnostic specimens are listed below in order of preference. Collect specimens using appropriate personal protective equipment, and prior to starting

antimicrobial therapy. Samples can still be taken and submitted for testing even if antibiotics have been given.

**Important note: All specimens being tested for tularemia should also be tested for plague. Both tests can be done on the same sample.*

1) Lymph node 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. Collect small quantities of exudates or pus on a sterile swab and place in bacterial transport medium for PCR testing.

2) Whole blood: Collect blood in a tube with anti-coagulant (purple-top EDTA collection tube) and submit for PCR testing, smear and gram stain, or culture (see below).

3) Tissue samples: Keep fresh tissues such as lymph node, liver, spleen or lung from biopsies or post-mortem exams 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. **Contact CDPHE Molecular Science lab (303-692-3286) before submitting specimens from sites other than those listed above.*

4) Blood cultures: *Francisella tularensis* can be isolated from blood of septicemic animals 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 CSU lab for culture.

5) Serum specimens*:* Humoral antibodies are usually detectable within 14 to 21 days. Thus, early in the course of disease, results of serologic tests are often negative because animals have not yet seroconverted. Collect serum from suspect animals during acute illness and again 2 to 3 weeks after illness onset (paired sera). Separate serum from the clot to prevent contamination due to cellular lysis. **Serum must be submitted to the CDC for testing, and results may not be available for several weeks.*

SPECIMEN SUBMISSIONS AND SHIPMENT:

Ship samples by same-day or overnight delivery to CSU or the state public health laboratory. Samples that cannot be tested by the state health lab, such as serum, may be routed to the CDC's laboratory. Call the contact numbers listed below for information on current testing costs and options.

All lab submissions are fee-for-service.

- CSU Veterinary Diagnostic Lab. Submission and guidance forms can be found at:

  http://www.dlab.colostate.edu

- Notify the state public health lab of any suspected tularemia case and provide details on the specimens being sent. Securely package specimens with enough absorbent material to prevent any spills or leakage. If you do not have a laboratory requisition form #272 call 303-692-3090 during regular business hours to have a form faxed to you for inclusion with the shipment.

Establish an account 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:

Treatment for animals is extrapolated from human recommendations since no systematic drug trials have been performed for animals. Antimicrobial treatment is recommended for 14 days to minimize the risk of relapse. Clinical response is usually rapid except in moribund cases, and animals are generally 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, macrolides and cephalosporins are not recommended.

Recommended Drug Therapy for Tularemia (adapted from Greene, 2013)

Drug	Dose [a]	Route	Duration (days)
Gentamicin [b]	Dogs and Cats: 5- 6.6 mg/kg q.d.	SC, IV, IM	7-14
Doxycycline [c, d]	Dogs: 5 mg/kg q.d. Cats: 50-100 mg total dose bid	PO PO	14 14
Chloramphenicol [d]	Dogs: 50 mg/kg q.d. Cats: 50 mg/kg tid	PO, SC, IM PO, SC, IM	14 14
Enrofloxacin [e]	Dogs: 5 mg/kg q.d. Cats: 5 mg/kg q.d.	PO, SC PO	10 10

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.
[d] Relapses can occur with bacteriostatic drugs such as doxycycline or chloramphenicol.

[e] Other veterinary Fluoroquinolones such as orbifloxacin, danofloxacin, or marbofloxacin may be substituted at an appropriate dose.
[f] Owners should wear gloves when giving Chloramphenicol to their pets.

CONSIDERATIONS FOR VETERINARY STAFF AND OWNERS:

The greatest exposure risk to veterinary staff occurs if they are bitten by an infected patient, during necropsy or when tissues or body fluids of an infected animal are directly handled, or from activities that potentially aerosolize *F. tularensis*. Veterinary staff and owners should be advised of these risks. In the event of known exposure (bite from pet or direct contact with tissues or body fluids) to *F. tularensis* or the abrupt onset of a febrile illness, a health care provider should be consulted. The health department should be notified of exposures to infected pets and can assist with evaluating transmission risk and make recommendations. Persons potentially exposed may either be recommended to start antibiotic prophylaxis, or a 14-day active fever watch, depending on the type and timing of the exposure to the infected animal.

PREVENTION:

Animal owners living in tularemia endemic areas are advised to 1) keep pets from roaming to decrease interactions with rodents and rabbits, 2) discourage hunting of wild prey, 3) maintain pets on a flea and tick control product, and 4) ensure any sick pet is examined promptly by a veterinarian. This is especially important during the most common periods of tularemia transmission (May through October). Pets should not be fed raw meats, especially from wild animals. Forward reports of die-offs of rodents or rabbits to the local health department, and avoid mowing and other aerosol generating activities in those areas.

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 holidays, weekends and after-hour emergencies.

Because of the low infective dose of F. tularensis, and the ease with which it could be released into food, water or aerosolized; it is classified as a Category A bioterrorism agent.

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