Tularemia

Summary

Tularemia, also known as rabbit fever, is a zoonotic disease caused by the bacterium *Francisella tularensis*. Tularemia is found throughout the northern hemisphere. The primary reservoir hosts are rabbits, hares, and rodents. Ticks serve as both reservoirs and vectors of tularemia. Typically, humans become infected through tick or deerfly bites or by handling infected animals. Less commonly, infection may be acquired by direct contact or ingestion of contaminated water, food or soil, inhaling airborne bacteria, or from animal bites. Dogs and cats are also susceptible to tularemia and typically become infected through ingestion of infected rodents or rabbits.

The most common clinical presentation is the ulceroglandular form as a skin ulcer or eschar at the site of inoculation of the organism together with swelling of the regional lymph nodes. Other presentations include glandular (lymphadenitis with no apparent primary ulcer), oropharyngeal (from ingestion of contaminated food or water), primary pneumonic (inhalation of infectious material), oculoglandular (conjunctivitis and lymphadenitis after inoculation of the conjunctival sac), and typhoidal with no localizing signs. All forms of tularemia can progress to secondary pneumonia, meningitis, or sepsis. Tularemia has not been shown to spread from person to person. Tularemia is treatable with antibiotics but has been fatal with inadequate or delayed treatment in less than 4% of cases. Tularemia preventive measures include: avoidance of tick and deer fly bites, use of impervious gloves when skinning or handling rabbits or rodents, cooking rabbit or rodent meat thoroughly; using tick control products on pets, and preventing pets from hunting.

Agent

Tularemia is caused by *Francisella tularensis,* a small, non-motile, gram-negative coccobacillus.

Transmission

Reservoir:

> Wild rodents and lagomorphs (rabbits and hares) are the natural vertebrate reservoirs of tularemia. Hard ticks (*Ixodidae*) can also serve as a reservoir, while deer fly bites, contaminated water or soil, and infected domestic cats may also be a source of infection to humans.

Vector:

> In New Mexico, hard ticks and deer flies are the most important vectors of tularemia to humans. In Europe, there has been demonstrated transmission from mosquitoes.

Mode of Transmission:

> Most humans acquire tularemia through handling infected rabbits or rodents, or from deer fly or tick bites. Tularemia may also be transmitted by: 1) direct contact with tissues and fluids of infected rodents and rabbits; 2) bites or scratches from an infected domestic cat; 3) inhalation of the organism from contaminated soil, grain, hay or aerosolized infected animal carcasses; 4) ingestion of contaminated water or undercooked meat from an infected animal; and 5) rarely the mishandling of tularemia cultures by laboratory workers.

Period of Communicability:

No direct person-to-person transmission has been reported. Infected cats or dogs may have draining lesions or saliva that should be considered infectious until 48 hours of appropriate antimicrobial therapy has been given and there is evidence of clinical improvement (including defervescence). The infectious agent may be found in the blood of untreated patients during the first two weeks of disease and in lesions for a month or more. Flies can be infective for 14 days and ticks throughout their lifetime (about two years). Frozen rabbit meat has remained infective for years. Tularemia organisms have been shown to survive for weeks at low temperatures in water, moist soil, hay, straw, and decaying animal carcasses.

Clinical Disease

Incubation period:

Related to size of inoculum, usually 3-5 days with a range of 1-21 days.

Illness:

The common symptoms of tularemia include sudden onset of high fever, chills, fatigue, general body aches, headache, and nausea. Tularemia can infect humans through the skin, mucous membranes, GI tract, and the lungs. Specific clinical presentations of tularemia include:

- Ulceroglandular: This is the most common form of tularemia, as a skin ulcer or eschar at the site of inoculation of the organism together with swelling of the regional lymph nodes.
- Glandular: Lymphadenitis with no apparent primary ulcer.
- Oropharyngeal: A painful pharyngitis can develop from ingestion of contaminated food or water, along with abdominal pain, diarrhea and vomiting.
- Oculoglandular: Follows direct contamination of the eye with ulceration of the conjunctiva, chemosis, vasculitis, and regional lymphadenitis.
- Pneumonic: Tularemia pneumonia can be the direct result of inhaling contaminated aerosols or be secondary to hematogenous spread from a distal site. Bronchiolitis, pleuropneumonitis, and hilar lymphadenitis accompanied by systemic illness may be present.
- Typhoidal: Systemic infection manifested as fever and other constitutional signs/symptom without cutaneous or mucosal membrane lesions or regional lymphadenitis.

Tularemia cannot be distinguished clinically from plague or many other gram-negative infections and should be considered in any patient who presents with fever and acute lymphadenitis and resides in a known tularemia area. Recent laboratory confirmed human cases in New Mexico have occurred in Bernalillo, Santa Fe, Rio Arriba, and San Juan counties while laboratory confirmed animal cases have occurred in San Juan, Torrance, Rio Arriba, Bernalillo, Santa Fe, Los Alamos, and San Miguel counties.

Laboratory Diagnosis

A single positive serologic test result ($\geq$1:128 for total antibody) by passive hemagglutination assay or enzyme immunoassay in an unimmunized patient who has not previously had tularemia provides presumptive evidence of infection. A 4-fold rise in total antibody titer

between two serum specimens obtained two or more weeks apart provides serologic confirmation.

Diagnosis of tularemia, preferably, is confirmed by culture of *F. tularensis* from blood, skin lesion, lymph node aspirate, or other clinical specimens. Samples should be submitted to the New Mexico Department of Health Scientific Laboratory Division (SLD) for microbiological confirmation. At SLD, contact the General Microbiology section (505-383-9127) or the Virology section (505-383-9124) for questions about specimen submission.

Treatment

Prompt diagnosis and treatment are critical for preventing tularemia from progressing to more serious clinical forms. When human tularemia 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: Streptomycin is considered the antibiotic of choice with gentamicin an acceptable alternative that is more widely available. Tetracyclines, chloramphenicol, and ciprofloxacin have also been shown to be effective. Treatment with aminoglycosides and ciprofloxacin should be continued for 10 days while treatment with bacteriostatic agents should be continued for 14-21 days to reduce chance of relapse.

It is important for physicians with suspected cases to consult with an infectious disease specialist.

Prophylactic therapy: Post-exposure prophylactic antibiotic treatment of close contacts of tularemia patients is not recommended since human-to-human transmission of *F. tularensis* is not known to occur. Persons exposed to a known case of tularemia in an animal (skinning an infected dead rabbit or rodent, scratch or bite from an infected cat) should consider antibiotic prophylaxis. A 14-day course of doxycycline or ciprofloxacin is recommended. If exposure is less certain, then a fever watch is recommended. Contacts should be instructed to measure their temperature twice a day for 14 days and see a physician immediately if fever greater than 100° F develops. Laboratory cultures of *F. tularensis* are easily aerosolized and antibiotic prophylaxis may be indicated if cultures were not kept under a hood while open. Contact the Epidemiology and Response Division at 505-827-0006 regarding specific recommendations for tularemia prophylaxis.

Surveillance

Case Definition:

> *Clinical diagnosis* is supported by evidence or history of a tick or deerfly bite, exposure to tissues of a mammalian host of *Francisella tularensis*, or exposure to potentially contaminated water.
>
> *Confirmed* – a clinically compatible case with confirmatory laboratory results (isolation of *F. tularensis* from a clinical specimen; four-fold or greater change in serum antibody titer to *F. tularensis* antigen).
>
> *Presumptive* – a clinically compatible case with presumptive laboratory results: Elevated serum antibody titer(s) to *F. tularensis* antigen (without documented fourfold or greater change) in a patient with no history of tularemia vaccination or detection of *F. tularensis* in a clinical specimen by direct fluorescent assay (DFA).

Reporting:

Report all suspected or confirmed cases of tularemia 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 tularemia case report form.

Case Investigation:

Complete the CDC Tularemia 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: Not recommended for tularemia patients given the lack of human-to-human transmission. In hospital settings, standard precautions are recommended. If plague has not yet been ruled out of the diagnosis then droplet isolation should be continued until 48 hours of appropriate antimicrobial therapy has been given and there has been a favorable clinical response (e.g., defervescence).

2. Contact management

   2.1. Isolation: None required.

   2.2. Prophylaxis (see Treatment section also):

   2.1.a Asymptomatic persons having direct exposure to infectious materials from sick or dead animals with tularemia or ingestion or inhalation of known tularemia infected material should receive post-exposure antibiotic prophylaxis for 14 days.

   2.1.b Contacts who have not had direct exposure to infectious material should measure their temperature twice a day for 14 days and see a physician immediately if fever greater than 100° F develops.

   2.1.c Laboratory workers in hospitals or other settings exposed to a potentially aerosolized tularemia culture may also need post-exposure prophylaxis. Consult with the Epidemiology and Response Division for further recommendations.

3. Prevention

   3.1. Immunization: A vaccine for tularemia has been developed but is not yet available to the general public.

   3.2. Surveillance of rabbits and rodents: The Department of Health Zoonoses team submits rodent and rabbit carcasses for routine plague surveillance. These carcasses will occasionally test positive for tularemia. Report rabbit and rodent die-offs to the Epidemiology and Response Division at 505-827-0006. Within Bernalillo County, report rabbit and rodent die-offs to the Albuquerque Environmental Health Department’s Urban Biology Division, 505-452-5300.

   3.3. Control of rabbits, rodents and vectors: Sylvatic (wildlife) tularemia defies most control measures because the wild rabbit and rodent reservoirs are so widespread and diverse as are the vectors (both ticks and deer flies).

   3.4. Public education: Educate the public about risk factors, preventive measures, and signs and symptoms of tularemia.

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

3.4.b Avoid contact with dead and sick animals, and potentially contaminated water.

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

3.4.d Rodent proof houses and outbuildings.

3.4.e Wear rubber gloves when handling wild game and thoroughly cook wild game meat.

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

References

Heymann, DL, ed. Control of Communicable Diseases Manual, 19th ed. Washington, DC: American Public Health Association; 2008.

Dennis D. T., T. V. Inglesby, D. A. Henderson, et al. Tularemia as a biological weapon: medical and public health management. JAMA. Jun 6 2001; 285(21):2763-2773.

Tularemia--United States, 1990-2000. MMWR Morb Mortal Wkly Rep. Mar 8 2002;51(9):181-184.

Feldman, K.; Tularemia; J Am Vet Med Assoc; 2003; 222: 725-730.

See Tularemia Fact Sheets (English) (Spanish).