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Tularemia

Overview^{1, 2, 3, 6, 8, 10}

Tularemia is a highly infectious disease of animals and humans caused by the bacterium *Francisella tularensis* (*F. tularensis*). The majority of human infections are caused by 2 subspecies of *F. tularensis*; *F. tularensis tularensis* (type A) and *F. tularensis holarctica* (type B). Type A is a more virulent serotype for humans, usually occurring in rabbits and rodents in the U.S. and Canada. Type B usually causes a mild ulceroglandular infection and occurs in water and aquatic animals in Europe and Asia. Rabbits, hares, and rodents are especially susceptible and often die in large numbers during outbreaks. *F. tularensis* is very infectious by the inhalation route; exposure to as few as 10-50 organisms can cause disease, but the bacteria are not spread from person-to-person. Humans may be infected by several different routes including tick and deer fly bites (and possibly other biting insects); skin contact with infected animals, ingestion of contaminated water, laboratory exposure, or inhalation of contaminated dusts or aerosols, exposure may also be the result of bioterrorism.

Symptoms of tularemia may include an abrupt onset of fever, chills, headaches, diarrhea, muscle aches, joint pain, dry cough, and progressive weakness. Symptoms usually appear three to five days after exposure to the bacteria, with a range of one to 21 days.² The symptoms typically last for several days, then remit for a brief interval, and then recur. There are several different [clinical presentations](#) of tularemia which are related to the route of exposure. Untreated tularemia has a mortality rate of 5-15%, but if treated the disease carries a mortality rate of 1-3%.

Tularemia can be difficult to diagnose. Therefore it is important to share any likely exposures such as tick and deer fly bites, or contact with sick or dead animals with your health care provider. Your health care provider will likely prescribe [antibiotics](#) if you are diagnosed with tularemia. Although symptoms may last for several weeks, most patients completely recover. However, in some people, tularemia may lead to months of debility usually associated with late lymph node suppuration or persistent fatigue.

Some steps to [prevent](#) tularemia include; the use of insect repellent, wearing gloves when handling sick or dead animals, cook game meat thoroughly before eating it, don't drink untreated water, and avoid mowing over animals.

For a complete description of tularemia refer to:

- *Control of Communicable Diseases Manual* (CCDM), American Public Health Association, 20th ed; 2015.
- American Academy of Pediatrics. *Red Book: 2015 Report of the Committee on Infectious Diseases*. 30th ed; 2015.
- *Mandell, Douglas, and Bennett's Principles and Practices of Infectious Diseases: Vol. 2*. 8th ed. 2015.



1999 Case Definition - Tularemia (*F. tularensis*)⁴ (4/16)

Clinical Description

An illness characterized by several distinct forms, including the following:

- **Ulceroglandular:** cutaneous ulcer with regional lymphadenopathy.
- **Glandular:** regional lymphadenopathy with no ulcer.
- **Oculoglandular:** conjunctivitis with preauricular lymphadenopathy.
- **Oropharyngeal:** stomatitis or pharyngitis or tonsillitis and cervical lymphadenopathy.
- **Intestinal:** intestinal pain, vomiting, and diarrhea.
- **Pneumonic:** primary pleuropulmonary disease.
- **Typhoidal:** febrile illness without early localizing signs and symptoms.

Laboratory Criteria for Diagnosis

Presumptive:

- 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 fluorescent assay.

Confirmatory:

- Isolation of *F. tularensis* in a clinical specimen, **OR**
- Fourfold or greater change in serum antibody titer to *F. tularensis* antigen.

Exposure

Clinical diagnosis is supported by evidence or history of a tick or deerfly bite, exposure to tissues of a mammalian host of *F. tularensis*, or exposure to potentially contaminated water.

Case Classification


Probable: A clinically compatible case with laboratory results indicative of presumptive infection.

Confirmed: A clinically compatible case with confirmatory laboratory results.

Information Needed for Investigation

Verify the diagnosis. What laboratory tests were conducted and what were the results? What is the primary clinical syndrome? Obtain demographic, clinical and laboratory information on the case from the attending physician, hospital, and/or laboratory. Obtain the other epidemiological information necessary to complete the [Disease Case Report](#) (CD-1) and the [Tularemia Case Investigation Report](#). The information may be obtained from the patient or a knowledgeable family member. **NOTE:** *People who have been exposed to the tularemia bacteria should be treated as soon as possible. The disease can be fatal if it is not treated with the appropriate antibiotics.*

Establish the extent of illness. Have there been other cases linked by travel, time, place, or person? Determine if household or other close contacts are, or have been ill by contacting the health care provider, patient, or family member. Identify symptomatic household members, child care contacts, associates / co-workers, travel companions and strongly urge them to contact their

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physician for a medical evaluation. **NOTE:** *Maintain a high index of suspicion regarding any cluster of cases of pneumonia diagnosed as being due to *F. tularensis*. This should be reported promptly to the [District Communicable Disease Coordinator](#) because of the potential of *F. tularensis* being used as a bioterrorism agent.*

Identifying the source of infection. Determine the source of infection. Human-to-human transmission has not been documented. *F. tularensis* can be transmitted to humans via various mechanisms: bites by infective insects; handling infectious animal tissues or fluids; direct contact with or ingestion of contaminated water, food, or soil; inhalation of infective aerosols generated by lawn mowing and brush cutting; accidental exposure in the laboratory setting; or exposure may be the result of [bioterrorism](#).

Establish the occupation of the case since this information may help narrow the search for the route of exposure. Shared activities or exposures should be investigated for cases among families and friends. Identify possible routes of exposure the 2 weeks preceding illness, did the patient report:

1. Travel?
2. Animal contact?
3. Recent tick and/or deer fly bites?
4. Ingested untreated water?
5. Work in a laboratory that processes tularemia specimens?
6. Performed aerosol-generating activities (e.g., brush-cutting or lawn mowing)?
7. If *F. tularensis* were used as a weapon, the bacteria would likely be made airborne for exposure by inhalation. People who inhale an infectious aerosol would generally experience severe respiratory illness, including life-threatening pneumonia and systemic infection if they are not treated.

COMMENT: *Sometimes the source of infection is not identified.*

Provide tularemia information to persons at risk for infection and the general public as needed. Efforts should be made to promote tularemia awareness and cases should be educated on the importance of [personal protective measures](#). Information is available from the Centers for Disease Control and Prevention for distribution - [Tularemia - Frequently Asked Questions](#) and a [Tularemia Fast Facts](#) sheet is available from the Center for Food Security & Public Health, Iowa State University. For managing potential laboratory exposures to *F. tularensis* see the [CDC Fact Sheet](#) on the subject.

Tularemia Surveillance. Review WebSurv to determine whether there have been other tularemia cases in the same geographic area. Every effort should be made to identify the source. Information obtained through the public health investigation will be used to identify a possible source of infection and to characterize persons or geographic areas in which additional efforts are needed to raise awareness and reduce disease incidence.

Notification

- The Local public health agency should immediately contact the [District Communicable Disease Coordinator](#), the District [Senior Epidemiology Specialist](#), or the Missouri



Department of Health and Senior Services (MDHSS) – Bureau of Communicable Disease Control and Prevention (CDCP), phone (573) 751-6113, Fax (573) 526-0235, or for after hours notification contact the MDHSS/Emergency Response Center (ERC) at (800) 392-0272 (24/7) upon learning of a suspected case of pneumonic tularemia; or if a **suspected intentional release** of tularemia is suspected.

Control Measures^{6, 8, 9}

When entering endemic areas, people should use tick-proof clothing and repellents. A thorough search for ticks should be done after leaving tick-infested areas. Ticks should be removed at once (see [Tick Bite Prevention](#)). When handling rabbits and rodents, especially in endemic areas, people should wear protective clothing; including rubber gloves and face mask, because organisms may be present in the animal and in tick feces on the animal’s fur. Wild birds and game must be thoroughly cooked before eating. Water that may be contaminated must be disinfected before use.

When hiking, camping or working outdoors:

1. Avoid bites from arthropods especially deerflies and ticks. Use insect repellants containing 20% to 30% DEET, picaridin or IR3535.
2. Wear long pants, long sleeves, and long socks; tuck pants into socks or tall boots to keep ticks off your skin. Wear light-colored clothing so ticks can be easily observed and removed.
3. Conduct body checks for ticks frequently and remove ticks promptly with fine-tipped tweezers.

Don’t drink untreated surface water. Avoid drinking, bathing, swimming, or working in untreated water, particularly in areas where tularemia is known to be endemic.

When mowing or landscaping:

1. Don’t mow over sick or dead animals.
2. Consider using dust masks to reduce your risk of inhaling the bacteria.


If you hunt, trap or skin animals:

1. Use gloves when handling animals, especially rabbits, muskrats, prairie dogs, and other rodents.
2. Cook game meat thoroughly before eating.

NOTE: A vaccine for tularemia is under review by the Food and Drug Administration and is not currently available in the United States.

If Biological Terrorism is suspected.

F. tularensis is very infectious. A small number (10-50 or so organisms) can cause disease. If *F. tularensis* were used as a weapon, the bacteria would likely be made airborne for exposure by inhalation. People who inhale an infectious aerosol would generally experience severe respiratory illness. This may include life-threatening pneumonia and systemic infection if they are not treated.

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Clinicians should be familiar with reporting requirements within their public health jurisdiction for these conditions. When clinicians suspect that illness is caused by an act of bioterrorism, they should contact their local public health agency (LPHA) immediately so that appropriate infection-control measures and outbreak investigations can begin. In the event of a bioterrorist attack, clinicians should review the CDC Emergency Preparedness and Response Web site at: <http://emergency.cdc.gov> for current information and specific prophylaxis and treatment guidelines or [USAMRIID's Pocket Reference Guide to Biological Select Agents & Toxins](#).

Public health authorities should be contacted before obtaining and submitting patient or environmental specimens for identification of suspected agents of bioterrorism. If tularemia is suspected to be the result of a terrorist act, or the intentional or deliberate release thereof; the LPHA should:

1. Notify local law enforcement and the [Senior Epidemiology Specialist](#) for the District or MDHSS/CDPCP phone (573) 751-6113, Fax (573) 526-0235, or for after-hours notification contact the MDHSS/ ERC at (800) 392-0272 (24/7) immediately.
2. Work with law enforcement and implement "Chain of Custody" procedures for all laboratory samples, as they will be considered evidence in a criminal investigation.
3. Work to define the population at risk which is essential to guide response activities. Public health authorities will play the lead role in this effort, but must consult with law enforcement, emergency response and other professionals in the process.
4. Once the mechanism and scope of delivery has been defined, identify symptomatic and asymptomatic individuals among the exposed and recommend treatment as appropriate.
5. Establish and maintain a detailed line listing of all cases and contacts with accurate identifying and locating information (complete a "[Suspect Tularemia Case Investigation Form](#)").

***NOTE:** The "[Consensus Statement: Tularemia as a Biological Weapon: Medical and Public Health Management](#)" also provides recommendations for measures to be taken by medical and public health professionals following the use of tularemia as a biological weapon against a civilian population.*

Laboratory Procedures⁸

Physicians who suspect tularemia should promptly collect appropriate specimens and alert the laboratory to the need for special diagnostic and safety procedures. Rapid diagnostic testing for tularemia is not widely available. Growth of *F. tularensis* in culture is the definitive means of confirming the diagnosis of tularemia. Appropriate specimens include swabs or scraping of skin lesions, lymph node aspirates or biopsies, pharyngeal washings, sputum specimens, or gastric aspirates, depending on the form of illness. Paradoxically, blood cultures are often negative.

A presumptive diagnosis of tularemia may be made through testing of specimens using direct fluorescent antibody, immunohistochemical staining, or PCR. The diagnosis of tularemia can also be established serologically by demonstrating a 4-fold change in specific antibody titers



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between acute and convalescent sera. Convalescent sera are best drawn at least 4 weeks after illness onset; hence this method is not useful for clinical management.

Routine clinical specimens for *F. tularensis* testing should be submitted to a commercial clinical laboratory for testing. However, the Missouri State Public Health Laboratory (MSPHL) conducts routine confirmatory testing for suspected *F. tularensis* **isolates**. Instructions on specimen collection and transport may be viewed at: <http://www.health.mo.gov/lab/specialbacteriology.php> or you may call the MSPHL – Special Microbiology Unit at (573) 751-3334.

In addition, the MSPHL has prepared specimen collection guidelines for bacteria that might be used in a bioterrorism event. These guidelines are specific to specimen collection during a suspected bioterrorism incident as determined by the Department of Health and Senior Services. The MSPHL would perform testing of **clinical specimens** and isolates under these circumstances. Instructions on clinical specimen collection and transport for testing by the MSPHL may be viewed at: <http://www.health.mo.gov/lab/pdf/TularemiaFactSheet.pdf>. Healthcare providers must call the MSPHL – Special Microbiology Unit at (573) 751-3334 before specimens are submitted.

***NOTE:** Remember that these samples may be highly infectious! Extreme caution should be taken in collecting, preparing for shipment and transporting any material suspected of being contaminated with a biological agent.*

Reporting Requirements

Tularemia (pneumonic) or where an **intentional release is suspected** is a Category 1(A) State Reportable Diseases and shall be reported to the [local health authority](#) or to MDHSS **immediately** upon first knowledge or suspicion by telephone, facsimile or other rapid communication. MDHSS/BCDCP may be contacted Monday through Friday, 8:00 AM to 5:00 PM, telephone (573) 751-6113 or fax (573) 526-0235; after hours and weekends telephone MDHSS/ERC (800) 392-0272.

Tularemia (non-pneumonic) or where intentional release is **not** suspected is a Category 2(A) State Reportable Diseases and shall be reported to the [local health authority](#) or to MDHSS within (1) calendar day of first knowledge or suspicion by telephone, facsimile or other rapid communication. MDHSS may be contacted Monday through Friday, 8:00 AM to 5:00 PM, telephone (573) 751-6113 or fax (573) 526-0235; after hours and weekends telephone (800) 392-0272.

As a Nationally Notifiable Condition, a **suspected intentional release** of tularemia is an **IMMEDIATE, EXTREMELY URGENT** report to the Centers for Disease Control and Prevention (CDC). **IMMEDIATE, EXTREMELY URGENT** reporting requires MDHSS to call the CDC EOC at 770-488-7100 within 4 hours of a case meeting the notification criteria; followed by submission of an electronic case notification via WebSurv in the next regularly scheduled electronic transmission.



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As a Nationally Notifiable Condition, all **confirmed** and **probable** tularemia cases, other than cases resulting from a **suspected intentional release** are a **STANDARD** report to CDC. MDHSS will submit these reports to the CDC by electronic case notification (WebSurv) within the next reporting cycle.

1. For all reported cases of tularemia complete a [Disease Case Report](#) (CD-1).
2. Entry of the completed CD-1 into WebSurv negates the need for the paper CD-1 to be forwarded to the District Health Office.
3. For all STANDARD confirmed and probable tularemia cases, complete a [Tularemia Case Investigation Report](#) (CDC 56.50 E) and send the completed report to the District Health Office.
4. For cases suspected of being part of an intentional release (bioterrorism), complete a [“Suspect Tularemia Case Investigation Form”](#).
5. Fax the completed Suspect Tularemia Case Investigation Form to the District Health Office.
6. MDHSS will report to CDC following the above reporting criteria (see boxes).
7. All outbreaks or “suspected” outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the [Missouri Outbreak Surveillance Report](#) (CD-51).
8. If an outbreak is associated with food, person-to-person transmission, environmental contamination, animal contact, or indeterminate/other/unknown etiology, a [National Outbreak Reporting System – Foodborne Disease Transmission, Person-to-Person Disease Transmission, Animal Contact](#) form (CDC 52.13) is to be completed and submitted to the District Health Office at the conclusion of the outbreak.
9. If an outbreak is associated with the consumption or use of water for drinking, or with ingestion, contact, or inhalation of recreational water, a [National Outbreak Reporting System - Waterborne Disease Transmission](#) form (CDC 52.12) is to be completed and submitted to the District Health Office at the conclusion of the outbreak.
10. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

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