**Tularemia**

**Revision Dates**

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**Case Definition**

**Confirmed case**  
Clinical illness\(^{(A)}\) with laboratory confirmation of infection:
- Isolation (i.e., culture) of *Francisella tularensis* from an appropriate clinical specimen (e.g., blood, swabs from primary lesions, tissue from biopsy, lymph node aspirates, gastric washings or respiratory samples)\(^{(B)}\);  
  **OR**
- Seroconversion or significant difference between acute and convalescent serum antibody titres to *F. tularensis* antigen.

**Probable case**  
Clinical illness\(^{(A)}\) with laboratory evidence:
- Detection of *F. tularensis* in an appropriate clinical specimen (e.g., ulcer exudate, lymph node biopsy)\(^{(B)}\) by fluorescent assay;  
  **OR**
- Detection of *F. tularensis* nucleic acid (e.g., PCR) in an appropriate clinical specimen (e.g., blood, CSF, biopsy tissue)\(^{(C)}\);  
  **OR**
- A single microagglutination titre of \(\geq 1:128\) or tube agglutination of \(\geq 1:160\) in a serum specimen.

*Denotes potential bioterrorism agent.*

\(^{(A)}\) 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. Clinical illness is characterized by onset of fever, chills, headache and malaise. Additional symptoms may present in several forms according to route/site of exposure with potential overlap:\(^{(1)}\)

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

\(^{(B)}\) Refer to the Provincial Laboratory for Public Health (ProvLab) Guide to Services for current specimen collection and submission information. Consultation with the ProvLab Microbiologist-On-Call is recommended before specimens are collected and submitted.

\(^{(C)}\) Refer to the National Microbiology Laboratory (NML) Guide to Services for current specimen collection and submission information.
Reporting Requirements

1. Physicians, Health Practitioners and others
   Physicians, health practitioners or others shall notify the Medical Officer of Health (MOH) (or designate) of the zone, of all confirmed and probable cases in the prescribed form by mail, fax or electronic transfer within 48 hours (two business days).

2. Laboratories
   All laboratories shall report all positive laboratory results by mail, fax or electronic transfer within 48 hours (two business days) to the:
   - Chief Medical Officer of Health (CMOH) (or designate), and
   - MOH (or designate) of the zone.

3. Alberta Health Services and First Nations and Inuit Health Branch
   - The MOH (or designate) of the zone where the case currently resides shall forward the initial Notifiable Disease Report (NDR) of all confirmed cases to the CMOH within two weeks of notification and the final NDR (amendment) within four weeks of notification.
   - For out-of-province and out-of-country reports, the following information should be forwarded to the CMOH (or designate) by phone, fax or electronic transfer within 48 hours (two business days):
     - name,
     - date of birth,
     - out-of-province health care number,
     - out-of-province address and phone number,
     - positive laboratory report, and
     - other relevant clinical / epidemiological information.

4. Exposure of Concern or Suspected Deliberate Release
   - The MOH (or designate) shall, by Fastest Means Possible, notify the CMOH (or designate) of all confirmed and probable cases where deliberate release is suspected.
   - In the case of an exposure of concern or suspected deliberate release (i.e., bioterrorism), the CMOH will notify the Alberta Security & Strategic Intelligence Support Team (ASSIST) Duty officer at 780-422-3787 and Alberta Health Emergency Preparedness on Call at ahweoc@gov.ab.ca.
Etiology
Tularemia (also called “rabbit fever” or “deer-fly fever”) is caused by the gram-negative coccobacillus Francisella tularensis. There are two main subspecies (ssp.) of F. tularensis that cause human disease:

1. F. tularensis ssp. tularensis (type A) is the most virulent and accounts for the majority of cases in North America.
2. F. tularensis ssp. holarctica (type B), occurs throughout the northern hemisphere. It is less virulent than ssp. tularensis.

Clinical Presentation
The clinical presentation of tularemia is determined by the portal of entry of F. tularensis, as well as the health of the individual and virulence of the organism. Symptoms can range from asymptomatic, to acute sepsis and rapid death. Most individuals experience abrupt onset of fever, chills, myalgia and headache (i.e., influenza-like illness). The following table outlines the different clinical presentations:

<table>
<thead>
<tr>
<th>Clinical classification</th>
<th>% of cases</th>
<th>Clinical presentation</th>
<th>Portals of entry</th>
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<tbody>
<tr>
<td>Ulceroglandular</td>
<td>60-80</td>
<td>Enlarged lymph nodes, non-healing maculopapular ulcer at inoculation site (i.e., insect or animal bite).</td>
<td>Tick or deer-fly bite, or direct inoculation across intact dermis.</td>
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<td>Painful, inflamed regional lymph nodes which can drain spontaneously.</td>
<td>Animal contact.</td>
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<td>Recovery can be lengthy.</td>
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<td>Rarely fatal (mortality rate &lt; 3%).</td>
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<tr>
<td>Glandular</td>
<td>≤20</td>
<td>Enlarged lymph nodes, no ulcer.</td>
<td>Direct inoculation across intact dermis.</td>
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<td>Most common in children</td>
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<td>Pneumonic</td>
<td>≤20</td>
<td>Fever, non-productive cough and pleuritic chest pain. Chest x-ray shows patchy bilateral infiltrates, pleural effusion and hilar lymphadenopathy.</td>
<td>Primary pneumonia is more common in certain occupations (e.g., laboratory workers, farmers, landscapers).</td>
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<td>May occur as secondary pneumonia in approximately 30% of ulceroglandular cases and 70% of typhoidal cases.</td>
<td>Inhalation of contaminated aerosols, aerosolized bioweapon exposures, or hematogenous spreading from glandular or typhoidal infections.</td>
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<tr>
<td>Oculoglandular</td>
<td>&lt;1</td>
<td>Enlarged lymph nodes, severe, painful conjunctivitis (usually unilateral).</td>
<td>Ocular inoculation of infectious fluids or animal dander, or autoinoculation from bite eschar or ulcers</td>
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<td>Oropharyngeal</td>
<td>&lt;1</td>
<td>Severe sore throat with exudates on the throat and tonsils and painful cervical lymphadenopathy</td>
<td>Ingestion of raw or undercooked infected game or bush meats</td>
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<tr>
<td>Intestinal</td>
<td></td>
<td>Intestinal pain, vomiting, and diarrhea</td>
<td>Ingestion of raw or undercooked infected game or bush meats</td>
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<td></td>
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<td>Can range from mild to acute, fatal disease with extensive ulceration of the bowel.</td>
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<tr>
<td>Typhoidal or Septicemic</td>
<td>&lt;1</td>
<td>Patients may present with a variety of symptoms including fever, chills, headache, muscle aches, sore throat, abdominal pain, diarrhea, and vomiting. This form of blood-borne infection can also lead to shock, disseminated intravascular coagulation or other complications.</td>
<td>May not be apparent. Can develop after any mode of acquisition.</td>
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<td>Mortality rate of 30 – 60%.</td>
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The most common complication observed in cases of tularemia is lymph node abscesses. Cases with more severe disease may also develop renal failure, disseminated intravascular coagulation (DIC), rhabdomyolysis, hepatitis and jaundice. Before the advent of antibiotic treatment, case-fatality rates were as high as 60%, but with treatment they are at approximately 4%. © 2003–2018 Government of Alberta
Diagnosis
The diagnosis of tularemia can be made via blood culture, immunofluorescent antibody (IFA) testing, microagglutination and polymerase chain reaction (PCR). The organism can be isolated in the blood for the first two weeks of illness and in skin lesions for a month or more. 

*F. tularensis* is a highly infectious organism, and can result in infection in laboratory workers if proper precautions are not taken. Clinicians should alert laboratory personnel regarding specimens where tularemia is suspected. Suspect cultures should be immediately sent to a reference laboratory with Bio Safety Level 3 capabilities. Intense caution should be used to avoid exposure by aerosol within the laboratory.

Epidemiology
Reservoir
*Francisella tularensis* ssp. *tularensis*, found more commonly in North America, is associated with dry environments, hares, and ticks or tabanid flies (horse or deer-fly). *F. tularensis* ssp. *holarctica*, which occurs throughout the Northern Hemisphere, is associated with fresh water, numerous rodent species, ticks, tabanid flies, or mosquitoes. Humans, other mammals (e.g., cats, dogs, hamsters, cows and primates), some species of bird, fish and amphibian are incidental hosts.

*F. tularensis* can survive for weeks to months in the environment.

Transmission
Person-to-person transmission has not been demonstrated. Transmission occurs through the bite of an infected tick or mosquito, through inoculation of the skin, eyes or nose with contaminated water, mud, blood or tissue while handling an infected carcass by drinking contaminated water, handling or eating poorly cooked infected meat, by inhaling dust from contaminated soil, grain or hay or from contaminated animal pelts or paws and by handling infected pets.

Laboratory-acquired infection has also been known to occur.

Incubation Period
The incubation period averages 3 – 5 days, but ranges from 1 – 21 days.

Period of Communicability
There is no evidence of person-to-person transmission. If the case remains untreated, the infectious agent may be found in the blood during the first two weeks of disease and in lesions for a month, sometimes longer.

Flies can remain infective for 14 days; ticks throughout their whole life cycle (about two years). *F. tularensis* is able to survive being frozen in rabbit meat at -15°C for three years and remain infective. *F. tularensis* can survive in water, mud and animal carcasses for prolonged periods.

Host Susceptibility
Susceptibility is universal however, underlying co-morbidity (e.g., alcohol abuse, diabetes), a delay in seeking medical care and a delay in commencing appropriate antibiotic therapy can affect severity of infection and result in poor outcomes. Immunity following recovery is believed to be long-term. Re-infection, although extremely rare, has been reported in laboratory workers.
Occurrence

General
Cases of tularemia are more common in North America, Europe and Asia, where the disease is considered endemic. Cases are less common or are sporadic in North Africa, Australia and the northern part of South America.\(^{(23)}\) Tick-transmitted tularemia occurs worldwide and is most commonly reported between May and August. Tularemia via contact with an infected animal occurs most often in the fall during hunting and trapping season.\(^{(4)}\)

Prior to World War II, tularemia was very common in the United States; however it steadily declined to fewer than 0.15 cases per 100,000 between 1965 and 1995 when it was removed from their national notifiable list.\(^{(24)}\) It became reportable again in 2000, due in part to concerns of its possible use as a bioterrorism agent.\(^{(4)}\) Between 2000 and 2010, the rate of tularemia in the United States has been less than 0.06 cases per 100,000.\(^{(25)}\)

Canada
Tularemia is a nationally notifiable disease in Canada. Tularemia is considered rare in Canada, however many cases likely remain undetected because they are mild. The first recorded case in Canada occurred in 1929.\(^{(26)}\) Between 2005 and 2011, between six and 22 cases were reported each year in Canada.\(^{(27)}\)

Alberta
Tularemia is a notifiable disease in Alberta. Between 1998 and 2014 there have been seven cases of tularemia reported in Alberta: 1998–2 cases, 2006–1 case, 2007–1 case, 2011–1 case, 2012–2 cases, 2013–1 case, 2014–2 cases.\(^{(28)}\) All of the cases were acquired within Alberta; the exposure source for two cases was animal exposure and unknown for the remaining five cases.

Key Investigation

Single case/cluster
- Confirm that the diagnosis meets the Alberta Health case definition.
- Review clinical presentation and history to determine possible source of infection of the case.
- Investigate possible exposures during the 1–21 days before onset, including a history of:\(^{(2,4,6,29)}\)
  - Contact with wild animals (e.g., bites or scratches, skinning or eviscerating wild game, especially rabbits or wild rodents),
  - Contact with domestic animals (e.g., bites or scratches),
  - Increased biting fly activity in the area and/or fly bites (deer and horse flies are usually active between late spring and early fall),
  - Recent tick bite,
  - Exposure to, or drinking of, untreated water,
  - Eating inadequately cooked wild game (especially rabbit),
  - Contact with dust or other aerosols associated with soil, grain or hay,
  - Work in a laboratory setting.
- Recent history of travel to or immigration from an area with known cases.
- Identify contacts that may have potentially been exposed to the same source or participated in the same activities.
Control

Management of a Case
- In addition to routine practices, contact precautions (due to discharges from ulcers, lymph nodes or conjunctival sacs) apply until the person is no longer considered infectious.\(^{(2)}\)

Treatment of a Case
- Antibiotics are used in the treatment of tularemia cases.\(^{(2)}\)
- Consultation with an Infectious Disease Specialist may be appropriate in some cases.

Management of Contacts
- As a general rule, contact follow-up of tularemia cases is not required. However, in the event that improperly cooked food or other suspected common environmental exposure is the suspected source, contacts that may have been exposed to the same source should be investigated and educated in the signs and symptoms of disease to observe for.
  - If any are ill, they should be referred to their healthcare professional in order to facilitate proper diagnosis and therapy.
- For high-risk exposures, such as laboratory personnel who worked with a specimen on an open bench or had direct skin contact, treatment with oral doxycycline or ciprofloxacin is recommended for 14 days.\(^{(30)}\)

Preventive Measures
Individuals should be educated on the following:\(^{(2)}\)
- Ways to reduce transmission of ticks around the home, including:
  - Removing brush and leaf litter and creating a desiccation zone of wood chips or gravel between forest and lawn.
- Use of personal protective measures to minimize exposure and reduce the risk of acquiring a tick bite:\(^{(4,31)}\)
  - Wear a long sleeved shirt and long pants, tight at the wrist and ankles or tucked into gloves or socks.
  - Light coloured clothing can aid in the detection of ticks that have not yet attached.
  - Small children should wear a hat where contact with vegetation such as in dense woods, high grasses, or thickets cannot be avoided. This is to help prevent the exposure of the head and neck to tick bites.
  - Apply insect repellents containing 20–30% N,N-diethyl-3-methylbenzamide (DEET) to the skin (adults). For children aged 2 – 12 years, insect repellent with <10% DEET may be used up to three times per day and once per day for children six months to two years of age. It is not recommended for use on children under six months of age.
  - Apply permethrin to tents and clothing. Do not apply directly to skin.
  - Check one’s body thoroughly for ticks.
  - Remove any attached ticks carefully without crushing.
    - Grasp gently with tweezers as close to its mouth as possible (the part sticking into the skin).
    - Slowly pull the tick straight out without jerking or twisting.
    - Check the bite area daily for at least two weeks.
    - If a red rash appears seek medical attention.
    - Protect hands with gloves, cloth or tissue when removing ticks from humans or animals.
    - Wash hands thoroughly following tick removal.
- When hunting, trapping or skinning animals:
  - Wear impervious gloves,
Avoid touching one’s eyes,
- Wash hands thoroughly afterwards and,
- Thoroughly cook wild animal meat.\(^{(4)}\)

- Do not mow over sick or dead animals.\(^{(32)}\)
- Do not drink untreated surface water.
- Antibiotic prophylaxis after potential exposures, such as tick bites, is not recommended.\(^{(4)}\)
- There is currently no vaccine licensed for the prevention of tularemia in Canada.
- Laboratory safety: Biosafety Level 3 practices are required.\(^{(33)}\)

**Bioterrorism Event**

- *F. tularensis* is of great concern as a bioterrorism agent because of:
  - its very low infectious dose (10–50 organisms),
  - its ability to survive in the environment,
  - the fact that it can be easily disseminated by aerosol and is infective by inhalation,
  - its potential of causing severe illness and death with untreated inhalational tularemia.\(^{(30)}\)

- In the event of an intentional release of tularemia, the local Zone MOH shall ensure that all exposed individuals are assessed and that appropriate antibiotic prophylaxis or treatment is provided.\(^{(30,34)}\)
References


(13) Klock LE, Olsen PF, Fukushima T. Tularemia epidemic associated with the deerfly. JAMA 1973 10/08;226(2):149-152.


