## 1. DISEASE REPORTING

### 1.1 Purpose of Reporting and Surveillance

1. To identify the source of infection of individual case-patients, to determine the risk of transmission from the source, and to stop transmission.
2. To identify swiftly and to mitigate any cluster of illness that might result from intentional release of this potential agent of bioterrorism.
3. To identify microbiology laboratory workers who may have been exposed through handling of specimens or cultures to ensure prompt recognition and treatment of any consequent illness.
4. To identify persons potentially exposed by the case-patient and to facilitate treatment.
5. To identify potential recurrent sources of transmission of enzootic tularemia to persons in Oregon.

### 1.2 Laboratory and Physician Reporting Requirements

Laboratories and physicians are required to report cases immediately upon diagnosis or identification.

### 1.3 Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed and presumptive cases to the Oregon Public Health Division (OPHD) immediately (971-673-1111).
2. OPHD would also like to hear about suspect cases, and can provide guidance to local health departments, providers, or laboratories as needed.
3. Begin follow-up investigation immediately. Complete the fields shown in Orpheus. Investigate and conduct follow up for potential exposures at laboratories within your health department’s jurisdiction (see §6.1). (If laboratories outside the case jurisdiction are involved, OPHD will notify the relevant LHDs to advise follow up.)
4. Coordinate with the Oregon State Public Health Laboratory (OSPHL) to ensure confirmatory testing (see §3.4).
5. The CDC Tularemia Case Investigation form, available at [http://public.health.oregon.gov/DiseasesConditions/DiseasesAZ/Pages/disease.aspx?did=14](http://public.health.oregon.gov/DiseasesConditions/DiseasesAZ/Pages/disease.aspx?did=14), will ordinarily be completed by OPHD. Counties with the time and inclination to complete it and send it to us may certainly do so, and we will be most appreciative.

## 2. THE DISEASE AND ITS EPIDEMIOLOGY

### 2.1 Etiologic Agent

*Francisella tularensis* is a small, non-motile, aerobic, non-spore-forming Gram-negative intracellular coccobacillus. *F. tularensis* is highly infectious (infectious dose: 10–50 organisms) and can survive for weeks to months on fomites. The organism can survive for years in frozen meat. It can be killed with 1% hypochlorite, 70% ethanol, glutaraldehyde, or formaldehyde, as well as by moist heat (121°C for 15 minutes) or dry heat (160°–170°C for at least 1 hour). Two major subspecies, with different biochemical and epidemiological characteristics, are found in the U.S.: *F. tularensis* subspecies tularensis (type A) and *F. tularensis* holarctica (type B). Type A is generally considered to be more virulent than type B (infective dose for type A: 10 bacteria when injected subcutaneously; 25 when given as an aerosol). Both subspecies are found in Oregon, though most cases here have been due to subspecies *holarctica* (type B).

### 2.2 Description of Illness

To a great extent, the nature of the illness reflects the route of transmission (see below, §2.4), as well as the virulence of the infecting strain. Symptoms could include rapid onset of fever, chills, headache, malaise, dry cough and fatigue. Bacteremia, should it develop, may last for two weeks if untreated; mouth and
1. **Ulceroglandular (majority of naturally occurring cases)**

   Patients present with enlarged, tender, localized lymphadenopathy and a painful papule in the region draining into these nodes, which develops into a slowly progressive, non-healing skin ulcer (21%–87% of cases in the U.S. [CSTE 2009]).

2. **Glandular**

   Similar to the ulceroglandular form, but without evidence of a cutaneous lesion. The skin lesion may have healed, or is minimal and therefore overlooked (3%–20% of cases in the U.S.).

3. **Oculoglandular**

   Early manifestations include photophobia and excessive lacrimation, progressing to painful, purulent conjunctivitis (usually unilateral) with preauricular, submandibular or cervical lymphadenopathy (0%–5% of cases in the U.S.).

4. **Oropharyngeal**

   Presents with fever and severe sore throat. Exudative pharyngitis or tonsillitis is seen on physical examination. Cervical, preauricular and retropharyngeal lymphadenopathy may be present. (0%–12% of cases in the U.S.).

5. **Typhoidal**

   This form of tularemia is difficult to diagnose, as it is not associated with prominent lymphadenopathy. Symptoms are nonspecific and could include high fever, nausea, vomiting, diarrhea, abdominal pain, cough, and pneumonia. (5%–30% of cases in the U.S.).

6. **Pneumonic (pulmonary)**

   Occurs as a primary infection following inhalation of organisms; or secondary to hematogenous spread, primarily from ulceroglandular or typhoidal forms. Certain occupations are at increased risk for primary pneumonic tularemia, including sheep shearsers, farmers, landscapers and laboratory workers. The pneumonic form is the most likely presentation from an intentional release of the organism. Pneumonic tularemia resembles pneumonic plague, with symptoms including nonproductive cough, dyspnea, and pleuritic chest pain. Chest X-ray may show patchy infiltrates and hilar adenopathy, or may be initially normal. Untreated, pneumonic tularemia has a 30%–60% mortality rate. (7%–20% of cases in the U.S.).

7. **Intestinal**

   A rare form of tularemia. Cases present with intestinal pain, vomiting, and diarrhea. Intestinal tularemia occurs after consumption of contaminated, undercooked meat or of contaminated water.

2.3 **Reservoirs**

   Tularemia is found in more than 250 species of mammals, birds, reptiles and fish. In the U.S., Cotton-tail rabbits (Sylvilagus spp.), are important reservoir hosts for type A strains. A wide variety of mammals, especially rodents (e.g., beaver, voles, muskrats) are associated with type B strains. Biting insects, such as the wood tick Dermacentor andersoni found in the Pacific Northwest, and deer flies can serve as mechanical vectors for the organism. Domestic cats are also at increased risk of infection due to their predation on small animals, and can be a source of human infection. Humans are usually dead-end hosts, and do not transmit the infection to others.

2.4 **Sources and Routes of Transmission**

   Probably no bacterial agent has more diversified modes of transmission than *F. tularensis*. Infection can occur (i) by direct contact with infected animals, infectious animal tissues or fluids; (ii), by arthropod bite; (iii) by ingestion of contaminated water or food; or, (iv) by inhalation of infective aerosols. There is no human-to-human transmission. As noted above, the infection progresses from the portal of entry, thereby determining the form of illness. Common routes of transmission include:

   1. **Direct contact**

      The most common route of natural transmission is contact while skinning/dressing wild game (especially rabbits and rodents). Infected body fluids (blood or lymph) may enter through cuts, abrasions, or possibly
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even intact skin (leading to ulceroglandular disease); or, by being splashed into the eyes (leading to oculo-
glandular disease).

Less common, transmission may result from the bites or scratches of dogs, cats, carnivorous mammals, or
birds of prey that have killed or fed on infected animals.

2. Arthropod Bite

Blood-feeding arthropods such as biting flies and ticks mechanically transmit the organism between ani-
imals and man. Ticks are important at transmitting *F. tularensis* among rodent or rabbit species, but most
of these ticks feed rarely if at all on man. In the Pacific Northwest, the only tick vector of any relevance to
human transmission is *Dermacentor andersoni*, the Rocky Mountain wood tick.

3. Waterborne/Foodborne

*F. tularensis* can be introduced into a stream or pond if an infected animal dies in or near water. Ingestion
or contamination of mucosal surfaces with this water can lead to oropharyngeal or typhoidal disease. Eat-
ing undercooked, contaminated rabbit or hare meat can result in typhoidal disease.

4. Airborne Transmission

Inhalation of *F. tularensis* can cause either pulmonary or typhoidal disease. If a large number of organisms
is inhaled, the infection may be fulminant and rapidly fatal. Infectious aerosols can be generated while
handling animal hides, cleaning areas contaminated with dried rodent carcasses (e.g., barns, feed bunks,
etc.), moving or winnowing contaminated grain, or by mowing or weed-whacking over infected animal
carcasses. Airborne transmission is also the most likely form of transmission in a bioterrorist attack.

Laboratory personnel are also at an increased risk for airborne transmission of *F. tularensis* as the organism
is highly infectious when grown in culture. Therefore, laboratory personnel should be alerted when tula-
remia is suspected, and all work with suspect cultures of *F. tularensis* should be done in a biological safety
cabinet. Contact OSPHL for additional information.

2.5 Incubation Period

Ranges from 1–14 days; but usually 3–5 days.

2.6 Period of Communicability

Not directly transmitted from person to person.

2.7 Treatment

Streptomycin or gentamicin for 10–14 days can be used in adults and children. Ciprofloxacin and other
fluoroquinolones have also been used. Tetracycline is a useful substitute, but relapses are common after
using it.

See model standing orders on our website for recommended treatment in a mass-casualty setting, as well as
options for post-exposure prophylaxis: https://public.health.oregon.gov/PreventionWellness/VaccinesImmuniza-
tion/ImmunizationProviderResources/Pages/stdgordr.aspx.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

3.1 Confirmed Case Definition(s)

Illness characterized by a clinical presentation of one or more distinct forms:

- 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
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AND

Isolation of *F. tularensis* in a clinical specimen, OR

Fourfold or greater change in serum antibody titer between acute and convalescent sera to *F. tularensis* antigen. Antibodies usually appear in week 2 of the disease.

(Note that, currently, a positive PCR for tularemia does not meet the laboratory component of the case definition.)

3.2 Presumptive Case Definition

A clinically compatible case

AND

Elevated serum antibody titer(s) to *F. tularensis* antigen (without documented fourfold or greater change) in a case with no history of tularemia vaccination, OR

Detection of *F. tularensis* in a clinical specimen by fluorescent assay

3.3 Suspect Case

Anyone with an undiagnosed compatible illness and a history of exposure to a known or suspected source of infection.

3.4 Services Available at the Oregon State Public Health Laboratories

OSPHL can arrange for antibody testing at a partner lab and offers presumptive and confirmatory testing of suspected *F. tularensis* isolates by standard culture methods and direct fluorescent antibody testing. It is unlikely that local health departments will be directly involved in packing or shipment of tularemia specimens. Just in case, here are the OSPHL links regarding collection and shipment of specimens for antibody testing: [https://public.health.oregon.gov/LaboratoryServices/Pages/test.aspx?TestID=57](https://public.health.oregon.gov/LaboratoryServices/Pages/test.aspx?TestID=57) and confirmatory testing: [https://public.health.oregon.gov/LaboratoryServices/Pages/test.aspx?TestID=21](https://public.health.oregon.gov/LaboratoryServices/Pages/test.aspx?TestID=21). If you get inquiries about this, feel free to refer questions to the OSPHL (503-693-4100) for consultation.

4. ROUTINE CASE INVESTIGATION

4.1 Identify the Source of Infection

Investigate possible exposures 1–14 days before onset, including a history of:

1. Skinning or eviscerating wild game (especially rabbits or wild rodents);
2. Bites or scratches by dogs, cats, birds of prey, or other animals;
3. Increased deer fly activity in the area or fly bites (in eastern Oregon, deer and horse flies are usually active between late spring and early fall);
4. Recent tick bite;
5. Drinking untreated water or eating wild game (especially rabbit);
6. Contact or possible contact with dust or other aerosols associated with livestock or grain farming activity;
7. Contact with postpartum fluid from an infected animal; or
8. Work in a medical laboratory.

4.2 Identify Potentially Exposed Persons (Contacts)

Identify persons who participated with the case in any of the activities listed above and contact them, as well as any acquaintance or household member with similar illness (n.b. – anyone meeting the presumptive case definition should be reported and investigated in the same manner as a confirmed case). If any persons with an exposure similar to that of the case-patient become ill, refer them for medical evaluation. For evaluation and management of laboratory workers’ exposures and evaluation of a possible bioterrorist event, see §6.

* Standard blood cultures are usually negative, and Gram stains of skin lesions, sputum, or lymph node aspirates are rarely informative.
5. CONTROLLING FURTHER SPREAD

1. If the infection appears to be associated with rabbit or rodent hunting, this fact should be publicized, to encourage proper handling of wild game carcasses. The Oregon Department of Fish and Wildlife should be given prior notice of any media releases on game-associated tularemia.

2. If the suspected source is a farm animal, contact the OPHD Epi on-call, and we will inform the Oregon Department of Agriculture.

3. If waterborne transmission is suspected, determine whether it involves a nominally potable water source. Consult with your local environmental health experts or the Oregon Public Health Division Drinking Water Section.

5.1 Education

1. Hunters should be instructed to wear gloves when skinning wild game and to keep their hands and gloves away from their eyes. They should wash their hands thoroughly after handling wild game carcasses.

Wild game meat should be cooked “well done” —i.e., to at least 65°C (150°F).

2. Persons should be instructed to drink only treated water when in the wilderness to avoid bacterial and protozoan diseases that can be transmitted via surface water.

3. DEET-based insect repellents can be used to reduce the possibility of bites by deer flies or ticks. Overuse of this repellent on children should be avoided, as excess application can lead to seizures.

5.2 Isolation and School or Day Care Restrictions

Cases with draining lesions should be cared for in accordance with standard precautions. No restrictions are indicated for outpatient management.

5.3 Follow up of Exposed Persons

Fever watch for 14 days after the exposure or post-exposure prophylaxis is recommended for laboratory personnel with unprotected exposure to \( F. \) tularensis and for persons who have been exposed to \( F. \) tularensis aerosols; for example, in the setting of an intentional release.

1. During a fever watch, exposed people should monitor their temperature and observe for signs and symptoms consistent with tularemia (e.g., chills, headache or body aches) for 14 days after their last exposure. (See the Health Assessment Form for Tularemia Exposure below as a medical monitoring tool.) Instruct exposed persons to seek medical attention immediately should they develop a fever (a single oral temperature above 101°F or 38.3°C) during this time.

2. Post-exposure prophylaxis model standing orders can be found at [https://public.health.oregon.gov/PreventionWellness/VaccinesImmunization/ImmunizationProviderResources/Pages/stdgordr.aspx](https://public.health.oregon.gov/PreventionWellness/VaccinesImmunization/ImmunizationProviderResources/Pages/stdgordr.aspx).

Also, see §6 for managing exposures to laboratory workers and bioterrorism events.

5.4 Protection of Contacts

Not necessary.

5.5 Environmental Measures

Generally, none necessary. In some cases, improvements to drinking water supplies may be warranted.

6. MANAGING SPECIAL SITUATIONS

6.1 Laboratory Worker Exposure

Immediately contact all laboratories that processed the specimen, as they may not be aware of the final isolate identification. Ask the laboratory manager to determine which laboratory personnel had contact with the specimen. If a laboratory worker has been exposed to \( Francisella \) tularensis, occupational health personnel should be notified immediately. With the consultation of OPHD, follow up with the laboratory and exposed workers to discuss post-exposure management options; depending on the type and extent of the exposure, these include a fever watch and post-exposure prophylaxis. See §5.3 for instructions for how to conduct a fever watch. There are no established criteria for determining whether a given worker should
be managed by a fever watch or with prophylaxis, but factors to consider include: (1) the extent of the exposure (workers who sniff the cultured plate are at greater risk than those who worked with the organism on the bench); (2) the incubation period, which may have passed by the time the specimen is identified as Francisella, making the question moot; and (3) the level of concern of the laboratory worker. OPHD epidemiologists should be consulted to help in this determination.

6.2 Bioterrorism Event

_F. tularensis_ has been classified as a "category A" agent (of greatest concern) for bioterrorism because of its very low infectious dose, its ability to survive in the environment, the fact that it can be easily disseminated by aerosol, and that untreated inhalational tularemia has the capacity to cause severe illness and death. One should suspect intentional spread of tularemia if there is a cluster of unusual pneumonia in persons who share a common exposure (e.g., a building with a common ventilation system). If a cluster of presumptive or confirmed pulmonary tularemia is recognized, people who have experienced the same exposure should be identified, given post-exposure prophylaxis, and instructed about how to do a fever watch as outlined in §5.3.

Call OPHD immediately, day or night if you suspect an intentional exposure.

**UPDATE LOG**

2002 Original version (K. Hedberg)
September 2010. Updated language, added reference to CDC form, and added medical monitoring form and guidance for exposed laboratory workers. (B. Progulske)
September 2013. Updated language, reference to case report form, and standing orders. Revised Sections 5C, 6A, and 6B to clarify response actions. (T. Watts)
November 2014. Edited and clarified “Local Health Department Responsibilities” (Section 1.3). Added information about relative frequency of various clinical presentations in Section 2.2. Updated “Laboratory Services” section (3.4). Minor edits for clarity throughout. Attached health assessment form. (Watts, Le-man)