

# Tularemia

## Surveillance and Investigation Protocol

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**Office of Epidemiology and Prevention Services**

**Division of Communicable Disease Epidemiology**

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### I. ABOUT THE DISEASE

Tularemia is a zoonotic disease caused by the bacteria *Francisella tularensis*, which spreads through multiple means of transmission to humans. The disease was first described in the United States in 1911 and was initially nationally notifiable up until 1994. Tularemia was made nationally notifiable again in 2000 due to concerns that the etiological agent could be used as a bioterrorist agent<sup>1</sup>. There are several forms the disease may take, each associated with a different route of transmission. There have been six cases of tularemia in West Virginia since 2014.

#### A. Clinical Presentation

The clinical presentation of tularemia can vary depending on the route of transmission, though all presentations are accompanied by fever. Symptoms may include headache, fatigue, anorexia, myalgia, vomiting, abdominal pain, or diarrhea. There are also more specific forms of presentation:

**Ulceroglandular:** a single skin ulcer at site of inoculation, accompanied by lymphadenopathy near the ulcer, typically associated with the bite of a tick or deer fly

**Glandular:** regional lymphadenopathy without an ulcer

**Oculoglandular:** conjunctivitis and photophobia with lymphadenopathy in front of the ears, under the jaw, and in the neck

**Oropharyngeal:** stomatitis, pharyngitis, or tonsillitis and cervical lymphadenopathy caused by ingestion or inhalation of contaminated materials

**Meningitic:** a rare manifestation of inflammation of the meninges and other neurological involvement

**Pneumonic:** primary pulmonary disease such as pneumonia or pleuritis with cough, chest pain, and difficulty breathing caused by contaminated and aerosolized materials inhalation

**Typhoidal:** febrile illness without localizing signs or symptoms

**Diagnosis:** For confirmatory diagnosis, there must be either isolation of *F. tularensis* in a clinical or autopsy specimen, **or** a fourfold or greater change in serum antibody titer to *F. tularensis* antigen between acute and convalescent specimens. A supportive diagnosis may be made if there is elevated serum antibody titer to *F. tularensis* antigen in a patient with no history of tularemia vaccination, **or** detection of *F. tularensis* in a clinical or autopsy specimen by either fluorescent assay or polymerase chain reaction (PCR).

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### **B. Etiologic Agent**

The etiologic agent of tularemia is the gram-negative obligate intracellular bacteria *Francisella tularensis*.

### **C. Reservoir**

The bacteria that cause tularemia exist in multiple different reservoirs. In mammals, the disease has been found in several rodents such as voles, mice, rats, muskrats, prairie dogs, and hamsters, as well as lagomorphs like rabbits<sup>2</sup>. Domestic cats are also susceptible and may transmit tularemia to humans<sup>3</sup>.

### **D. Incubation Period**

The incubation period is on average 3-5 days, with a range of 1-14 days, after inoculation by arthropod or animal bite, or inhalation or ingestion of infected materials.

### **E. Mode of Transmission**

Tularemia has many routes of transmission. Humans may be exposed to tularemia through the bite of an infected tick or deer fly, or through the handling or ingestion of infectious animal tissues or fluids. Transmission may also occur through the bite of an infected animal; inhalation of infected aerosols caused by the aerosolization of animal carcasses or feces; inhalation of aerosols of contaminated dust, soil, or hay; or by drinking contaminated water. Laboratory workers may become infected through the handling of tularemia specimens or cultures.

### **F. Period of Communicability**

Person-to-person transmission of tularemia has not been documented. There has been documentation of tularemia through solid organ donation<sup>4</sup>.

## **II. DISEASE CONTROL AND PREVENTION**

### **A. Disease Control Objectives**

1. Reduce severe complications of disease by educating healthcare providers about the occurrence of tularemia and the importance of obtaining a thorough history of clinical symptoms, patient travel and exposure history, and proper laboratory testing.

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### **B. Disease Prevention Objectives**

1. Reduce disease risk through public education regarding use of personal protective measures.
2. In the event of deliberate infection, respond promptly to identify exposed individuals, and offer prophylactic treatment and tularemia education where appropriate to curb serious illness through early detection and intervention.

### **C. Disease Prevention and Control Intervention**

A person bitten by a tick or deer fly should be alert for symptoms suggestive of tularemia and consult a physician if fever, ulcer, or other symptoms of concern develop. Tularemia vaccine is no longer available in the United States.

Avoiding tick or deer fly bites is the mainstay of tularemia prevention. The following are important personal protective measures that should be followed, especially for people that live, work, or spend leisure time in an area likely to have ticks or deer flies:

- Stick to main pathways and the centers of trails when hiking.
- Wear long-sleeved, light-colored shirts, and long pants tucked into socks when weather permits.
- Talk to a veterinarian about the best ways to protect pets and livestock from ticks.
- Use repellents containing DEET (N, N-diethyl-meta-toluamide) and choose a product that will provide sufficient protection for time spent outdoors. DEET products should not be used on children <2 months of age. The following precautions should be observed when using DEET products:
  - Avoid using DEET products that combine repellent with sunscreen. Sunscreens may need to be applied too often, resulting in an over application of DEET.
  - Apply DEET on exposed skin, using only as much as needed.
  - Do not use DEET on the hands of young children and avoid applying repellent to areas around the eyes and mouth.
  - DO not use DEET over cuts, wounds, or irritated skin.
  - Wash treated skin with soap and water after returning indoors, and wash treated clothing
  - Avoid spraying DEET products in enclosed areas.
- Permethrin-containing products will kill deer flies and ticks on contact. Permethrin products are not designed to be applied to the skin. Clothing should be treated and allowed to dry in a well-ventilated area prior to wearing.

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- Check yourself, children, and pets for ticks upon returning from outdoors. Make sure to check the following areas: between the toes, back of the knees, groin, armpits, neck, along the hairline and behind the ears.
- Promptly remove attached ticks using fine-point tweezers. Grasp the tick close to the skin and pull straight up using steady pressure. Do not squeeze or twist the tick.

### ***Environmental Exposures:***

Prevention of tularemia can also involve actions to keep ticks out of yards.

- Keep the grass cut short.
- Remove leaf litter and brush from around the yard.
- Prune low lying bushes to let in more sunlight.
- Keep woodpiles and bird feeders off the ground and away from the home.
- Keep the plants around stone walls cut short.
- Use a three-foot wide woodchip, mulch, or gravel barrier where the lawn meets the woods and remind children not to cross that barrier.
- Ask a landscaper or local nursery about plants to use in the yard that do not attract deer.
- Use deer fencing (for yards 15 acres or more).

If applying a pesticide outdoors, a licensed applicator experienced with tick control should be hired. In general, good tick control can be achieved with no more than two pesticide applications in a year.

Pneumonic tularemia is associated with breathing aerosolized infectious particles, usually during yardwork or farming. When operating landscaping equipment, such as lawnmowers or weed eaters, check the area first for animal carcasses and avoid macerating dead or sick animals.

### ***Other Prevention Measures:***

Oropharyngeal tularemia is associated with the ingestion of contaminated game meat and water. Thoroughly cook game meat and avoid drinking untreated surface water.

Tularemia may also spread through the bite of an infected animal. Wear gloves when handling wild animals, especially rodents or lagomorphs like rabbits and hares. Always wash hands after handling a dead or sick animal.

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### D. Treatment

#### ***For adults:***

Doxycycline 100 mg intravenous (IV) or per os (PO) twice daily for 14-21 days is recommended for tularemia. For severe tularemia infection, gentamicin 5 mg/kg intramuscular (IM) or IV daily for 10-14 days is recommended by the Centers for Disease Control and Prevention (CDC), though this is not a Food and Drug Administration (FDA) approved use for the antibiotic. For patients unable to take either doxycycline or gentamicin, the CDC recommendation is ciprofloxacin 400 mg IV/500 mg PO for 10-14 days, though it is also not FDA-approved for tularemia.

#### ***For children:***

Doxycycline 2.2mg/kg IV or PO twice daily, with a limit of 100 mg IV or PO per day, for 14-21 days is recommended for tularemia in pediatric patients. For severe tularemia infection, gentamicin 2.5 mg/kg IM or IV three times a day for 10-14 days is recommended by the CDC, though this is not an FDA-approved use for the antibiotic. For pediatric patients using gentamicin, serum drug levels should be monitored, and consultation made to a pediatric infectious disease doctor. For patients unable to take either doxycycline or gentamicin, children may use ciprofloxacin 15 mg/kg IV or PO twice daily, with a limit of 800 mg a day, for 10-14 days.

For meningitic tularemia, combination therapy should be considered under consultation of an infectious disease doctor.

## III. DISEASE INVESTIGATION

### A. Criteria for Case Ascertainment

Report any infection to public health authorities that meets any of the following criteria:

#### **Clinical Criteria for Reporting**

N/A

#### **Laboratory/Imaging Criteria for Reporting**

- Isolation of *F. tularensis* from a clinical specimen
- A positive IgM and/or IgG antibody specimen in sera
- Positive *F. tularensis* identification via direct immunofluorescence assay (DFA), immunohistochemical staining, sequence-based technologies, or PCR

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### Epidemiologic Linkage Criteria for Reporting

N/A

### Vital Records Criteria for Reporting

- A person whose death certificate lists tularemia as an underlying cause of death or a significant condition contributing to death.

### Other Criteria for Reporting

- A person whose healthcare record contains a diagnosis of tularemia.

## **B. Case Definition and Case Classification**

### Clinical Criteria

Illness which may occur in one of the following forms:

- **Ulceroglandular:** a single skin ulcer at site of inoculation, accompanied by lymphadenopathy near the ulcer
- **Glandular:** regional lymphadenopathy without an ulcer
- **Oculoglandular:** conjunctivitis and photophobia with lymphadenopathy in front of the ears, under the jaw, and in the neck
- **Oropharyngeal:** stomatitis, pharyngitis, or tonsillitis and cervical lymphadenopathy
- **Pneumonic:** primary pulmonary disease such as pneumonia or pleuritis with cough, chest pain, and difficulty breathing
- **Typhoidal:** febrile illness without localizing signs or symptoms

### Laboratory/Imaging Criteria

*Confirmatory laboratory evidence:*

- Isolation of *F. tularensis* from a clinical or autopsy specimen **OR**
- Fourfold or greater change in serum antibody titer to *F. tularensis* from acute to convalescent specimens

*Supportive laboratory evidence:*

- Elevated serum antibody titer (without fourfold or greater increase) to *F. tularensis* without prior history of vaccination **OR**
- Detection of *F. tularensis* in a clinical or autopsy specimen by fluorescent assay **OR**
- Detection of *F. tularensis* in a clinical or autopsy specimen by PCR

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### Epidemiologic Linkage

- Clinical diagnosis is supported by patient history or evidence of a tick or deer fly bite, exposure to the mammalian tissues of a host reservoir known to carry *F. tularensis*, including via animal bite, or exposure to potentially contaminated water.

### Vital Records Criteria

N/A

### Other Classification Criteria

N/A

### Case Classifications

*Confirmed:* Any clinically compatible case with a confirmatory lab result.

*Probable:* Any clinically compatible case with a supportive lab result.

*Criteria for a new case:*

- A person previously reported as a probable or confirmed case patient may be counted as a new case when there is an episode of new clinically compatible illness with confirmatory laboratory evidence if an epidemiological exposure is identified. Positive laboratory results and a new epidemiological exposure within the last 12 months alone without clinically compatible illness may not indicate new infection, especially in areas where tularemia is endemic.

### **C. Reporting Timeframe to Public Health**

All probable or confirmed cases of tularemia should be reported to the Local Health Department **immediately** upon diagnosis.

### **D. Outbreak Recognition**

An outbreak of tularemia under natural conditions is highly unlikely, due to the self-contained nature of the disease and lack of person-to-person transmission.

**However**, given the prior history of tularemia as a proposed biological warfare agent, deliberate infection would most likely be used in an aerosolized fashion, producing unexplained pneumonia and severe systemic, febrile illness among a localized population regardless of age or sex in previously healthy individuals, with a high

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proportion of cases displaying pleuropneumonitis. In such instances, healthcare providers must work closely with the Office of Laboratory Services, Office of Epidemiology and Prevention Services, and the Center for Threat Preparedness to determine if such cases are from naturally occurring infection or deliberate bioterrorism.

### E. Healthcare Provider Responsibilities

1. Report suspect and confirmed cases of tularemia (including copies of lab results) to the Local Health Department **immediately**. Supply requested clinical information to the Local Health Department to assist with case ascertainment.
2. Follow recommended testing and treatment guidelines for tularemia.
3. Notify the laboratory staff testing the patient's specimens of the suspicion for tularemia **immediately** to ensure proper biosafety protocols are followed. If laboratory staff were exposed to specimens containing *F. tularensis* prior to a diagnosis being made, educate on signs and symptoms of tularemia for early intervention or possible prophylactic treatment.
4. **In the event bioterrorism or deliberate infection is suspected**, contact law enforcement, the Local Health Department, and the Office of Epidemiology and Prevention Services' Epi-On-Call at (304) 558-5358 ext. 2 **immediately**. Follow law enforcement directive on maintaining chain of custody for evidence, as bioterrorism constitutes a criminal offense.

### F. Laboratory Responsibilities

1. Communicate with the Office of Laboratory Services and the worksite safety coordinator within the lab if *F. tularensis* testing is requested to ensure proper safety precautions are practiced.
  - a. If any laboratory staff were exposed to specimens containing *F. tularensis*, educate them on the signs and symptoms of tularemia, and coordinate with occupational health professionals to obtain prophylactic treatment if requested.
  - b. If *F. tularensis* is identified or cannot be ruled out, contact the Office of Laboratory Services to arrange transport of isolate for confirmation.
2. Report positive laboratory results for tularemia to the Local Health Department **immediately**.

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### G. Local Health Responsibilities

1. Conduct an appropriate case investigation.
  - a. Contact the healthcare provider who ordered the laboratory test to obtain clinical information for the West Virginia Electronic Disease Surveillance System (WVEDSS) tularemia page, such as organ donation and primary clinical syndrome (typhoid, ulceroglandular, etc.).
  - b. Interview the patient to obtain information regarding arthropod or animal exposure, occupational history, and travel history.
  - c. Educate the patient and the patient's family on tularemia prevention.
  - d. Report all other case data using WVEDSS.
2. Institute appropriate control measures in select cases:
  - a. If case is a **landscaper, farmer, or other agricultural worker**:
    - i. Interview immediate supervisor for any other members of their organization who may be experiencing illness.
    - ii. Provide educational information to employees on the signs and symptoms of tularemia, and to seek immediate medical attention if any employees develop symptoms.
    - iii. Identify locations of possible exposure, such as private residences where landscaping was performed, in the previous 14 days prior to the index patient's illness onset date. Interview residents for unexplained febrile illness and suggest testing if found to be ill.
  - b. If case is associated with **an animal from a pet store or newly purchased pet**:
    - i. Determine infection status of the animal through veterinary testing if the animal is still available.
    - ii. If the animal has died, is unavailable, or tested positive for *F. tularensis*, determine the source of the animal to conduct further environmental investigation and testing. Ask if there have been unexpected, sudden illness or deaths among animal stock in the facility.
    - iii. Educate staff at the facility about the signs and symptoms of tularemia, and to seek immediate medical attention if any develop. Suggest rat traps to control possible rodent vectors.
    - iv. Obtain a list of customers who bought animals starting 28 days prior to the index patient's illness onset date and since investigations began. Locate and interview customers for possible unexplained febrile illness and suggest testing if found to be ill.

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3. Educate the public about tularemia, especially regarding the mode of tick or deer fly transmission and use of personal protection. Prevention messages for these diseases are also effective for other tickborne diseases (e.g. Lyme disease).
4. Educate healthcare providers and laboratories to report cases of tularemia to the Local Health Department in the patient's county of residence **immediately**.
5. **In the event of deliberate infection**, cooperate with law enforcement, the Center for Threat Preparedness, and the West Virginia Department of Health to disseminate education, manage possible exposures, and assist in further investigation.
  - a. Ensure sanitarians and other environmental health professionals are aware of the signs and symptoms of tularemia, and to seek immediate medical attention if displaying signs or symptoms during environmental investigation.

### H. State Health Responsibilities

1. Review completed case reports from Local Health Departments within one week.
2. Report all confirmed and probable cases to CDC upon confirmation of case status. Complete the supplemental case report form entitled, "Tularemia Case Report" and submit it to CDC for all confirmed and probable cases.
3. Provide training and consultation to Local Health Departments regarding case ascertainment for tularemia.
4. Collaborate with the West Virginia Division of Natural Resources to identify possible die-offs of reservoir populations such as rabbits, muskrats, groundhogs, and other wild rodents which may carry *F. tularensis* and therefore pose a transmission risk.
5. Notify and collaborate with the Center for Threat Preparedness and law enforcement if suspicion of deliberate infection arises for further investigation and additional precautions.
6. **In the case of deliberate infection**, identify persons exposed to the bioterrorist agent and collaborate with the Department of Homeland Security, the Center for Threat Preparedness, and the Office of Laboratory Services to conduct active surveillance and disperse prophylaxis and/or education to the affected population to seek medical attention should signs or symptoms arise.
7. Follow the National Incident Management system framework for timely response.
8. Inform the State Health Commissioner upon report of suspected bioterrorist activity for situational awareness purposes.

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### **I. Occupational Health**

1. In the event of laboratory exposure, infection preventionists within hospitals and other healthcare systems should identify lab workers who have been exposed to tularemia specimens, identify routes of exposure (e.g., aerosolizing activities), and collaborate with the Office of Epidemiology and Prevention Services to determine the need for further testing and prophylaxis.
2. For organizations with an occupational health program but are not a healthcare facility, collaborate with the Local Health Department to arrange education on tularemia as well as coordinate testing for exposed employees.

### **IV. DISEASE SURVEILLANCE**

#### **A. Public Health Significance**

Tularemia is a serious disease with multiple means of environmental and zoonotic transmission to humans. While rare, incidence of tularemia in West Virginia has increased slightly since 2014, with 50% of cases occurring between 2021-2023. Given the nature of tularemia as a possible warfare agent, it is imperative to examine the epidemiology of tularemia cases as soon as possible.

Surveillance for tularemia can help to inform healthcare providers of the seasonality, incidence, and geographic distribution of these diseases. This information can be useful in facilitating appropriate diagnoses. Surveillance data can also help identify less common routes of transmission such as inhalation.

#### **B. Disease Surveillance Objectives**

1. To identify and monitor the epidemiologic characteristics of tularemia in West Virginia, including the geographic distribution of cases.

#### **C. Surveillance Indicators**

1. Proportion of cases with complete demographic information.
2. Proportion of cases with complete clinical information (i.e., presence of fever and other clinical signs meeting clinical criteria of case definition).
3. Proportion of cases with risk factor information (e.g., history of potential tick or deer fly exposure through recreational or occupational activities).

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