Tularemia

Organism: *Francisella tularensis* is the causative agent for tularemia. The signs and symptoms of tularemia vary depending on how the bacteria enter the body. Illness ranges from mild to life-threatening. All forms are accompanied by fever, which can be as high as 104 °F.

Incubation period: ~3 to 5 days, but can vary from 1-14 depending on route of transmission.

Infectious period: Direct transmission from another person has not been reported.

Transmission route: May vary and will inform the clinical picture. See below for a description of the distinct forms.

a. Wound/skin-break usually causes a localized lesion with regional lymphadenopathy; this is the most commonly reported type in Alaska.
b. Concern for aerosols in a bioterrorist attack. Note that "naturally-occurring" aerosol exposures have also been described among landscapers in situations such as a lawnmower macerating an infected animal carcass.

Treatment:

- Streptomycin is the drug of choice based on experience, efficacy and FDA approval. Gentamicin is considered an acceptable alternative, but some series have reported a lower primary success rate. Treatment with aminoglycosides should be continued for 10 days.
- Tetracyclines may be a suitable alternative to aminoglycosides for patients who are less severely ill. Tetracyclines are static agents and should be given for at least 14 days to avoid relapse.
- Ciprofloxacin and other fluoroquinolones are not FDA-approved for treatment of tularemia but have shown good efficacy in vitro, in animals, and in humans.

Information Needed for the Investigation

Verify the Diagnosis

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 (this is really rare)
- Pneumonic: primary pleuropulmonary disease
- Typhoidal: febrile illness without early localizing signs and symptoms

Epidemiologic criteria:

Most of the Alaska cases have involved some contact with animals, whether skinning a trapped muskrat, snowshoe hare; or contact with a dog that had recently killed a hare. There have also been cases among veterinarians and other persons who were bitten by a clinically affected cat. Most cases have been exposed in Interior Alaska; although other locations have been reported. Cases of tularemia are not unexpected in these circumstances; if however, there was a cluster of cases that did not seem consistent with the historical epi/findings and could be related to an intentional release, we will need to consult with CDC and local law enforcement.

Laboratory criteria:

Supportive

- 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 or autopsy specimen by fluorescent assay, **OR**
- Detection of *F. tularensis* in a clinical or autopsy specimen by a polymerase chain reaction (PCR)

Confirmatory

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

Determine the Extent of Illness

- Determine if cluster exists depending on suspected exposure source. Consider the potential for an intentional inhalational release based on the number of cases reported, the location, and the lack of reported animal exposure.
- If a specific animal exposure was reported, interview others who may have been in contact with the animal. For example, if an animal carcass was shared with others, or an animal subsequently died and was taken to a veterinary clinic, etc., interview/notify those persons of the potential exposure. There is no routine antimicrobial prophylaxis, but consult with CDC SME for unusual situations.

Laboratory Specimens

****Notify Lab prior to submission; specimens require Select Agent biosafety precautions.****

- ASPHL can work with: isolate, swab of affected area, aspirates (e.g., lymph node), tissue biopsy, bronchial/tracheal wash, pleural fluid, sputum, blood, serum, autopsy specimens; animal samples from necropsy (e.g., abscess, sections of lymph nodes, liver, spleen, bone marrow); vector samples e.g., (e.g., mosquitoes, ticks, flies); environmental samples (e.g., water, soil, air, grass, food, other); and evidentiary materials (e.g., dried desiccated organics - hair, wood liquids; nonorganics - powders, paper, containers).
- ASPHL will perform LRN testing on all specimens, and titer quantification on sera. PCR positive results would be presumptive not confirmatory.
- Laboratory personnel should be alerted when tularemia is suspected. Diagnostic procedures with clinical materials can be performed in biosafety level 3 conditions. All

work with suspect cultures of *F. tularensis* must be done in a biological safety cabinet. Manipulation of cultures and other procedures that might produce aerosols or droplets (e.g., catalase assay, Gram stain smear, transfers for subculture, etc.) should be conducted under a biosafety cabinet with biosafety level 3 precautions.

- NOTE that testing at commercial labs may not be a quantitative assay (as for a true titer). Interpret results in light of the clinical picture and consider recommending additional confirmatory testing, i.e., culture or demonstration of 4-fold increase in titer.
- In limited circumstances, ASPHL will test animal specimens. Consult with ASPHL on a case-by case basis.

Contact and Control Measures

- Ensure that if isolate/culture was processed at a hospital lab, there is appropriate follow-up to ensure that correct PPE was used. More information on post-exposure monitoring and possible antibiotic prophylaxis for laboratory personnel/settings is available at: http://www.cdc.gov/tularemia/laboratoryexposure/ and http://www.cdc.gov/tularemia/resources/lab/TularemiaLabExposureFactSheet.pdf.
- Bodies of patients who die of tularemia should be handled using standard precautions. Autopsy procedures likely to produce aerosols or droplets should be avoided.
- Consider working with Alaska Department of Fish and Game (ADFG) and Department of Environmental Conservation's Office of the State Veterinarian (OSV) to put out a press release to alert the public and veterinarians about increased activity among wildlife and potential infection of domestic pets. ADFG contact is Dr. Kimberlee Beckmen: dfg.dwc.vet@alaska.gov or 907-328-8354. OSV phone contacts are: Bob Gerlach 375-8214; Sarah Coburn 375-8213 (main 907-375-8200).
- CDC SMEs for tularemia are located in Fort Collins:

  Bacterial Diseases Branch, CDC
  3150 Rampart Road
  Ft Collins, Colorado
  970-221-6400 (fax 970-494-6631)
- Consider the potential of a bioterrorist attack; involve appropriate personnel accordingly. CDC'S EOC phone # is 770-488-7100.

Hospital Considerations

- Isolation is not recommended for tularemia patients, given the lack of person-to-person transmission. In hospitals, standard precautions are recommended.
- Clothing or linens contaminated with body fluids of patients with tularemia should be disinfected per standard hospital procedure.
- Direct transmission from another person has not been reported.

Reporting Requirements

- FTR: write up cluster investigations
- AK STARS: enter all *confirmed* and *probable* cases.

- CDC Case Definition is used to define *confirmed* and *probable* cases; see above.
- Fax a tularemia case report form to CDC: http://www.cdc.gov/tularemia/resources/TularemiaCaseReportForm.pdf
- Because *F. tularensis* is a Select Agent, when notifying partners of a suspected/confirmed case, be sure to notify Preparedness regardless of whether the case appears to be a potential bioterror threat.
- If *F. tularensis* is confirmed in any specimens, ASPHL is required to ask laboratories in the specimen referral pathway to complete Forms 3 and 4 as part of the Select Agent requirements. ASPHL takes care of this; forms are available here FYI: http://www.selectagents.gov/Forms.html

Alaska Wildlife Disease Resource
ADFG Division of Wildlife Conservation information on tularemia in animals:
http://www.adfg.alaska.gov/index.cfm?adfg=disease.internal3

Hospital Resources:

- Centers for Disease Control and Prevention (CDC) tularemia website: http://www.cdc.gov/Tularemia/
- Siegel JD, Rhinehart E, Jackson M, Chiarello L, and the Healthcare Infection Control Practices Advisory Committee. 2007 Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings. Available at http://www.cdc.gov/hicpac/pdf/isolation/isolation2007.pdf

Other References:

- CDC. Tularemia FAQs; available at: http://www.cdc.gov/tularemia/faq/index.html
- Section of Epidemiology *Bulletin*. Two Cases of Tularemia – Interior Alaska, June 2009. http://www.epi.alaska.gov/bulletins/docs/b2009_20.pdf

Tularemia (*Francisella tularensis*)
2017 Case Definition

Clinical Criteria

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
- Pneumonic: primary pulmonary disease
- Typhoidal: febrile illness without localizing signs and symptoms

Laboratory Criteria for Diagnosis

Supportive

- 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 or autopsy specimen by fluorescent assay, **OR**
- Detection of *F. tularensis* in a clinical or autopsy specimen by a polymerase chain reaction (PCR)

Confirmatory

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

Epidemiologic Linkage

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

Criteria to Distinguish a New Case from an Existing Case

Serial or subsequent cases of tularemia experienced by one individual should only be counted if there is an additional epidemiologically compatible exposure and new onset of symptoms. Because the duration of antibodies to *F. tularensis* is not known, mere presence of antibodies without a clinically-compatible illness **AND** an epidemiologically compatible exposure within 12 months of onset may not indicate a new infection, especially among persons who live in endemic areas.

Case Classification

Probable

A clinically-compatible case with supportive laboratory evidence.

Confirmed

A clinically-compatible case with confirmatory laboratory evidence.

https://wwwn.cdc.gov/nndss/conditions/tularemia/case-definition/2017/

Alaska Division of Public Health
Prevention Promotion Protection

Tularemia Fact Sheet

What is tularemia?
Tularemia, also known as "rabbit fever," is a disease caused by the bacterium *Francisella tularensis*. Cases of tularemia occur in animals, especially snowshoe hares, muskrats, and beavers that live in the interior region of Alaska. More information about tularemia in wildlife can be found at the Wildlife Diseases webpage of the Alaska Department of Fish and Game (ADFG): http://www.adfg.alaska.gov/index.cfm?adfg=disease.internal3

How do people become infected with the agent that causes tularemia?
People can become infected with *F. tularensis* through the bite of infected insects, by handling infected sick or dead animals, by eating or drinking contaminated food or water, or by inhaling airborne bacteria. In Alaska, most people have become ill after handling an infected animal -- usually skinning or cleaning a hare or muskrat. In a few instances, people have become ill after being bitten by a domestic cat that was sick with tularemia.

How often does Alaska record a case of tularemia in a human?
In Alaska, tularemia is an uncommon but expected disease, with an average of one human case reported about every 2 years. More information about human cases of tularemia in Alaska is available at http://epibulletins.dhss.alaska.gov/Bulletin/DisplayClassificationBulletins/130. Cats and/or dogs are more frequently affected than humans. There are usually several cases in domestic pets reported each year in the Interior.

What are the signs and symptoms of tularemia?
The signs and symptoms people develop depend on how they were exposed to tularemia. Possible symptoms include skin ulcers, swollen and painful lymph glands, inflamed eyes, sore throat, mouth sores, diarrhea or pneumonia. If the bacteria are inhaled, symptoms can include abrupt onset of fever, chills, headache, muscle aches, joint pain, dry cough, and progressive weakness. People with pneumonia can develop chest pain, difficulty breathing, bloody sputum, and respiratory failure. Tularemia can be fatal if the person is not treated with appropriate antibiotics.

How can I protect myself from getting tularemia?
Wear gloves when gutting out hares, muskrats or beavers. Always wash your hands well after handling any wildlife. Try to avoid letting your cats or dogs play with wildlife, especially sick or dead animals. Report dead hares to the Fairbanks ADFG Division of Wildlife Conservation Wildlife Disease Surveillance hotline at 907-328-8354 or via email at dfg.dwc.vet@alaska.gov.

3601 C Street, Suite 540
Anchorage, AK 99503
(p) 907-269-8000; (f) 907-562-7802