Tularemia

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To determine whether the source of infection may be a major public health concern (e.g., a water supply, group camp, rodent die-off, bioterrorist act) and stop transmission from such a source.
2. To identify the source of infection and determine the risk of transmission from that source to others.
3. To identify other cases.

B. Laboratory And Physician Reporting Requirements

Laboratories and physicians are required to report cases within one day of diagnosis or identification.

C. Local Health Department Reporting and Follow-Up Responsibilities

1. Report all confirmed and presumptive (but *not* suspect) cases to OHS (see definitions below) *immediately*. Use the standard case report form.
2. Begin follow-up investigation *immediately*. Use the Tularemia case investigation form. Send a copy of the completed form to OHS within seven days of initial report.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Francisella tularensis, an aerobic, non-motile, Gram-negative rod.

Francisella. tularensis comes in two basic flavors, or biovars: type A, which is highly virulent in humans and animals and is the most common type in North America; and type B, which is less virulent and thought to cause most of the human cases in Europe and Asia. As few as 10–50 organisms of type A can cause disease.

F. tularensis is quite hardy, surviving weeks to months in cool water or mud, in tap water for up to 3 months, and in dry straw litter as much as 6 months. Frozen (e.g., in rabbit meat), it may remain infective for several years. Concentrations of chlorine attained in routine water purification are very effective at killing *F. tularensis*, as are trace amounts of copper sulfate or zinc.

B. Description of Illness

To a great extent, the nature of the illness reflects the route of transmission (see below, §D), as well as the virulence of the infecting strain. Almost all cases have a rapid onset of fever and lymphadenopathy. Bacteremia, should it develop, may last for two weeks if untreated, and mouth and throat lesions may contain the organism for up to a month. Illness usually falls into one of the following categories:

1. Ulceroglandular (75–85% of naturally occurring cases)

Patients present with large, tender nodes and a papule that develops into a non-healing skin ulcer, often accompanied by headache, fatigue, chills, and malaise.

2. Pneumonic (pulmonary)

Occurs as a primary infection following inhalation of organisms, or secondary to ulceroglandu-

lar bacteremia. The pneumonic form is the most probable presentation of illness in a bioterrorist attack. Resembles plague, with symptoms including non-productive cough, dypsnea, and pleuritic chest pain. Patchy bilateral infiltrates are seen on chest X-ray. Untreated, pneumonic tularemia has a 30–60% mortality rate.

3. Typhoidal

A rare form of tularemia, with development of mesenteric lymph adenopathy, abdominal pain (often protracted), diarrhea, vomiting, and GI bleeding.

4. Oculoglandular

Painful, purulent conjunctivitis (usually unilateral) with cervical or preauricular lymphadenopathy with more or less systemic involvement: fever, chills, and malaise.

5. Glandular

Similar to ulceroglandular form but without skin lesions.

6. Oropharyngeal

Usually accompanied by very painful sore throat, and occasionally abdominal pain, nausea and vomiting.

C. Reservoirs

Type A infections are acquired from cottontail rabbits or *Dermacentor* ticks; type B infections are associated with a wide variety of mammalian hosts; rabbits, hares, and some rodents (e.g. beavers, muskrats) are particularly important. The life cycle is in part maintained by tick, mosquito, and fly vectors. Humans are usually dead-end hosts (i.e., they do not transmit the infection to others).

D. Sources and Routes of Transmission

Probably no bacterial agent has more diversified modes of transmission than *F. tularensis*; infection can occur by direct contact, by arthropod bite, by ingestion, or by inhalation. As noted above, the infection progresses from the portal of entry, thereby determining the form of illness. Common scenarios include:

1. Direct Contact

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

Less commonly, 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

Tabanid flies (deer and horse flies) that are blood sucking, mechanically transmit the organism between rodents, rabbits, and man. This form of transmission occurs in Eastern Oregon, accounting for perhaps 1 to 3 cases a year—typically ulceroglandular disease.

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. Tick-borne transmission of tularemia to humans is rare.

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 orophyaryngeal or typhoidal disease. Eating 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 are inhaled, the infection may be fulminant and rapidly fatal. Airborne transmission

is the most likely form of transmission in a bioterrorist attack. Infectious aerosols can be generated while handling animal hides, cleaning areas (barns, feed bunks, etc.) contaminated with dried rodent carcasses, moving or loading contaminated grain or winnowing grain (a common practice in third world and poorly mechanized agriculture), or, in at least one instance, by running a lawn mower over a bunny rabbit.

This organism is extremely dangerous to handle in the medical laboratory; culture of material from patients with suspected tularemia should not be attempted without special containment facilities. Contact the OSPHL for additional information.

E. Incubation Period

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

F. Period of Communicability

Not directly transmitted from person to person.

G. Treatment

Streptomycin for 10–14 days is the drug of choice for adults and children. Gentamicin for 10–14 days is an acceptable alternative for adults and children. Ciprofloxacin and other fluoroquinolones have also been used. Tetracycline and chloramphenicol are useful substitutes for the above two drugs; however, relapses are common after using them.

3. CASE DEFINITIONS, DIAGNOSIS, AND LABORATORY SERVICES

A. Confirmed Case Definition

1. Serologic Test Confirmation

Patients with at least a 4-fold rise in antibody titer between acute and convalescent sera. Antibodies usually appear in week 2 of the disease.

2. Culture Confirmed

Patients from whom *F. tularensis* is cultured. (This usually requires cysteine supplementation of the media for good growth.) This organism is extremely dangerous to handle in the medical laboratory; culture of material from patients *with suspected tularemia should not be attempted without special containment facilities.* Note that standard blood cultures are usually negative and that Gram stains of material from skin lesions, sputum, or lymph node aspirates are rarely informative.

B. Presumptive Case Definition

For surveillance purposes, a presumptive case is a patient with “typical” tularemia signs/symptoms, a history of exposure to a known or suspected source of infection, and an antibody titer $\geqslant$160 in a serum specimen collected after onset.

C. Suspect Case

Anyone with an undiagnosed compatible illness. While not "officially" reportable, we want to hear about cases of unexplained illness of possible public health significance.

D. Center for Public Health Laboratories Services

1. For antibody testing, 1–2 ml of both acute and convalescent (collected at least 2 weeks after onset) serum are needed. A single convalescent specimen can be tested, but results may be inconclusive.
2. The OSPHL provides identification of *F. tularensis* from pure isolates as well as culturing of clinical specimens. Contact the OSPHL prior to collection and shipment of specimens. When specimens are shipped, they must be properly packaged in triple packaging with absorbent material around the primary container; use the Bacteriology/Parasitology form (#75) and instructions for shipping and handling of diagnostic specimens. Isolates must be packaged following instructions for shipping and handling an infectious substance.

4. CASE INVESTIGATION

Interview the case and others who may be able to provide pertinent information. (For evaluation of a possible bioterrorist event, see §6.)

A. Identify Source of Infection

Investigate possible exposures during the period 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 tabanid fly activity in the area and / 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;
8. work in a medical laboratory.

B. Identify Other Potentially Exposed Persons.

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 are ill, inform them (or their physician) of possible exposure, in order to facilitate proper diagnosis and therapy.

C. Environmental Evaluation

1. If the source of infection appears to be associated with rabbit or rodent hunting, this fact should be publicized, in order 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 in farm animals, contact the Oregon Department of Agriculture.
3. If waterborne transmission is suspected, a determination should be made if it is nominally a potable water source. Consult with your local environmental health experts or the Oregon Health Services Drinking Water Section.

5. CONTROLLING FURTHER SPREAD

A. Education

1. Hunters should be instructed to wear gloves when skinning wild game and to keep their hands / gloves away from their eyes. They should thoroughly wash their hands after handling wild game carcasses. Wild game meat should be cooked "well done" (to at least 65°C / 150°F)
2. Persons should be instructed to drink only treated water when in wilderness areas to avoid all of the bacterial and protozoan disease that can be transmitted via surface water.
3. DEET-based insect repellents can be used to reduce the possibility of tabanid fly or tick bite. Overuse of this repellent on children should be avoided, however; excess application can lead to convulsive seizures.

B. Isolation and Work or Day Care Restrictions

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

C. Follow Up of Case — None.

D. Protection of Contacts— Not necessary.

E. Environmental Measures

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

6. MANAGING SPECIAL SITUATIONS

A. Bioterrorist Event

F. tularensis has been classified as a "category A" agent (of greatest concern) for bioterrorism 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 that untreated inhalational tularemia has the capacity to cause severe illness and death. One should suspect bioterrorist spread of tularemia if there is a cluster of unusual pneumonia (atypical patient profile, e.g. young, otherwise healthy individuals, severe illness, widened mediastinum, low response to standard treatment) in persons in a building with a common ventilation system. Call the Bioterrorism Preparedness Program of the Communicable Disease Section *immediately, day or night*.