7 | *FRANCISELLA TULARENSIS*

7.1 | Disease agent

- *Francisella tularensis*

7.2 | Disease agent characteristics

- Gram-negative coccobacillus, aerobic, nonmotile, nonspore-forming bacterium.
- Order: Thiotrichales; Family: *Francisellaceae*.
- Size: 0.2–0.7 μm × 0.2 μm.
- Nucleic acid: 1892 kb of DNA.
- While the organism grows in appropriate cell-free bacteriologic media, it is widely regarded to be an intracellular pathogen.
- The organism survives long-term freezing (i.e., up to 3 years in frozen rabbit meat).
- 10% bleach can be used for surface decontamination.

7.3 | Disease name

- Tularemia
- Rabbit fever

7.4 | Priority level

- Scientific/Epidemiologic evidence regarding blood safety: Theoretical
- Public perception and/or regulatory concern regarding blood safety: Absent
- Public concern regarding disease agent: Very low, but low in regions where outbreaks have occurred

7.5 | Background

- The disease is named after Tulare County, California where the disease was discovered in 1911.
- Occurs naturally in several areas of the US, usually in rural areas. Historically, most cases of tularemia occurred in the summer (arthropod bites) and winter (hunters coming into contact with infected rabbit carcasses).
- First described in the United States in 1911 and has been reported from all states except Hawaii
- Removed from the list of nationally notifiable diseases in 1994, but it was reinstated in 2000 because of increased concern about potential use of *F. tularensis* as a biologic weapon
- Classified among the highest priority for bioterrorism agents by the CDC (Category A)
  - *Francisella tularensis* is a viable biological weapons agent because it is easy to aerosolize, highly infectious, easy to decontaminate, highly incapacitating and has a low fatality rate when treated

7.6 | Common human exposure routes

- Inhalation: bacterium aerosolized when animals skinned or shredded by mowers
- Tick or fly bites by infected vectors
- Skin contact with infected animals
- Drinking contaminated water (5%–10% of all tularemia reported in the United States)

7.7 | Likelihood of secondary transmission

- Highly unlikely; transmission of tularemia from person to person has not been reported.

7.8 | At-risk populations

- Taxidermists, landscape workers, hunters
- A threat as a bioterrorist weapon for susceptible populations

7.9 | Vector and reservoir involved

- Blood-feeding arthropods and flies are the most important vectors for. Ticks are most important in the United States.
- At least 13 species of ticks have been found to be naturally infected with *F. tularensis*, and transovarial passage may occur with some but not all vectors. Biting flies, specifically the deer fly (*Chrysops* spp.)
- Mosquitoes are the most frequent vectors in Scandinavia.
  - In Europe, a large number of cases have been reported from Finland and Sweden; e.g., in Sweden from 1984 to 2012, a total of 4830 cases were reported.
- Infected mammals (rodents, rabbits and hares) are the reservoir.

7.10 | Blood phase

- Bacteremia can persist for weeks in symptomatic infections; asymptomatic bacteremia has not been demonstrated.
- Agent found in monocytes.

7.11 | Survival/persistence in blood products

- Unknown

7.12 | Transmission by blood transfusion

- Theoretical

7.13 | Cases/frequency in population

- Approximately 200–300 cases reported in the United States each year.
- In recent years, a seasonal increase in incidence has occurred (late spring and summer), when arthropod bites are most common.
- Outbreaks of tularemia in the United States have been associated with muskrat handling, tick bites, deerfly bites, and lawn mowing or cutting brush.
- Sporadic cases in the United States have been associated with contaminated drinking water and various laboratory exposures.

7.14 | Incubation period

- Usually 3–5 days, but can take weeks

7.15 | Likelihood of clinical disease

- Disease likelihood will vary based on exposure rate and immune status of host. There are six characteristic clinical variants: the most common representing 75% of all forms is ulceroglandular (others include glandular, oropharyngeal, pneumonic, oculoglandular, and typhoidal).
- Subclinical infections are common.
- Immunocompromised persons are more likely to have complications.

7.16 | Primary disease symptoms

- Skin ulcers, swollen and painful lymph nodes, sudden fever (moderate or very high), chills, headaches, diarrhea, muscle aches, joint pain, dry cough, and progressive weakness; inflammation spreads to the lymph nodes which enlarge and may be suppurate and accompanied by high fever.
- Pneumonia-like symptoms also are possible, particularly when the agent is inhaled.

7.17 | Severity of clinical disease

- More severe infections can be and are fatal, particularly if left untreated.

7.18 | Mortality

- Varies by exposure route and subspecies but untreated inhalation tularemia may have a mortality rate of from 30% to 60%, but less than 4% if appropriately treated with antibiotics.

7.19 | Chronic carriage

- Unknown in humans

7.20 | Treatment available/efficacious

- Once diagnosed, infection is treatable with antibiotics (tetracyclines and fluoroquinolones). Antibiotic treatment is efficacious.
- There are no approved vaccines; live attenuated vaccines are being research and most promising for approval. Killed-whole cell vaccines are also under investigation.

7.21 | Agent-specific screening question(s)

- No specific question is in use.
- Not indicated because of the low incidence of infection and lack of evidence of transfusion transmission.
- No sensitive or specific question is feasible.
- Under circumstances of a bioterrorism threat, the need for and potential effectiveness of specific donor-screening questions would need to be addressed.

7.22 | Laboratory test(s) available

- No FDA-licensed blood donor screening test exists.
- Culture, microagglutination based on fourfold rise in titers, enzyme immunoassay, and polymerase chain reaction available.

7.23 | Currently recommended donor deferral period

- No FDA Guidance or AABB Standard exists.
- Prudent practice would be to defer donor until signs and symptoms are gone and any course of treatment is complete.

7.24 | Impact on blood availability

- Agent-specific screening question(s): Not applicable; in response to a bioterrorism threat, impact of a local deferral would be significant.
- Laboratory test(s) available: Not applicable.

7.25 | Impact on blood safety

- Agent-specific screening question(s): Not applicable; unknown impact in response to a bioterrorism threat
- Laboratory test(s) available: Not applicable

7.26 | Leukoreduction efficacy

- Unknown

7.27 | Pathogen reduction efficacy for plasma derivatives

- Specific data indicate that the multiple steps in the fractionation process are robust and capable of inactivating and/or removing bacteria at concentrations that may be present in plasma.

7.28 | Other prevention measures

- Vector avoidance
- Limiting direct exposure (particularly when handling infectious animals)

7.29 | Other comments

- Outbreaks of pneumonic tularemia, particularly in low-incidence areas, should prompt consideration of bioterrorism.

SUGGESTED READING

1. Auwaerter PG, Penn RL. *Francisella tularensis* (Tularemia). Mandell, Douglas and Bennett's principles and practice of infectious diseases. 9th ed. 2019. ch. 227. p. 2759–73.
2. CDC. Managing potential laboratory exposures to *Francisella tularensis*. Accessed 4 May 2021. https://www.cdc.gov/tularemia/laboratoryexposure/index.html
3. CDC. Tularemia—United States, 1990-2000. Morb Mortal Wkly Rep MMWR. 2002;51:182–4.
4. CDC. Tularemia—United States, 1990-2000. MMWR Morb Mortal Wkly Rep. 62(47):963–6.
5. Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a biological weapon: medical and public health management. JAMA. 2001;285:2763–73.
6. Eisen RJ, Mead PS, Meyer AM, Pfaff LE, Bradley KK, Eisen L. Ecoepidemiology of tularemia in the southcentral United States. Am J Trop Med Hyg. 2008;78(4):586–94.
7. Eliasson H, Broman T, Forsman M, Bäck E. Tularemia: current epidemiology and disease management. Infect Dis Clin North Am. 2006;20:289–311.
8. Farlow J, Wagner DM, Dukerish M, Stanley M, Chu M, Kubota K, et al. *Francisella tularensis* in the United States. Emgerg Infect Dis. 2005;11:1835–41.
9. Feldman KA, Enscore R, Lathrop S, et al. An outbreak of primary pneumonic tularemia on Martha's Vineyard. N Engl J Med. 2001;345:1601–6.
10. Harrist A, Cherry C, Kwit NA, et al. *Francisella tularensis* exposure among National Park Service employees during an epizootic: Devils Tower National Monument, Wyoming, 2015 external icon. Vector Borne Zoonotic Dis. 2019;19(5):316–22.
11. Kugeler KJ, Mead PS, Janusz AM, et al. Molecular epidemiology of *Francisella tularensis* in the United States. Clin Infect Dis. 2009;48(7):863–70.
12. Schmid GP, Kornball AN, Connors CA, et al. Clinically mild tularemia associated with tick-borne *Francisella tularensis*. J Infect Dis. 1983;148:63–7.
13. Staples JE, Kubota KA, Chalcraft LG, Mead PS, Petersen JM. Epidemiologic and molecular analysis of human tularemia, United States, 1964-2004. Emerg Infect Dis. 2006;12(7):1113–8.
14. Tarnvik A. WHO Guidelines on Tularaemia.pdf icon [PDF – 125 pages] external icon. Vol. WHO/CDS/EPR/2007.7. Geneva: World Health Organization 2007.
15. Weber IB, Turabelidze G, Patrick S, Griffith KS, Kugeler KJ, Mead PS. Clinical recognition and management of tularemia in Missouri: a retrospective records review of 121 cases. Clin Infect Dis. 2012;55(10):1283–90.