TULAREMIA A SERIOUS INFECTIOUS DISEASE: A REVIEW

Vinayak Gaware*¹, Kiran Kotade², Ramdas Dolas³, Kiran Dhamak¹, Sachin Somwanshi³, Vikrant Nikam³, Atul Khadse¹, Vivekanand Kashid³

- 1.Department of Pharmaceutical Chemistry, College of Pharmacy Chincholi, Sinnar, Nashik, M.S, 422101.
- 2. Department of Pharmacology, College of Pharmacy Chincholi, Sinnar, Nashik, M.S, 422101.
- 3. Department of Pharmaceutics, College of Pharmacy Chincholi, Sinnar, Nashik, M.S, 422101.

Summary

Tularemia also known as Pahvant Valley plague, Rabbit Fever, Deer Fly Fever, Ohara's fever is a serious infectious disease caused by the bacterium *Francisella tularensis* (Type A) & (Type B) and is highly virulent for humans and domestic rabbits. The vectors who are responsible for the transmission of the disease is ticks and deer flies. Tularemia may also be spread by direct contact with contaminated animals or material, by ingestion of poorly cooked flesh of infected animals or contaminated water, or by inhalation. In the present review we have mostly focused on the causes, symptoms, diagnosis, treatment, preventions, complication and various research which are been made to overcome from this infectious disease.

Keywords: Deer flies, Francisella Tularensis, Ohara's fever, Tularemia.

Address for correspondence: Vinayak Madhukar Gaware Department of Pharmaceutical Chemistry, College of Pharmacy, Chincholi, A/P: Chincholi, Tal: Sinnar, Dist: Nashik, 422101, (M.S), India E-mail: vins_gaware1@rediffmail.com Mobile No: 09423572791.

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Introduction

Tularemia (also known as **Pahvant Valley Plague**, **Rabbit Fever**, **Deer Fly Fever**, **Ohara's Fever** is a serious infectious disease caused by the bacterium *Francisella tularensis*. A Gram-negative, nonmotile coccobacillus, the bacterium has several subspecies with varying degrees of virulence. The most important of those is *F. tularensis tularensis* (Type A), which is found in lagomorphs in North America and is highly virulent for humans and domestic rabbits. *F. tularensis palaearctica* (Type B) occurs mainly in aquatic rodents (beavers, muskrats) in North America and in hares and small rodents in northern Eurasia. It is less virulent for humans and rabbits. The primary vectors are ticks and deer flies, but the disease can also be spread through other arthropods. The disease is named after Tulare County, California¹.

History

The bacterium was first isolated by GW McCoy of the US Public Health Service plague lab and reported in 1912. Scientists determined that tularemia could be dangerous to humans; a human being may catch the infection after contacting an infected animal. The ailment soon became frequent with hunters, cooks and agricultural workers².

Epidemiology^{3, 4, 5}

The disease is endemic in North America and parts of Europe and Asia. The most common mode of transmission is via arthropod vectors. Rodents, rabbits and hares often serve as reservoir hosts, but waterborne infection accounts for 5 to 10% of all tularemia in the US. Tularemia can also be transmitted by biting flies, particularly the deer fly *Chrysops discalis*. Individual flies can remain infective for 14 days and ticks for over 2 years. Tularemia may also be spread by direct contact with contaminated animals or material, by ingestion of poorly cooked flesh of infected animals or contaminated water, or by inhalation. The most likely method for bioterrorist transmission is through an aerosol. In the United States, although records show that tularemia was never particularly common, incidence rates continued to drop over the course of the 20th century so that between 1990 and 2000, the rate was less than 1 per 1,000,000, meaning the disease is extremely rare in the US today.

Causes ^{6,7}

Tularemia is caused by the bacterium called *Francisella tularensis*. This bacterium is found naturally in small mammals such as rabbits, rodents and hares, as well as the bugs that feed on these animals. The bacterium can survive for weeks at low temperatures in water, moist soil, hay, straw, or decaying animal carcasses. *F. tularensis* has two subspecies.

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- Type A is common in North America and may be highly virulent (potent) in humans and animals.
- Type B probably causes all human tularemia in Europe and Asia.

Transmission^{8,9,10}

The most common ways you can get tularemia are by

- Being bitten by flies, ticks, or other bugs carrying the disease
- Handling infected animal tissue or fluids
- Eating or drinking food or water contaminated by the bacteria
- Breathing in the bacteria

You can also get tularemia by

- Having direct contact with or ingesting bacteria-contaminated water, food, or soil
- Handling contaminated animal skins
- Inhaling infective aerosols from materials containing the bacteria

In Europe, there have been cases where the disease was caused by inhaling airborne bacteria generated during farm work, such as transporting infected hay. A small number (about 10 to 50 bacteria) can cause disease. Laboratory workers also can become infected by inhaling bacteria while examining an open culture plate.

Symptoms ^{11, 12}

Tularemia infection varies from a mild illness to acute sepsis (serious infection of the blood or other tissues) and rapid death. After exposure to the bacteria, you will usually develop symptoms within 3 to 5 days, but they can take up to 21 days to appear. Symptoms include:

- Sudden fever
- Chills
- Headaches
- Diarrhea
- Muscle aches
- Joint stiffness or pain
- Dry cough
- Weakness

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In most people, progressive weakness leads to a dry cough and pneumonia. Tularemia-induced pneumonia can cause chest pain, bloody sputum (saliva or mucus) and trouble breathing. Depending on how you were exposed to the bacteria, other symptoms may include

- A red spot on the skin that enlarges to an ulcer
- Ulcers in the mouth

Diagnosis^{13, 14}

- Blood culture for tularemia
- Blood test measuring the body's immune response to the infection (serology for tularemia)
- Chest x-ray
- Polymerase chain reaction (PCR) test of a sample from an ulcer

This disease may also affect the results of febrile/cold agglutinins.

Prevention^{15, 16}

Several precautions can protect individuals from tularemia:

- Avoid drinking, bathing, swimming or working in untreated water where infection may be common among wild animals.
- Use impervious gloves when skinning or handling animals, especially rabbits.
- Cook the meat of wild rabbits and rodents thoroughly.
- Avoid being bitten by deer flies and ticks. The following suggestions may help:
- Check your clothing often for ticks climbing toward open skin. Wear white or light-colored longsleeved shirts and long pants so the tiny ticks are easier to see. Tuck long pants into your socks and boots. Wear a head covering or hat for added protection.
- For those who may not tolerate wearing all of these clothes in hot, muggy weather apply insect repellent containing DEET (30 percent or less) to exposed skin (except the face). Be sure to wash treated skin after coming indoors. If you do cover up, use repellents containing permethrin to treat clothes (especially pants, socks and shoes) while in locations where ticks may be common. Follow label directions; do not misuse or overuse repellents. Always supervise children in the use of repellents.
- Walk in the center of trails so weeds do not brush against you.

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- Check yourself, children and other family members every two to three hours for ticks. Most ticks seldom attach quickly and rarely transmit tick borne disease until they have been attached for four or more hours.
- If you let your pets outdoors, check them often for ticks. Infected ticks also can transmit some tick borne diseases to them. (Check with your veterinarian about preventive measures against tick borne diseases.) You are at risk from ticks that "hitch a ride" on your pets but fall off in your home before they feed.
- Make sure the property around your home is unattractive to ticks. Keep your grass mowed and keep weeds cut.

Treatment ^{17, 18}

The goal of treatment is to cure the infection with antibiotics. Streptomycin and tetracycline are commonly used to treat this infection. Once daily gentamycin treatment has been tried with excellent results as an alternative therapy to streptomycin. However, only a few cases have been studied to date. Tetracycline and Chloramphenicol can be used alone, but they are not considered a first-line treatment. Oral tetracycline is usually not prescribed for children until after all their permanent teeth have come in. It can permanently discolor teeth that are still forming.

Possible Complications ^{18, 19}

- Bone infection (osteomyelitis)
- Infection of the sac around the heart (pericarditis)
- Meningitis
- Pneumonia

Research²⁰

The National Institute of Allergy and Infectious Diseases (NIAID) supports research on the diagnosis, prevention and treatment of infections caused by microbes, including those that have the potential for use as biological weapons. The research program to address biodefense includes both short- and long-term studies targeted at designing, developing, evaluating and approving specific tools (diagnostics, therapies and vaccines) needed to defend against possible bioterrorist-caused disease outbreaks.

NIAID research goals to diagnose, prevent and treat tularemia include

- Supporting basic research to identify mechanisms of *F. tularensis* virulence and pathogenesis and to define host responses to pathogen
- Developing quick and inexpensive ways to diagnose tularemia

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- Developing antimicrobials and immunotherapies with novel mechanisms of action to treat tularemia
- Identifying new $F_{\underline{\cdot}}$ tularensis vaccine candidates that can prevent or modulate infection both before and after exposure
- Conducting clinical trials of vaccine candidates

Conclusion

Tularemia is a serious infectious disease caused by the bacterium *Francisella tularensis*. The history and physical examination are essential to making the diagnosis. The signs and symptoms usually include sudden fever, chills, headaches, diarrhea, muscle aches, joint stiffness or pain, dry cough and weakness. Tularemia is a serious disease but there are various preventive measures which can keep the indivual far away from this infectious disease.

References

- 1. Rapini, Ronald P.; Bolognia, Jean L.; Jorizzo, Joseph L. Dermatology, 2007,2: 123-126.
- James, William D.; Berger, Timothy G.; et al. Andrews' Diseases of the Skin: clinical Dermatology. Saunders Elsevier, 2006, 14: 114-120.
- 3. Ryan KJ, Ray CG, Sherris Medical Microbiology, McGraw Hill. 2004: 4:488–90.
- Pearson A . Zoonoses: biology, clinical practice and public health control (Soulsby EJ, Palmer SL eds.). Oxford [Oxfordshire]: Oxford University Press. 1998, 276–9.
- 5. A. Tärnvik1 and L. Berglund, Tularaemia. Eur Respir J 2003; 21:361-373.
- 6. McCoy GW, Chapin CW. Bacterium tularense, the cause of a plaguelike disease of rodents. Public Health Bull 1912;53:17–23.
- 7. http://english.pravda.ru/main/18/90/363/14923_tularemia.html
- 8. Mörner T. "The ecology of tularaemia". Rev. Sci. Tech. 1992,11 (4): 1123–30.
- Jellison WL, Owen C, Bell JF, Kohls GM. "Tularemia and animal populations". Wildl Dis 1961, 17: 1–22.
- 10. Hayes E, Marshall S, Dennis D, et al. "Tularemia--United States, 1990-2000". MMWR, 2002, 51: 181–4.
- 11. Plourde PJ, Embree J, Friesen F, Lindsay G, Williams T. "Glandular tularemia with typhoidal features in a Manitoba child". CMAJ, 1992, 146 (11): 1953–5.

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- Office international des épizooties. Manual of standards for diagnostic tests and vaccines: lists A and B diseases of mammals, birds and bees. Paris, France: Office international des épizooties, 2000, 494–6, 1394.
- 13. Enderlin G, Morales L, Jacobs RF, Cross JT "Streptomycin and alternative agents for the treatment of tularemia: review of the literature". Clin. Infect. Dis. 1994, 19 (1): 42–7.
- 14. "Tularemia: FAQ About Tularemia". CDC. 2003-10-08.
- 15. Dennis DT, Inglesby TV, Henderson DA, et al.. "Tularemia as a biological weapon: medical and public health management". , 285 (21): 2763–73.
- Sjöstedt A, "Tularemia: history, epidemiology, pathogen physiology and clinical manifestations". Ann. N. Y. Acad. Sci. 2007, 1105: 1–29..
- 17. Kanti Ghosh, Tushar, Prelas, Mark, Viswanath, Dabir: Science and Technology of Terrorism and Counterterrorism. CRC Press, 2002, 97.
- "Fact Sheet Red Cloud", Office of the Assistant Secretary of Defense (Health Affairs), Deployment Health Support Directorate.
- Feldman KA, Enscore RE, Lathrop SL, et al. . "An outbreak of primary pneumonic tularemia on Martha's Vineyard". N. Engl. J. Med, 2001, 345 (22): 1601–6.
- 20. "Medscape & eMedicine Log In". http://www.medscape.com/viewarticle/431539.