Agent

Francesella tularensis is a small gram-negative coccobacillus that is carried in numerous animal species, especially rabbits, and is the causal agent of tularemia (Rabbit fever, Deer fly fever, Ohara disease, or Francis disease) in humans. F. tularensis can be divided into three subspecies, F. tularensis (Type A), F. holarctica (Type B) and F. novicida, based on virulence testing, 16S sequence, biochemical reactions and epidemiologic features. Type A and Type B strains are highly infectious, requiring only 10-50 organisms to cause disease. Francesella tularensis is a Select Agent.

1. Disease/Infection
Francesella tularensis is causal agent of tularemia, a zoonotic disease (Rabbit fever, Deer fly fever, Ohara disease, or Francis disease.)

2. Pathogenicity
Human tularemia presents as a local papule at site of inoculation 3-5 days after exposure, followed by an indolent ulcer at site of infection (2-4 days later), accompanied by swelling of the regional lymph nodes (ulceroglandular) followed by sudden onset of pain and fever. Fever generally lasts 3 - 6 weeks without treatment. Infection can present in the glandular form only when the initial ulcer has already healed. In setting of contact with eye or ingestion, disease can present with oculeoglandular or pharyngeal manifestations. Inhalation of the agent may be followed by a pneumonic disease or primary systemic (typhoidal) picture. The Type B strains has a 5-15% fatality rate; Type A strains has approximately 35% mortality rate resulting from pulmonary tularemia.

3. Biosafety Information
   a. Risk Group/BSL
      Risk Group 3
      Biosafety Level 3 practices
   b. Modes of Transmission

<table>
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<th>Transmission</th>
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<tr>
<td>Skin Exposure (Needlestick, animal bite, or scratch):</td>
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<tr>
<td>Mucous Membrane Exposure Splash to Eye(s), Nose or Mouth:</td>
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<tr>
<td>Inhalation:</td>
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<td>Consumption of undercooked or raw meat products or dairy products from infected animals</td>
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   c. Host Range/Reservoir
      Over a hundred species of wild animals, especially rabbits, hares, muskrats, beavers and some domestic animals; various hard ticks; deerfly (Chrysops discalis), mosquito, and birds; rodent - mosquito cycle in Scandinavia and Russia
   d. Symptoms
      Febrile illness – temperature of more than 100.4 F in individuals who have worked with Francisella tularensis within the past 3 weeks. Illness ranges from mild to life-threatening. All forms are accompanied by fever. Main forms of this disease are listed below:
      • Ulceroglandular – This is the most common form of tularemia an. A skin ulcer appears at the site where the organism entered the body. The ulcer is accompanied by swelling of regional lymph glands, usually in the armpit or groin.
Francisella tularensis

- **Glandular** – Similar to ulceroglandular tularemia but without an ulcer. Also generally acquired through unprotected (without proper PPE) when handling animals.
- **Oculoglandular** – This form occurs when the bacteria enter through the eye. This can occur when a person touches his or her eyes through an unprotected exposure to the bacteria or an infected animal. Symptoms include irritation and inflammation of eye conjunctivitis and swelling of lymph glands in front of the ear.
- **Oropharyngeal** – This form results from splash of secretions of animal or bacteria. Workers with oropharyngeal tularemia may have sore throat, mouth ulcers, tonsillitis, and swelling of lymph glands in the neck.
- **Pneumonic** – This is the most serious form of tularemia. Symptoms include cough, chest pain, and difficulty breathing. This form results from breathing aerosols containing the organism. It can also occur when other forms of tularemia (e.g. ulceroglandular) are left untreated and the bacteria spread through the blood stream to the lungs.

**e. Incubation Period**
The incubation period varies with the virulence of the strain, dose and route of introduction but ranges from 1-14 days with most cases exhibiting symptoms in 3-5 days.

**f. Viability**
The agent is susceptible to 10% sodium hypochlorite, 70% ethanol.

**g. Survival Outside Host**
- Carcasses and organs - up to 133 days; grain dust; bedbugs - 136 days; rabbit meat - 31 days; straw - 192 days; water - up to 90 days, infected rabbit meat stored frozen at -15° C has remained infective longer than 3 years

**Information for Lab Workers**

1. **Laboratory PPE**
   - BSL3 personal protective equipment includes hooded-PAPR, disposable full suits, disposable gloves, booties.

2. **Containment**
   - BSL-3 and ABSL3 practices, containment equipment, and facilities are recommended for all manipulations of suspect cultures, animal necropsies and for experimental animal studies. Preparatory work on cultures or contaminated materials for automated identification systems should be performed at BSL-3. Characterized strains of reduced virulence such as *F. tularensis* Type B (strain LVS) and *F. tularensis* subsp novicida (strain U112) can be manipulated in BSL-2. Manipulation of reduced virulence strains at high concentrations should be conducted using BSL-3 practices.
   - BSL-2 practices, containment equipment, and facilities are recommended for activities involving clinical materials of human or animal origin suspected or known to contain *F. tularensis*. Laboratory personnel should be informed of the possibility of tularemia as a differential diagnosis when samples are submitted for diagnostic tests.

3. **In Case of Exposure/Disease**
   1. For injuries in the lab which are major medical emergencies (heart attacks, seizures, etc…):
      a. **Medical Campus:** call or have a coworker call the Control Center at 4-4144.
      b. **Charles River Campus:** call or have a coworker call campus security at 617-353-2121.
         You will be referred to or transported to the appropriate health care location by the emergency response team.
   2. For lab exposures (needle sticks, bite, cut, scratch, splash, etc…) involving animals or infectious agents, or for unexplained symptoms or illness call the ROHP 24/7 hour number (1-617-414-ROHP (7647); or, 4-ROHP (7647) if calling from an on-campus location) to be connected with the BU Research Occupational Health Program (ROHP) medical officer. ROHP will refer you to the appropriate health care location.
   3. Under any of these scenarios, always inform the physician of your work in the laboratory and the agent(s) that you work with.
   4. Provide the wallet-size agent ID card to the physician.
4. Vaccination
Currently, no vaccine is available, only intradermal live attenuated experimental vaccine from USAMRID.

Information for First Responders/Medical Personnel

1. Public Health Issues
Person to person transmission of tularemia has not been documented. Hospitalized patients with tularemia do not need special isolation. Hence, standard precautions can be used in managing a case of potential exposure to the agent. However, clinical laboratory staff should be made aware of the suspicion of tularemia when samples are submitted for diagnosis so that appropriate biosafety practices may be employed.

2. Diagnosis/Surveillance
Presumptive: Elevated serum antibody titer(s) to F. tularensis antigen in a worker with no history of tularemia vaccination, or, detection of F. tularensis in a clinical specimen by fluorescent antibody or PCR DNA test
Confirmatory: Isolation of F. tularensis in a clinical specimen or Fourfold or greater change in serum antibody titer to F. tularensis antigen
Growth of F. tularensis in culture is the definitive means of confirming the diagnosis of tularemia. Appropriate specimens include swabs or scraping of skin lesions, lymph node aspirates or biopsies, pharyngeal washings, sputum specimens, or gastric aspirates, depending on the form of illness. Paradoxically, blood cultures are often negative.

3. First Aid/Post Exposure Prophylaxis
Doxycycline or ciprofloxacin given orally for 14 days is recommended for adults with suspected or proven high-risk exposure to F. tularensis. Individuals with low risk exposures or exposures in vaccinated employees can be observed for clinical signs without antibiotics.

Perform one of the following actions:

<table>
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<tr>
<th>Skin Exposure (Needlestick or scratch):</th>
<th>Immediately go to the sink and thoroughly wash the wound with soap and water for 15 minutes. Decontaminate any exposed skin surfaces with an antiseptic scrub solution.</th>
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<td>Mucous Membrane Splash to Eye(s), Nose or Mouth:</td>
<td>Exposure should be irrigated vigorously.</td>
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<td>Splash Affecting Garments:</td>
<td>Remove garments that may have become soiled or contaminated and place them in a double red plastic bag.</td>
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4. Treatment
Susceptible to aminoglycosides, streptomycin, gentamycin, tobramycin and kanamycin (bactericidal) and tetracyclines, chloramphenicol (bacteriostatic); streptomycin is the drug of choice for severe disease; gentamycin is an acceptable alternate. Doxycycline can be used for low grade disease.

5. References
Center for Disease Control - http://www.cdc.gov/tularemia/laboratoryexposure/
Biosafety in Microbiological and Biomedical Laboratories; Deborah E. Wilson, DrPH, CBSP Director Division of Occupational Health and Safety National Institutes of Health Bethesda, Maryland L. Casey Chosewood, M.D. Director Office of Health and Safety Centers for Disease Control and Prevention Atlanta, Georgia; US Government Printing Office, Washington DC. 5th Edition; 2007