

HEALTH CARE PROVIDER FACT SHEET

TULAREMIA

Information for Health Care Providers

Physicians • Nurses • Laboratory Personnel • Infection Control Practitioners

Tularemia

Caused by *Francisella tularensis*, a small, pleomorphic, gram-negative coccobacillus found naturally in the northern hemisphere and throughout the United States. Transmission to humans usually occurs through a tick bite or direct contact with infected animals.

- Naturally occurring tularemia in humans most commonly involves the skin and lymph nodes, (ulceroglandular or glandular tularemia); pneumonic tularemia and other forms of tularemia are not as common
- **Pneumonic tularemia, caused by inhaling aerosolized bacteria, would be the most likely outcome of an intentional (bioterrorist) aerosol release of *F. tularensis***
- Person-to-person transmission does NOT occur with pneumonic or other forms of tularemia

**Any confirmed or suspected case of tularemia
(*Francisella tularensis*) must be reported IMMEDIATELY
to the Clark County Health District at 383-1378
Alert your laboratory personnel.**

Pneumonic Tularemia

Incubation: commonly 3-5 days (range 1-21 days)

Clinical Illness:

- Fever, non- to minimally productive cough, sub-sternal tightness, pleuritic chest pain, occasional hemoptysis (though uncommon), as well as chills, headache, malaise, anorexia, and fatigue
- May be primary pneumonia or secondary due to bacteremic spread from other tularemia syndromes
 - Chest X-ray may show infiltrates without symptoms
 - Other CXR findings include: subsegmental/lobar infiltrates, hilar adenopathy, pleural effusion, or miliary infiltrates
 - Miliary infiltrates may mimic tuberculosis.
 - Caseating granulomas can be seen on lung biopsy which may also lead to confusion with TB
- Can manifest as a community acquired pneumonia.

Laboratory Clues to *F. tularensis*:

- Pleural fluid usually exudative with more than 1000 leukocytes/mm³
- Granulomas may develop (and occasionally caseate) and thus may be confused with tuberculosis

Laboratory Confirmation of Diagnosis

- A *Francisella tularensis* antibody test is available from American Medical Laboratories. This IgG agglutinin test is run Monday - Friday.
- Culture takes several days to become positive and **MUST** be done at the Nevada State Public Health Laboratory, which is a bio-safety level 2 laboratory. **IF TULAREMIA IS SUSPECTED – INFORM LABORATORY IMMEDIATELY SO PROPER LABORATORY SAFETY PRECAUTIONS MAY BE TAKEN.**
- **Transport and packaging of culture specimens must be coordinated with the Clark County Health District and NSPHL**

Treatment of Pneumonic Tularemia

- If untreated, fatality rate may be as high as 35%.
 - Recommendations¹ for the treatment of patients with tularemia in the contained and mass casualty settings and for postexposure prophylaxis²
- (** indicated medications which will be supplied as a part of the Strategic National Stockpile (SNS) maintained at the CDC)

Patient Category	Recommended Therapy
Adults	Preferred choices **Gentamicin, 5mg/kg IM or IV once daily or 2 mg/kg loading dose followed by 1.7 mg/kg IM or IV 3 times daily ³ Streptomycin, 1 g IM twice daily
	Alternative choices **Doxycycline, 100 mg IV twice daily **Ciprofloxacin, 400 mg IV twice daily ⁴ Chloramphenicol, 15 mg/kg IV 4 times daily ⁵
Children ⁶	Preferred choices **Gentamicin, 2.5 mg/kg IM or IV 3 times daily ³ Streptomycin, 15 mg/kg IM twice daily (maximum daily dose, 2 g)
	Alternative choices **Doxycycline, If ≥ 45 kg, give adult dosage If < 45 kg, give 2.2 mg/kg IV twice daily **Ciprofloxacin, 15 mg/kg IV twice daily ⁴ Chloramphenicol, 15 mg/kg IV 4 times daily ⁵
Pregnant women ⁷	Preferred choice **Gentamicin, 5mg/kg IM or IV once daily or 2 mg/kg loading dose followed by 1.7 mg/kg IM or IV 3 times daily ³ Streptomycin, 1 g IM twice daily
	Alternative choices **Doxycycline, 100 mg IV twice daily **Ciprofloxacin, 400 mg IV twice daily ⁵

Post-Exposure Prophylaxis

- Antibiotic prophylaxis is not commonly used to prevent naturally-acquired tularemia. In the case of a suspected bioterrorist release prophylaxis may be indicated
 - Initiation of prophylaxis with oral medications, especially in children, should be coordinated with the Clark County Health District, Office of Epidemiology
 - Oral prophylaxis should continue for at least 14 days if the exposure is confirmed
Physicians may be asked to get an informed consent signed administration of certain medications supplied by the Strategic National Stockpile (SNS)
1. These are adapted from consensus recommendations of the Working Group on Civilian Biodefense and are not necessarily approved by

Patient Category	Recommendations
Adults	Preferred choices **Doxycycline, 100 mg orally twice daily ⁹ **Ciprofloxacin, 500 mg orally twice daily ⁵
Children ⁶	Preferred choices **Doxycycline ⁹ , If ≥ 45 kg, give adult dosage If < 45 kg, give 2.2 mg/kg orally twice daily **Ciprofloxacin, 15 mg/kg orally twice daily ⁵
Pregnant women ⁷	Preferred choices **Ciprofloxacin, 500 mg orally twice daily ⁵ **Doxycycline, 100 mg orally twice daily ⁹

the Food and Drug Administration. In non-bioterrorism response situations, routine treatment guidelines should be followed. Please refer to original publication (Dennis DT, Inglesby TV, Henderson DA, et al. Tularemia as a biological weapon: Medical and public health management, JAMA, in press) for explanations and further discussion.

2. One antimicrobial agent should be selected. Therapy with streptomycin, gentamicin or ciprofloxacin should be continued for 10 days; treatment with doxycycline or chloramphenicol should be continued for 14-21 days. Persons beginning treatment with parenteral doxycycline, ciprofloxacin, or chloramphenicol can be switched to PO when clinically indicated.
3. Aminoglycosides must be adjusted according to renal function. Neonates up to 1 week of age and premature infants should receive gentamicin, 2.5 mg/kg IV twice daily.
4. Other fluoroquinolones can be substituted at doses appropriate for age. Ciprofloxacin dosage should not exceed 1 g daily in children.
5. Concentration should be maintained between 5 and 20 μ g/mL. Concentrations greater than 25 μ g/mL can cause reversible bone marrow suppression. Children younger than 2 years should not receive chloramphenicol.
6. In children, ciprofloxacin dose should not exceed 1 g daily, chloramphenicol should not exceed 4 g daily. Children younger than 2 years should not receive chloramphenicol. In neonates, gentamicin loading dose of 4 mg/kg should be given initially.
7. Alternatives to breastfeeding may be required while mother is taking certain antibiotics, see specific antibiotic package insert for information on breastfeeding
8. One antibiotic, appropriate for patient's age, should be chosen from among alternatives. Duration of prophylaxis for tularemia in mass casualty situations is 14 days. Duration of treatment with doxycycline or chloramphenicol is 14-21 days.
9. Tetracycline may be substituted for doxycycline.

Systemic Tularemia

- Febrile illness caused by *F. tularensis* without typical clinical features of other forms of tularemia
- May be more common in persons with chronic illnesses and lead to rapid death or protracted illness
- Non-descript symptoms: fever with chills, headache, myalgias, sore throat, anorexia, nausea, vomiting, diarrhea, abdominal pain, cough
- Patients may develop sepsis with complication of bleeding and organ failure
- Treatment is the same as for pneumonic tularemia (see Pneumonic Tularemia Treatment Protocol)

Oropharyngeal, Ulceroglandular or Glandular Tularemia

- A possible, though unlikely outcome of a terrorist aerosol release of *F. tularensis*
- Pharyngeal form results from direct invasion of oral pharynx (contaminated food/water) causing sore throat with exudative tonsillitis/pharyngitis with one or more ulcers. Also, may involve cervical, preauricular and retropharyngeal lymph nodes with possible abscess formation.
- Ulceroglandular form usually recognized as tularemia
 - Enlarged, local tender lymph nodes
 - Skin lesion (can appear before, simultaneously or after lymphadenopathy) starts as red, painful papule that progresses to necrotic painful draining ulcer with raised borders.
 - Multiple lesions may occur.
 - Glandular form is as above without skin lesions.
- Systemic symptoms and pneumonic symptoms (see pneumonic tularemia for both) may be present.
- Oculoglandular tularemia is a rare form resulting from inoculation of bacterium in eye – complaint of photophobia and excessive lacrimation. Patients have swollen eyelids, painful infected conjunctiva with small, yellowish conjunctival ulcers.
- Inhalation or inoculation of the eye from an aerosolized release may result in pharyngeal or ocular tularemia
- Treatment is the same as for pneumonic tularemia

Infection Control

- Standard (Universal) Precautions for care and transport of patients and during post-mortem care
- Wound precautions for patients with cutaneous tularemia
- Isolation of patients is NOT necessary; however, the following extra precautions are advised:
 - After an invasive procedure, instruments and the area used should be autoclaved
 - Contaminated clothing/bedding should be placed in labeled, plastic bags for later incineration, steam sterilization, or laundry with hot water and bleach.
 - Spills of potentially infected body fluid or tissue:
 - Gently cover, then liberally apply 0.5% hypochlorite (a 1:10 dilution of household bleach)
 - Let sit for at least 20 minutes before cleaning up (work from perimeter to center)
 - Any materials used in the clean-up must be autoclaved or incinerated
- Contamination of personnel
 - Remove outer clothing carefully where spill occurred and place in a labeled, plastic bag
 - Remove rest of clothing in the locker room and place in a labeled, plastic bag
 - Shower thoroughly with soap and water
- If exposure to contaminated sharps occurs:
 - Follow standard reporting procedures for sharps exposures
 - Thoroughly irrigate site with soap and water and apply a disinfectant solution such as 0.5% hypochlorite solution. DO NOT SCRUB AREA.
- Decontamination of environment
 - Use a decontamination solution such as 0.5% hypochlorite (a 1:10 dilution of household bleach) for surfaces
 - Let sit for at least 20 minutes before cleaning up (work from perimeter to center)
 - Routinely clean non-sterilizable equipment with a sterilizing solution

References

1. Dennis, DT, Inglesby TV, Henderson DA, Barlett JG, et al. Tularemia as a biological weapon: Medical and public health management. *JAMA*, June 6, 2001;285(21):2763-2773.
2. Cross T, Penn R. *Francisella tularensis* (tularemia) from *Principles and Practices of Infectious Diseases* 5th edition, Gerald L. Mandell, John E. Bennett and Raphael Dolin editors. Churchill Livingstone 2000.
3. 1997 Red Book, Report of Committee on Infectious Diseases, 24th Edition, American Academy of Pediatrics
4. Mandell, Douglas, and Bennett's, *Principles and Practices of Infectious Diseases*, 5th Edition
5. *Control of Communicable Diseases Manual*, 16th Edition, 1995 use the 17th edition
6. Red Book 2000, American Academy of Pediatrics, 25th Edition.

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**When You See Unusual,
Think Outbreak!**