Naturally occurring tularemia is a zoonotic disease that is transmitted to humans via contact with infected animals or from the bite of arthropods that have fed on infected animals. It is caused by the highly infectious, slow-growing, aerobic, non-sporulating, Gram negative coccobacillus *Francisella tularensis*. As few as 10-50 organisms are sufficient to cause disease if inhaled or inoculated into the skin. Discovered in the early 20th century, the disease has caused multiple sporadic outbreaks but no large epidemics. It is endemic in rural areas in moderate climates, particularly in the midwestern United States. Over the last decade, annual incidence has been less than 200 cases nationwide. Pneumonic tularemia is considered one of the diseases most likely to be encountered in a bioterrorism event. Intentional aerosol release should be suspected if cases occur in nonendemic areas when no discernible risk factors for exposure are identified. Outbreaks of any form of tularemia should be rapidly investigated to rule out a bioterrorism event. There are six forms of tularemia, classified by clinical presentation and determined by route of exposure:

- **Pneumonic tularemia**
  Although up to half of all tularemia cases present with lung involvement from hematogenous spread of systemic infection (secondary pneumonic), this term is generally used to describe infection in the lung as a result of direct inhalation of aerosolized bacteria (primary pneumonic), which is not associated with skin ulcers or lymphadenopathy. Primary pneumonic accounts for <5% of all tularemia cases, but is associated with the highest mortality of 30-60% when untreated. This form is the most likely to be seen in a bioterrorism setting, but can also be seen after handling infected animals or contaminated soil.

- **Typhoidal tularemia**
  Presents as severe systemic disease without skin ulcers, lymphadenopathy or pneumonia. Any route of infection possible. 5-15% of tularemia cases. Mortality similar to pneumonic. Could be seen in bioterrorism setting, but less likely than pneumonic.

- **Ulceroglandular tularemia**
  Characterized by skin ulcer and regional lymphadenopathy. Occurs via contact with an infected animal (particularly rabbits) or by arthropod (particularly tick) bite. Most common natural form of disease, 50-85%. Mortality <5%.

- **Glandular tularemia**
  Regional lymphadenopathy without a skin ulcer. Approx. 10% of cases. Mortality similar to ulceroglandular.

- **Oculoglandular tularemia**
  Conjunctivitis and local lymphadenopathy following inoculation into the eye. Theoretically possible from aerosol or from direct contact with infected material. <5% of cases. Mortality similar to ulceroglandular.

- **Oropharyngeal tularemia**
  Pharyngitis and cervical lymphadenopathy following ingestion of inadequately cooked meat from an infected animal. <5% of cases. Mortality similar to ulceroglandular.
Decontamination

Treatment should be initiated as soon as a diagnosis of tularemia is suspected, and should not be delayed for confirmatory testing. Cure rates are high if antibiotics are started prior to development of severe illness, and survivors have no long term sequelae. Naturally-occurring \textit{F. tularensis} exhibits reliable susceptibility patterns, however, unusual resistance patterns could be a concern in a bioterrorism event. Until sensitivities are known, treat as follows: continue treatment for 10-14 days if aminoglycosides or fluoroquinolones are used, or up to 21 days for other agents. Intravenous therapy can be switched to the oral equivalent (when available) upon clinical improvement and the patient’s ability to eat and absorb medications. Intensive supportive care will be required for severe cases.

- **Adults**
  streptomycin 1 g IM q 12 hrs (should be avoided in pregnant or lactating women)
  gentamicin 3-5 mg/kg IV/IM q day

- **Children**
  streptomycin 15 mg/kg IM q 12 hrs, maximum 2 grams per day
  gentamicin 2.5 mg/kg IV q 8 hrs

Alternative therapies include:
  ciprofloxacin (very active in vitro, limited clinical data)
  doxycycline (high risk of relapse if duration <21 days)
  chloramphenicol (high risk of relapse, but best for meningitis)

Noneffective therapies include:
  Beta-lactams (including 3rd generation cephalosporins) and macrolides

In mass casualty incidents, parenteral administration may not be feasible; substitution with oral antibiotics, as recommended for post-exposure prophylaxis, may be necessary.
Post-Exposure Prophylaxis

Prophylactic therapy for tularemia should be provided for 14 days for the following:
- persons who were likely exposed to known intentional release within the last few days (asymptomatic persons who may have been exposed to a covert infectious aerosol from which other cases have been identified should be observed, and started on full treatment antibiotics if a fever or flu-like illness develops within 14 days of probable exposure).
- laboratory workers with a high-risk exposure (spill of culture, centrifuge aerosolization)
- Note: contacts of cases do not require prophylaxis if not exposed to original aerosol

Prophylactic regimen:
- **Adults** (including pregnant/lactating women)
  - doxycycline 100 mg PO bid or
  - ciprofloxacin 500 mg PO bid
- **Children** (benefits of therapy likely outweigh the risks)
  - doxycycline 2.2 mg/kg PO bid, up to 100 mg PO bid or
  - ciprofloxacin 20 mg/kg PO bid, up to 500 mg PO bid

Vaccination

A safe, live attenuated vaccine offering moderate protection versus pneumonic tularemia has been used in the U.S. since 1959 with very limited availability for laboratory workers at high risk. As tularemia has a relatively short incubation period, and the vaccine has a delayed effect, it is not recommended for post-exposure prophylaxis.

Reporting

Report suspected cases or suspected intentional release of tularemia to your local health department. The local health department is responsible for notifying the state health department, FBI, and local law enforcement. The state health department will notify the CDC.

Disclaimer

Information contained in this fact sheet was current as of October 2001, and was designed for educational purposes only. Medication information should always be researched and verified before initiation of patient treatment.

Additional information and references available at www.bioterrorism.slu.edu