Tularemia is a zoonotic disease caused by *Francisella tularensis*. Tularemia presents with various clinical illnesses, but meningitis is rare.

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Arch Neurol. 2009;66(4):523-527

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Tularemic meningitis is rare; only 16 cases have been reported (Table). The worldwide incidence of tularemia is unknown and likely underrecognized. Tularemia not infrequently occurs in the United States and other developed countries in the northern hemisphere. Between 1990 and 2005, 2000 human cases from 44 states were reported to the Centers for Disease Control and Prevention.21,22

The early clinical picture of tularemic meningitis may be relatively nonspecific. Most cases occur in late spring and summer,21 when individuals are exposed to infected arthropods (ticks and biting flies) or to aerosolized bacteria from handling hay, cutting brush, or mowing over dead infected animals.23,24 Occupational exposure has been reported in landscapers in Martha’s Vineyard in Massachusetts, with an outbreak of 59 cases of mostly pulmonary tularemia beginning in 2000 and continuing through 2006.25 A serosurvey of landscapers in Martha’s Vineyard reported F tularensis antibody titers in up to 15% of workers, and the highest titers were in those who mowed grass, cut brush, and used a power blower.24 Winter outbreaks also occur, although more rarely, and are usually related to hunters coming in contact with infected animal carcasses.21 Cases of tularemia have been reported from 44 states, but 56% of all cases are reported from Arkansas, Missouri, South Dakota, and Oklahoma.21

Francisella tularensis is highly infectious, requiring as few as 10 inhaled bacteria to cause disease, making aerosolization an environmental risk and a potential mode of transmission as a bioterrorist agent.28 Francisella tularensis was studied in several countries as a potential bioterrorist agent and was weaponized by the US military in the 1950s to 1960s as part of an offensive biowarfare program.27 The US military terminated its biological weapons development in 1970, and all stockpiles were destroyed by 1973.27 Francisella tularensis is classified as a class A bioterrorist agent due to its potential ease of dissemination and high morbidity and mortality. All human cases of tularemia must be reported to the Centers for Disease Control and Prevention.28 Postexposure prophylaxis with ciprofloxacin, 500 mg orally twice daily, or doxycycline hyclate, 100 mg orally twice daily, for 14 days is thought to be protective against symptomatic infection.

The incubation period of tularemia is usually 3 to 6 days, but it may range from 1 to 14 days after inoculation.27 In patients with tularemia meningitis, signs and symptoms of meningitis typically developed 5 days after the onset of initial illness but ranged from 3 to 30 days. Seven patients with meningitis presented with ulceroglandular disease, defined as ulcerations on the skin with regional lymph node enlargement. Five patients had the typhoidal form, characterized by an influenzalike syndrome with chills, fever, headache, and generalized aches without lymphadenopathy, skin ulcers, or pneumonia. Four patients had pharyngeal disease (painful sore throat with enlarged tonsils and formation of a yellow-white pseudomembrane). In this series with often incomplete histories and examinations, most patients had confusion, headaches, meningismus, and fevers. Seizures were reported in only 1 patient. Our patient had some symptoms consistent with typhoidal tularemia, but he also had symptoms consistent with possible pneumonia, with crackles and wheezing on physical examination but negative findings on chest radiography. The patient most likely acquired his infection through inhalation as a landscaper.

In tularemia meningitis, patients usually had marked CSF pleocytosis, with a mean white blood cell count of 1788×10^6/L (range, 2-13 200×10^6/L). In contrast to most other causes of acute bacterial meningitis, in tularemia meningitis, there was usually a mononuclear predominance ranging from 70% to 100%. Levels of CSF glucose were depressed, with a mean of 32 mg/dL (range, 9-59 mg/dL). The mean CSF protein level was 3600 g/dL (range, 230-18 900 g/dL). In addition, as was found in our patient, the Gram stain of CSF sediment was negative in 90%. Although the reason for the low sensitivity...
of Gram staining is unclear, it may reflect that an *F. tularensis* Gram stain is weak, is intracellular, or is in low numbers in the CSF (≤10^3 colony-forming units/mL). Patients with tularemia meningitis had similar blood changes as patients with tularemia without meningitis. Some peripheral white blood cell counts were normal, but most were elevated (range, 3000-49 000×10^6/μL), with a mononuclear predominance.

The differential diagnosis of mononuclear pleocytosis is broad. Viral infections, including herpes simplex virus, may cause a mononuclear predominance; however, it would be expected that the CSF would have an elevated glucose level. Other etiologies include *Mycobacterium* and *Cryptococcus*; however, these infections would be expected in immunocompromised hosts. Spirochete infections with *Treponema pallidum* or *Borrelia burgdorferi* may also cause mononuclear pleocytosis along with other infections, including *Brucella*, *Bartonella henselae*, and *Leptospira*. Our patient did not have risk factors for these diseases.

Isolation of *F. tularensis* is difficult and slow because *F. tularensis* is fastidious. Most isolates appear in 2 to 4 days, but it may take as long as 14 days to grow in culture. In our patient, CSF isolation required 4 days, and the blood specimen did not grow the organism. It is important to notify the microbiology laboratory of suspected tularemia so that they will take appropriate safety precautions and hold the cultures longer. Routine clinical specimens require a biosafety level 2 laboratory, but further processing of initial isolates suspected of being

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**Table. Case Histories of Tularemia Meningitis**

<table>
<thead>
<tr>
<th>Source</th>
<th>Patient Sex/Age</th>
<th>Work</th>
<th>Presumed Source of Infection</th>
<th>Days From First Symptom to Meningitis</th>
<th>Worst CSF Findings, WBC/mm³</th>
<th>Diagnosis °</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Primary Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haight and O'Neil, 1931</td>
<td>M/45 y</td>
<td>Night watchman</td>
<td>Rabbit or squirrel</td>
<td>5</td>
<td>2100 (70% PMN)</td>
<td>Bacterial isolation: blood</td>
<td>None</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>Bryant and Hirsch, 1931</td>
<td>M/48 y</td>
<td>Chef</td>
<td>Rabbit</td>
<td>8</td>
<td>400 (84%) M P (75 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>None</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>Hutman, 1932</td>
<td>M/12 mo</td>
<td>None</td>
<td>Unknown</td>
<td>8</td>
<td>2620 (63%) PMN G (39 mg/dL) P (174 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>CSF, T</td>
<td>Recovered</td>
<td>Death</td>
</tr>
<tr>
<td>David and Olsen, 1944</td>
<td>F/5 mo</td>
<td>None</td>
<td>Cat</td>
<td>11</td>
<td>13 200 (100%) M</td>
<td>Bacterial isolation: blood</td>
<td>Chloramphenicol</td>
<td>OP</td>
<td>OP</td>
</tr>
<tr>
<td>Stuart and Pullen, 1945</td>
<td>M/34 y</td>
<td>Unknown</td>
<td>Unknown</td>
<td>5</td>
<td>960 (100%) M G (45.4 mg/dL) P (643 mg/cm³)</td>
<td>Bacterial isolation: blood</td>
<td>None</td>
<td>Death</td>
<td></td>
</tr>
<tr>
<td>Fields, 1949</td>
<td>F/16 mo</td>
<td>Unknown</td>
<td>Skimming rabbit</td>
<td>155</td>
<td>330 (70%) M G (28 mg/dL) P (730 mg/cm³)</td>
<td>Bacterial isolation: blood</td>
<td>CSF serology</td>
<td>Antitularemia horse serum intrathecally and intravenously</td>
<td>Recovered with sequelae</td>
</tr>
<tr>
<td>Hutton and Everett, 1985</td>
<td>M/60 y</td>
<td>Unknown</td>
<td>Tick</td>
<td>9</td>
<td>2620 (63%) PMN G (39 mg/dL) P (174 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>CSF, T</td>
<td>Chloramphenicol</td>
<td>Recovered T</td>
</tr>
<tr>
<td>Lovell et al, 1986</td>
<td>F/3 mo</td>
<td>None</td>
<td>Cat scratch</td>
<td>59</td>
<td>13 200 (100%) M</td>
<td>Bacterial isolation: blood</td>
<td>Chloramphenicol</td>
<td>OP</td>
<td>OP</td>
</tr>
<tr>
<td>Harper et al, 1986</td>
<td>M/18 mo</td>
<td>None</td>
<td>Unknown</td>
<td>8</td>
<td>3470 (96%) M G (33 mg/dL) P (205 mg/dL)</td>
<td>Bacterial isolation: CSF</td>
<td>Chloramphenicol</td>
<td>Recovered OP</td>
<td>OP</td>
</tr>
<tr>
<td>Hill et al, 1990</td>
<td>M/64 y</td>
<td>Unknown</td>
<td>Unknown</td>
<td>7</td>
<td>5240 (60%) M G (32 mg/dL) P (540 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>CSF, T</td>
<td>Chloramphenicol, rifampicin, gentamicin</td>
<td>Recovered T</td>
</tr>
<tr>
<td>Allis and Ayers, 1990</td>
<td>M/19 y</td>
<td>Construction</td>
<td>Rabbit</td>
<td>7</td>
<td>2127 (100%) L G (30 mg/dL) P (115 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>CSF, T</td>
<td>Chloramphenicol, streptomycin, chloramphenicol</td>
<td>Recovered OP</td>
</tr>
<tr>
<td>Pittman, 1996</td>
<td>M/5 y</td>
<td>None</td>
<td>Rabbit</td>
<td>3</td>
<td>1570 (66%) L G (34 mg/dL) P (120 mg/dL) 2 (62%) M G (25 mg/dL) P (48 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>CSF, T</td>
<td>Chloramphenicol, streptomycin followed by tetracycline</td>
<td>Recovered T</td>
</tr>
<tr>
<td>Rodgers et al, 1998</td>
<td>F/4 mo</td>
<td>None</td>
<td>Unknown</td>
<td>9</td>
<td>1570 (66%) L G (34 mg/dL) P (120 mg/dL) 2 (62%) M G (25 mg/dL) P (48 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>CSF, T</td>
<td>Chloramphenicol, doxycycline</td>
<td>Recovered</td>
</tr>
<tr>
<td>Weiner et al, 2004</td>
<td>M/17 mo</td>
<td>None</td>
<td>Tick</td>
<td>Unknown</td>
<td>1000 mg/dL</td>
<td>Bacterial isolation: blood</td>
<td>CSF</td>
<td>Ceftriaxone</td>
<td>Death</td>
</tr>
<tr>
<td>Gangat, 2007</td>
<td>F/51 y</td>
<td>Unknown</td>
<td>Rabbit</td>
<td>30</td>
<td>2926 (94%) PMN G (33 mg/dL) P (1800 mg/dL) 1416 (73%) L G (41 mg/dL) P (266 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>CSF, T</td>
<td>Streptomycin, doxycycline</td>
<td>Recovered T</td>
</tr>
<tr>
<td>Present study</td>
<td>M/21 y</td>
<td>Landscaper</td>
<td>Rabbit</td>
<td>7</td>
<td>1570 (66%) L G (34 mg/dL) P (120 mg/dL) 2 (62%) M G (25 mg/dL) P (48 mg/dL)</td>
<td>Bacterial isolation: blood</td>
<td>CSF, T</td>
<td>Chloramphenicol</td>
<td>Recovered T</td>
</tr>
</tbody>
</table>

Abbreviations: CSF, cerebrospinal fluid; G, glucose; L, lymphocyte; M, monocyte; OP, oropharyngeal; P, protein; PMN, polymorphonuclear cell; T, typhoidal; UG, ulceroglandular; WBC, white blood cell.

° Serology indicates serum agglutination or CSF agglutination.

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