# A case of fevers in a 65 year-old carpenter

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## HPI

- 65-year-old male was admitted for liver transplant evaluation for newly diagnosed cirrhosis when he reported fevers and fatigue, abdominal distension, leg swelling, & dry cough. He was febrile for several days early on in his admission.
- He denied shortness of breath, hemoptysis, headaches, joint pain, rashes, skin nodules, vomiting, diarrhea, changes in urinary habits, recent trauma, wounds or ulcer.

- PMH: Hypothyroidism
- Medication: None
- Social Hx: Carpenter, deroofs & renovates older residential homes & buildings - cleaned friend's attic 2 months ago that had racoon droppings
  - Lives at home with wife & dog x 8 yrs
  - One month ago took care of granddaughter's pet rabbit at his home for approximately 1 week. Rabbit stayed in cage & he fed it snacks w/o touching it.
  - Drinks alcohol at social events and denies smoking, IV drug use, homelessness or incarceration
  - Has not visited forest reserves, gone hiking or consumed well or stream water.

## Physical Exam

T: 100.8F, BP: 124/83 mm Hg, HR: 79, RR: 20, O2 saturation: 100% on room air
**HEENT:** Well-appearing although fatigued and sleepy. No conjunctival injection or scleral icterus. No cervical, axillary or groin lymphadenopathy.
**CVS:** Regular, S1 and S2 normal without murmurs.
**Chest:** Decreased breath sounds over lung bases. Remainder of exam normal.
**Abdomen:** Soft, distended, non-tender, fluid thrill present and bowel sounds positive.
**Skin:** No skin rashes, nodules or wounds.
**Neurological:** Cranial nerves II-XII intact. Strength in upper and lower extremities 5/5 and sensation intact.

## Studies

**WBC** 8.0 x$10^3$/L
**Hgb:** 10.3 g/dL
**Platelets:** 66 x $10^9$/L
**Sodium:** 124 mEq/L
**Creatinine:** 1.2 mg/dL
**LFTs:** normal
**Bilirubin:** 4.4 mg/dL
**Transthoracic and Transesophageal Echocardiogram:** No evidence of endocarditis or valvular pathology.
**CT Chest:** Cirrhotic changes of liver, splenomegaly with ascites, tree-in-bud opacities in lung bases (Figure 1)
**Blood culture and gram stain:** Gram-negative coccobacilli on gram stain, culture pending prior to discharge (Figure 2)

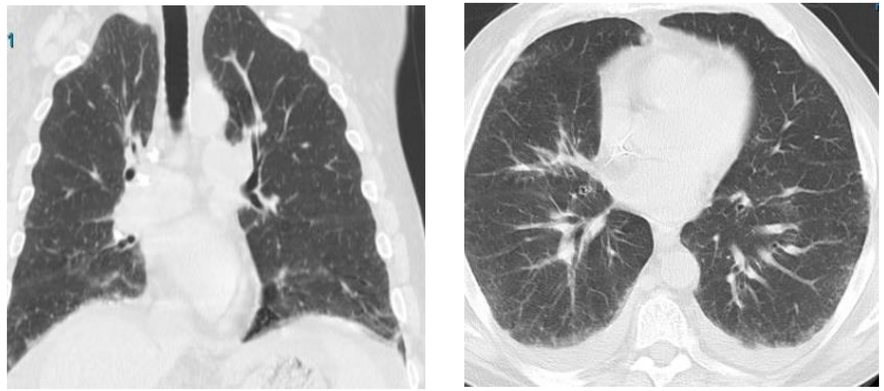



**Figure 1.** CT chest showing tree-in-bud opacities in lungs.

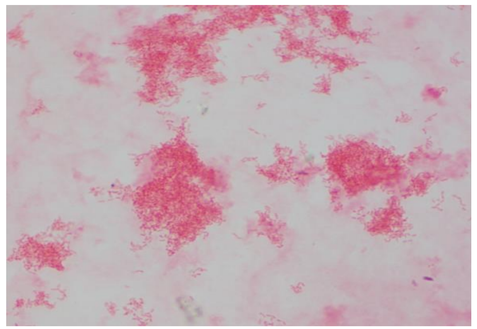

**Figure 2.** Blood culture Gram stain with gram-negative coccobacilli.

## Differential Diagnosis

A. *Kingella*
B. *Brucella*
C. *Francisella*
D. *Yersinia*
E. *Pasteurella*
F. *Leptospira*

## Hospital Course

- The patient was discharged prior to final identification of the organism isolated from blood cultures. He was prescribed a 10-day course of piperacillin-tazobactam. Repeat blood cultures prior to discharge were negative and the patient had clinically improved.
- Ten days after discharge, the patient was readmitted for fevers and fatigue.
- Blood cultures were repeated on admission and after 3 days of incubation again revealed gram-negative coccobacilli

## Diagnosis and Treatment

- After 12 days, the gram-negative coccobacillus reported on initial blood cultures was identified as *Francisella tularensis* subsp. *novicida*
- Ciprofloxacin 400 mg twice daily was given for 2 weeks and repeat blood cultures were negative.
- The patient's condition remained stable and 1 month after bacteremia, a successful liver transplant was completed.

## The Pathogen

*Francisella tularensis* is a facultative intracellular gram-negative coccobacillus. It has a low incidence rate in the United States [1, 2, 11]. Surveillance records of all tularemia cases in Arkansas found that of 138 confirmed cases identified 2009-2013, 41% were hospitalized and 3% had a fatal outcome [12]. Without treatment, death occurs in 30-60% of cases with the pneumonic form [7, 8, 9, 11].

- 4 subtypes of F. tularensis (F.t) including F.t. Type A, F.t. holarctica Type B, F.t. mediasiatica, and F.t. novicida (Figure 3). F.t. tularensis Type A can be divided into two subspecies of A.I and A.II. [1, 10].
- The severity of infection is dependent on the subtypes and strains, with F.t. tularensis Type A.I being the most virulent subspecies and F.t. novicida the least virulent and resulting in mild typhoidal disease [1, 10]. (Figure 3)
- Virulent → 10-15 organisms enough to cause infection

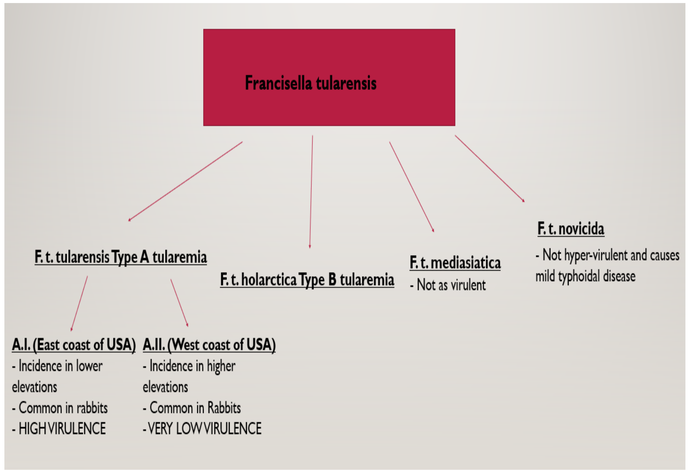


**Figure 3.** Classification of *Francisella* subtypes and species [1].

## Epidemiology/Transmission

- Transmission: tick or deer flies, drinking or exposure to contaminated water, trauma with fish hooks, inhalation of contaminated dusts or aerosols or direct contact [2].
- Host: mammals (rabbits), birds, amphibia
- Potential bioterrorism agent, can aerosolize; lab workers must be immediately notified to take precautions when managing the pathogen samples [4].
- Occupational risks: lab work, farming, landscaping, hunting and meat handling [3, 7].
- Incubation period: 3-5 days, often an abrupt onset, and most common May through September [7].
- Multiple tularemia syndromes have been identified (Table 1) [2, 3, 6, 7, 8].
- A detailed history is vital to identify possible epidemiologic links to the infection.

## Clinical Presentation

| Tularemia Syndrome | Characteristics | Portal of Entry |
|---|---|---|
| Ulceroglandular | Skin papule followed by an ulcer, tender lymphadenopathy, fever | Skin |
| Glandular | Tender lymphadenopathy, fever | Unknown – possibly sin |
| Oropharyngeal | Severe pharyngitis, cervical lymphadenitis, fever | Oropharyngeal mucosa |
| Oculoglandular | Conjunctivitis, Parinaud's oculoglandular syndrome | Conjunctiva |
| Typhoidal | Fever of unknown origin, sepsis, myalgias, headaches | Oropharyngeal mucosa or respiratory tract |
| Pneumonic | Pneumonia, fever (usually from aerosolized infected animal carcass) | Respiratory tract |

**Table 1.** Tularemia Syndromes [6, 7, 9].

## Complications

- Respiratory failure
- ARDS
- Rhabdomyolysis
- Renal failure
- Endocarditis
- Suppurative lymphadenopathy
- Pericarditis
- Peritonitis
- Perisplenitis
- Osteomyelitis
- GBS
- Hepatitis

## Diagnosis

- Samples can include blood, respiratory specimen, fine needle aspirate, swab or scraping of throat, ulcer skin lesion or lymph node
  - Culture—often requires >.1 week
  - Direct Fluorescent Antibody (DFA) or immunohistochemical stain
  - PCR
- Serology can also be used

## PCR Testing Challenges

- Four subspecies with differences in genetic organization due to chromosomal differences on a molecular level, each vary in virulence [1].
- Methods currently available to genotype *F. tularensis* can't conclusively identify the subpopulation without using time-consuming testing or complex scoring systems [1].
- Single and multiplex quantitative real-time PCR (qPCR) assays have been developed that detect and identify the various *F. tularensis* strains
  - Hypervirulent strains (such as A.I strain) can be distinguished from less virulent strains (such as *F. tularensis* subsp. *novicida*) [1, 8, 11]

## References

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