West Coast TID Meeting

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Disclosures

None

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Fever in a returning traveler

Pt is a [redacted]yo with hx of ESRD due to DM s/p renal transplant 202X on tacrolimus, mycophenolate, prednisone 5mg daily who presents with 1 day of fever following ~1 week of chills, subjective fevers and intermittent, non-bloody diarrhea following a trip to Mexico.

+long-standing low back pain. No respiratory sxs, urinary sxs or rash.

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Additional Hx

PMH

- Htn, HL
- Hypothyroidism
- CVA
- Dematiaceous fungal infection of skin/soft tissue 2022
  - Corynespora (wrist)
  - Alternaria (calf) s/p excision after failure to respond to isavuconazole

Social Hx

- Exposure to pet cats and dogs
- Lives in [redacted] suburbs
- Occasionally does landscaping work

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Pre-Transplant Labs

- CMV+
- EBV+
- VZV +
- HIV Ag/Ab neg
- RPR +1:8
- Hep A IgG+
- HBsAg neg/HBsAb+/HBcAb neg
- HCV Ab neg
- Quantiferon neg
- Toxoplasma Ab neg
- Strongyloides Ab neg
- Coccidioides Ab neg

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Travel details

- ~2-week trip to Nayarit, return to US ~3 weeks prior to presentation
- Mother had respiratory tract infection
- Denies mosquito or other insect bites
- +Unpasteurized dairy consumption

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Initial Work-Up

- WBC 9.6, hgb 12.2, plt 173
- Cr 1.48
- LFTs unremarkable
- Flu/COVID/RSV negative
- Urine screen negative
- BCxs NGTD
- Stool testing: **GI panel** + **norovirus**; C diff negative

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Imaging

- **CXR**: clear lungs

- **MRI spine:** multilevel degenerative changes

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Pt discharged home

- MMF stopped, azathioprine started
- BUT…fevers persisted

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Second admission

- Fever, myalgias/arthralgias, dry cough but non-toxic and satting well on room air
- Diarrhea resolved
- CT chest with new RML and RLL consolidations
- TTE unremarkable
- Started on empiric ceftriaxone + doxycycline but fevers persist -> ambisome initiated

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Additional Laboratory Work-Up

- Legionella urine Ag
- 1,3-beta-D-glucan
- Serum galactomannan
- Serum Cryptococcal antigen
- Urine Histoplasma Ag
- Fungal Abs
- Brucella Abs
- Bartonella henselae Abs
- Leptospira Ab
- BCxs
- CMV, adenovirus PCR
- West Nile Virus antibodies
- Dengue antibodies
- HIV Ag/Ab
- Quantiferon
- Malaria smear
- Respiratory viral panel

All negative

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Bronch w/BAL

- Cx +nl flora
- AFB negative, cx NGTD
- Fungal cx NGTD
- Nocardia cx negative
- Legionella PCR negative
- Galactomannan negative
- PJP PCR negative
- Cytology w/o organisms on GMS
- Broad range PCR with multiple bacterial templates, NGS pending

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A real head-scratcher

What is in your ddx at this point?

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Finally, some answers!

Broad range PCR from BAL:

Multiple bacterial templates detected

NGS: oral flora + **Francisella tularensis**

F. tularensis IgG and IgM positive

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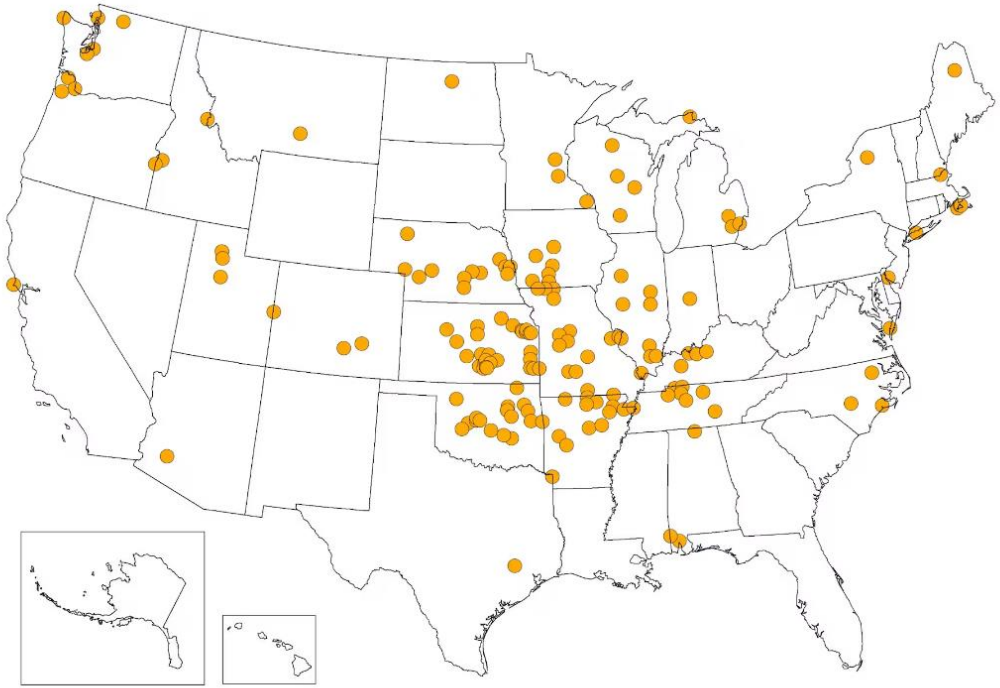
Tularemia Cases - 2022



1 dot placed within state of residence for each reported case

https://www.cdc.gov/tularemia/data-research/index.html Accessed 9/27.24.
Nelson, et al. CID. 2024.

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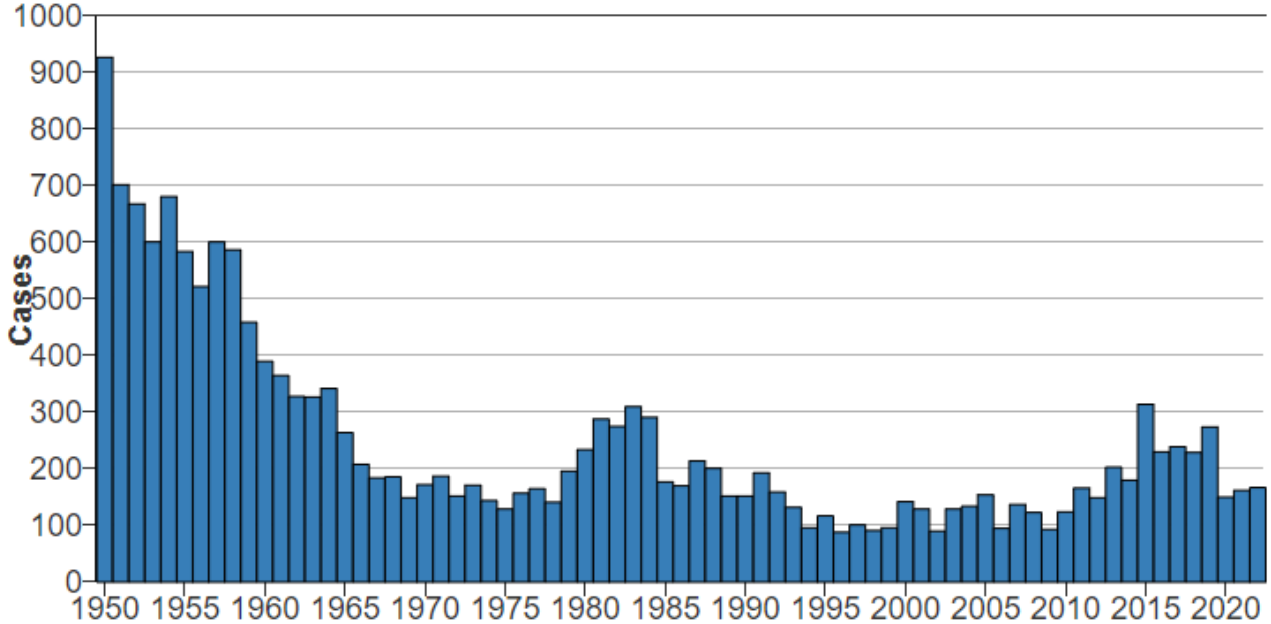
Yearly Reported Tularemia Cases – 1950-2022



https://www.cdc.gov/tularemia/data-research/index.html

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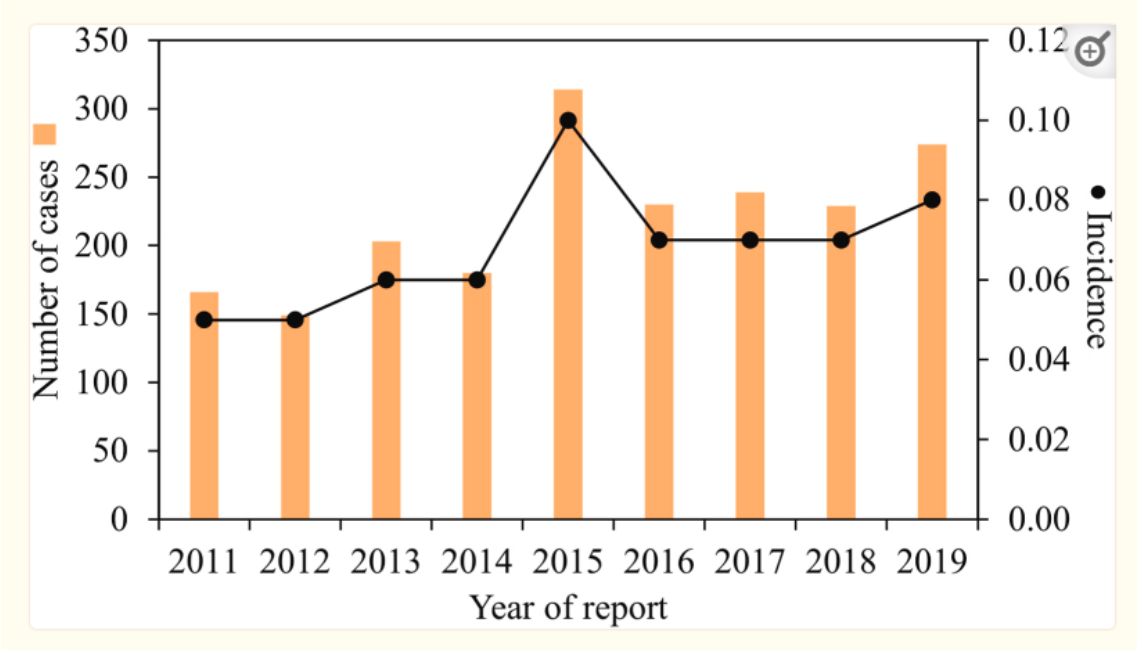
Reported Cases and Incidence of Tularemia – US 2011-2019



Bishop, et al. Current Research in Parasitology and Vector-Borne Diseases. 2023.

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Tularemia in SOT

- Rare reports of tularemia in SOT recipients (7 cases)
  - Presentations include fever + non-specific sxs, pneumonia unresponsive to standard therapy
  - Typhoidal +/- pulmonary involvement seems more common
  - 5 of 7 treated with fluoroquinolone
  - Recovery in all 7 cases

- Report of donor-derived tularemia
  - Renal recipient #1 deceased prior to dx of tularemia
  - Renal recipient #2 recovered, tx with doxy
  - Heart recipient -> no clear tularemia dx, tx with cipro x 10d

Bahuaud, et al. BMC ID. 2019. Limaye and Hooper. CID. 1999. Khoury, et al. Am J Kidney Dis. 2005. Mittalhenkle, et al. Clin Transpl. 2006. Faucon, et al. Presse Med. 2011. Ozkok, et al. Am J Kidney Dis. 2012. Nelson, et al. Emerg Infect Dis. 2019.

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What antibiotic/s would you initiate?

A. Doxycycline
B. Fluoroquinolone
C. Fluoroquinolone + gentamicin
D. Doxycycline + gentamicin
E. Doxycycline + fluoroquinolone

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Tularemia Treatment

- No resistance detected in US isolates (2009-2018) to recommended drugs

- Aminoglycosides
  - Streptomycin historically considered tx of choice -> reported rate of cure 97%, no relapses
  - Gentamicin 86% cure rate, 6% relapse rate

- Fluoroquinolones
  - Reports of clinical success similar to aminoglycosides

- Tetracyclines
  - Reports of lower cure rates, greater relapse rate

- Signal for possible higher case fatality rate with monotherapy vs. combination therapy (Nelson, et. al.) ; ?reserve for most severe cases

Choat, et al. CID. 2024.; Enderlin, et al. CID. 1994; Nelson, et al. CID. 2024.; Limaye and Hooper. CID. 1999.; Johansson, et al. Pediatr Infect Dis. 2000.; Piercy, et al. J Antimicrob Chemother. 2005.; Meric, et al. APMIS. 2008.

How did our patient become infected?

- Suspect his landscaping work led to inhalational exposure

- **What could have been done to prevent this?**

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How do you counsel SOT recipients re occupational risk (e.g., farming, landscaping) for respiratory infection?

A. No counseling
B. Avoid high-risk work for a defined period of time post-transplant +/- during any episodes of tx for rejection
C. Ok to return to work with mask use once incisions healed and able to perform physical activity required
D. Unsure

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Safe Living After Transplant – AST Guidelines

- If possible, avoid occupational risks including working in
  - Certain animal care settings
  - Construction
  - Gardening
  - **Landscaping** (in US cases where exposure source provided, 24% of pneumonic cases were related to landscaping (Nelson, et al.)
  - Farming

- Decisions to work in high-risk areas should be made by the patient after consultation with the transplant team and PCP so that risks and benefits can be appropriately discussed and precautions implemented if the patient chooses to accept these risks

Avery, et al. 2019.
Nelson, et al. CID. 2024

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Prevention Tips

For mowing or landscaping:

- Check for carcasses prior to mowing
- Use of masks during mowing and other activities may reduce risk (but this has not been studied)

For outdoor work:

- Use EPA-registered insect repellant
- Long sleeves and pants
- Prompt tick removal with fine-tipped tweezers

https://www.cdc.gov/tularemia/prevention/index.html Accessed 9/29/24.

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Clinical Update

- Treated with cipro x 21 days

- Pt doing well with resolution of fevers

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Summary

- Tularemia is rare but consider in ddx for patients with risk factors for exposure presenting with FUO, pneumonia of uncertain etiology not responding to standard therapy
- Fluoroquinolones and aminoglycosides are preferred therapy
- Don’t forget to ask about occupation and counseling on occupational risk for exposure

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Thank You