Illustrative Cases in Infectious Diseases: Pitfalls and Good Pickups

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Disclosure

I have no financial interests or relationships to disclose.

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Illustrative Cases in Infectious Diseases: My Past Year as an I.D. Consultant

Sharing of Some Remarkable Cases That Highlight

- Potential pitfalls during the earliest stages of progressive and life-threatening infections.
- Astute laboratory workups that clinch early diagnoses and achieve early cures.

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Illustrative Case #1

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Case Presentation

- 28 y.o. female presented with fevers, pharyngeal pain on **12/31/24** to U.C. site, and diagnosed with mononucleosis with a positive Monospot test.
- On **1/4/25 ,** went to local hospital with worsening throat symptoms, swollen tonsils and prescribed toradol and prednisone. Strep screen negative, and throat culture sent to lab – culture positive - resulted as **Strep/not Group A**.
- Worsening pain and difficulty managing secretions led to return to ED on **1/6/25** and CT neck performed revealing 1.4 x 1.6 x 1.7 cm R peritonsillar abscess.
- To protect her airway, she was intubated and transferred to tertiary care hospital for ENT care on **1/7/25**.
- Upon admission to ENT service , began on Clindamycin IV rx

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Case Presentation Cont.

- PMH - healthy; had laparoscopic surgery for endometriosis/appendectomy on 11/27/24
- Soc – works as a surgical P.A. in Upstate NY
- No substance use issues
- No additional medications

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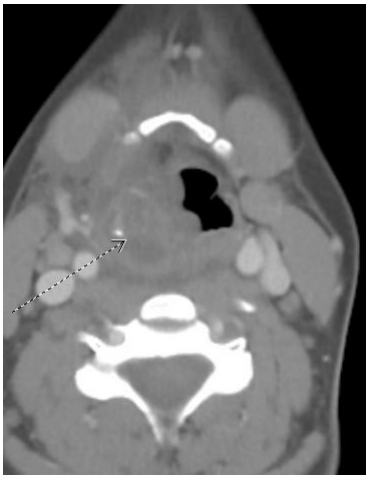
C.T. Neck 1/6/25 at OSH



IMPRESSION:

Extensive soft tissue swelling/edema at the right-sided pharyngeal and parapharyngeal structures with fluid collection at right posterior margin of hypopharynx with measurements provided as above. The fluid collection is suspect for abscess.

There is some mild stranding-like soft tissue density in the anterior mediastinum, but this could be due to residual thymic tissue in a patient of this age. A component of mediastinitis is not entirely excluded.

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Case Presentation

- I.D. consultation 1/8/25 in AM. Recommended prompt surgical exploration and drainage and changed abx to Ampicillin-Sulbactam.

Findings: OR 1/8/25 – Transoral drainage of R tonsillar abscess

- Bilateral tonsillar hypertrophy 3+ was noted with right more than left tonsil crypts spontaneously draining purulence and swabbed for culture.
- Mild right parapharyngeal fullness just posterior to the right tonsil incised; in total approximately 7 ml of purulence expressed and swabbed for culture.
- **Culture positive for Group B Streptococcus; eventual three (3) different Prevotella species grew in anaerobic culture.**

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Case Presentation Cont.

- Post op day #2, patient had been extubated, but complained of mid back pain, worse with inspiration.
- Follow up C.T. scan revealed progression of abscess into the posterior mediastinum.
- Returned to O.R. 1/10/25 with ENT and Thoracic surgery, for wider excision via R submandibular incision and a VATS, respectively.

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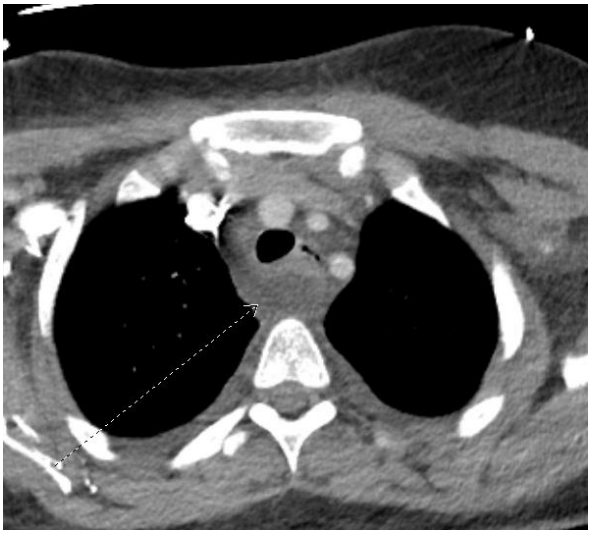
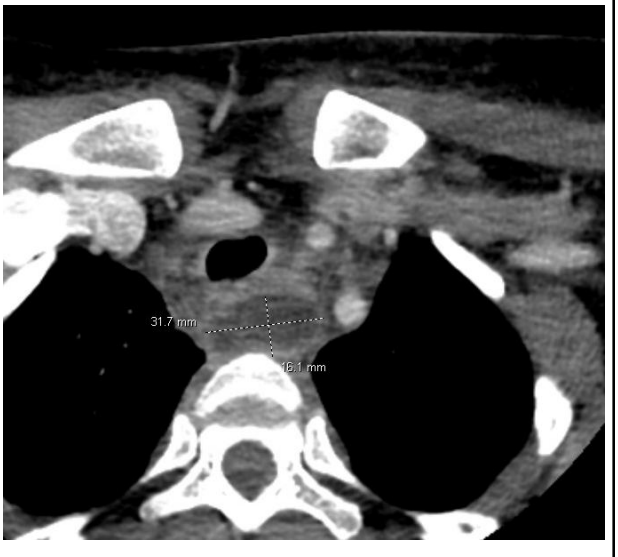
CT Chest 1/10/25





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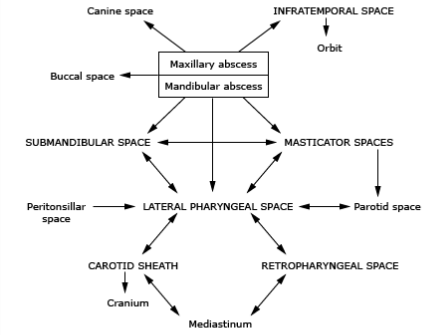
Potential pathways of extension in deep cervical fascial space infections



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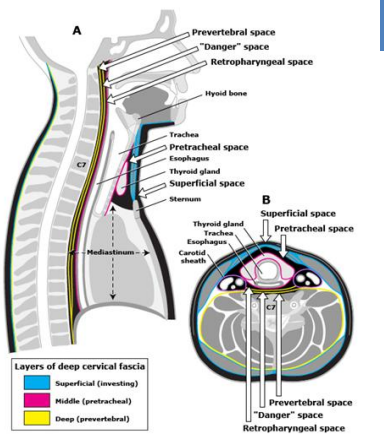
Relationship of various cervical fascial spaces to the superficial and deep layers of the cervical fascia



The "danger" space lies behind the anatomic retropharyngeal space. It is a potential space that provides a path for retropharyngeal infections to extend into the mediastinum.

(A) Sagittal section of the neck.

(B) Coronal section at the level of C7.

Adapted with permission from: Chow, AW. Life-threatening infections of the head, neck, and upper respiratory tract. In: Principles of Critical Care, 2nd ed. Hall, JB, Schmidt, GA, Wood, LH (Eds), McGraw-Hill, New York 1998. p.888. Copyright © 1998 McGraw-Hill.

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Questions Raised by This Case

- Asked reference lab to type the " non-A Strep" from 1/4/25 throat culture- identified as **Group B Streptococcus** -
- Initial use of Clindamycin monotherapy for complicated H+N infection (GBS is routinely resistant)

Question for the conferees:

1. Who would treat a non-A Streptococcal throat culture in a young adult with mononucleosis (EBV panel- confirmed true acute infection) presenting with progressive tonsillar pain/swelling?
2. Are steroids to be prescribed along with empiric antibiotics?

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Clinical Practice Guideline for the Diagnosis and Management of Group A Streptococcal Pharyngitis: 2012 Update by the Infectious Diseases Society of America: Microbial Etiology of Acute Pharyngitis doi.org/10.1093/cid/cis629

- **Antibiotic Therapy Recommended**

Group A streptococcus
Neisseria gonorrhoeae
Corynebacterium diphtheriae

- **Antibiotic Therapy NOT routinely recommended**

Group C and group G streptococcus
Arcanobacterium haemolyticum
Fusobacterium necrophorum
Francisella tularensis

- Routine culture following a negative RADT is NOT recommended in adults due to low prevalence of GAS and resultant Rheumatic Fever.

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Non- GAS Bacterial Pharyngitis: Who Gets Antibiotics, Who Gets Steroids With Progressive Mononucleosis?

- GAS accounts for about 25% of pharyngitis cases in children. Predominant causes are viral (Adenovirus/EBV, Coxsackie).
- Group C/G Strep are relatively uncommon but seen more in college students/adults; Group G has been associated with food borne outbreaks – ? true etiologic role for C/G as cause for acute pharyngitis/ or role for any antibiotic rx.
- **No mention of GBS Pharyngitis in IDSA Guidelines,** or recent Eur J of Peds Review: 2023 182:5259-5273.
- RADT test has specificity of 88-99%, so back up cultures may not be done unless high risk/high prevalence scenarios.

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Take Home Points

- Complicating, even polymicrobic supra-infections can occur in the acute setting of EBV-Mononucleosis
- Corticosteroid role for anything other than acute airway compromise is not supported in the literature Cochrane Database 2015 doi.org/10.1002/14651858.CD004402
- Introduction of empiric antibiotic for complicated tonsilitis, even with negative GAS growth, instead of steroids may need to be considered on case-by-case basis.
- Group B Streptococcus can clearly be a pathogen in complicated H+N infections…

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Illustrative Case #2

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Case Presentation #2

- Previously healthy 57 y.o. male presented to ED in early **July 2025** with significant anemia, acute kidney injury and new onset of fever
- History dated back **nearly 6 months**, with initial low back pain
- Seen by Ortho, with a negative radiographs, and treated with NSAIDS.
- Ongoing myalgias, moderate weight loss led PCP to get blood work and pt. found to be anemic in **April** (Hcrit in low 30% range)
- Sent to G.I. with no notable findings on upper and lower endoscopies in **May**, and developed SVT during upper endoscopy

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Case Presentation #2

- Refer to Rheum for ongoing myalgias/arthralgias and anemia in **June**, and workup found a RF of > 120. Pt. reported a 30# wt. loss **over the 5 mos.** Was started on prednisone at 50mg/d and tapered to 20 mg/d by early July.
- Upon return to Rheum found to have **creatinine rise to over 3. Hgb at 8.0,** with possible vasculitic-like lesions on legs and edema and sent to ED July 9, 2025.
- STOP! What critical lab test has still not been done months into an illness that led to weight loss, anemia and new inflammatory results?

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Case Presentation #2

- In ED , pt, was febrile to 40.0 C (***no prior reports/complaints of fever***). Creatinine of 3.2, Hgb of 9, hypocomplementemia
- As part of workup in ED , had TTE which found concern for vegetations on: AV (all 3 leaflets), MV and TV!
- Initial diagnostic concern was marantic/Libman-Sachs endocarditis with underlying undefined auto-immune disease.
- Blood cultures obtained, empiric Pip/tazo and Linezolid started.
- CT imaging revealed only concerns for splenomegaly and splenic infarct.

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Case Presentation #2 Continued

- Hospital Day # 2 – two sets of blood cultures positive and identified the following as *Granulicatella* species; this is considered a Nutritionally Variant/Deficient Streptococcus (as often difficult to grow – potential "culture negative I.E")
- Ceftriaxone initiated based on sensitivity.
- AKI felt most likely due to immune-complex GN.
- Due to significant valvular involvement, had AVR, MV annuloplasty, and TV debridement on D#7 – all operative vegetations grew *Granulicatella*.
- Discharged on 42 days of Ceftriaxone, and renal function returned to normal

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Sub-Acute Bacterial Endocarditis: Spectrum of Clinical Features

Mandell's Principles and Practice of Infectious Diseases 9th Edition 2020

- Median interval of **approximately 5 weeks** of symptoms before the diagnosis of subacute form of endocarditis, mainly due to Streptococcal, and less often HACEK/"Culture Negative" pathogens.
- Fever may be absent up 5-10% of the time and other symptoms maybe protean due to metastatic foci, immunopathologic factors and immune complexes
- Arthralgias, myalgias, weight loss and anemia of chronic disease
- Failure to recognize the syndromic features leads to delay in diagnosis due to lack of BLOOD CULTURES!. Patients are in fact continuously bacteremic once with the established vegetation

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The 2023 Duke-International Society for Cardiovascular Infectious Diseases Criteria for Infective Endocarditis: Updating the Modified Duke Criteria. Clin Infect Dis. 2023;77(4):518.

Duke's Minor Criteria- Immunologic phenomena
•Positive rheumatoid factor, Osler nodes, Roth spots, or immune complex-mediated glomerulonephritis

New Major Criteria in 2023

- PCR/metagenomic sequencing, serologic testing for Coxiella, Bartonella, T.whipplei.
- PET/Cardiac CT imaging
- Intraoperative inspection of aneurysm, vegetations, abscess, valvular destruction.

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Nutritionally Deficient Streptococcus: *Granulicatella* and *Abiotrophia*

1. Epidemiology, clinical characteristics, and outcome of infective endocarditis due to *Abiotrophia* and *Granulicatella* in a Tertiary Hospital in China, 2015–2023: a retrospective study. *BMC Infect Dis* 24, 1022 (2024). doi.org/10.1186/s12879-024-09943-4
2. Epid., Clin Features and Outcome of IE due to *Abiotrophia and Granulicatella* species: 2000-15; CID 2018;66(1):104-11 doi10.1093/cid/cix752

- 45 cases, which made up 2.9% of all cases of endocarditis in Zhongshan Hospital over 8 years (1531 total cases)
- Fever in only 69% of *Granulicatella* cases (less common than *Strep viridans* cases)
- **Duration of symptoms with median of 60 days**
- 92% were native valve infections
- 45.5 y.o. was median age
- 26% required in-hospital surgery
- Similar presentations/demographics in a Spanish report of 76 cases in 2018, yet with much higher operative needs (75%)

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Illustrative Case # 3: Great Pickup, But Poor Outcome

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Case #3

- 65 y.o. male with active IVDU (heroin/fentanyl) and EtOH.
- Presented to rural hospital in Northern VT 6/2/25 after being found down x hours. Admitted to nasal fentanyl/IV heroin just prior to admission
- Not septic by parameters, or febrile, upon transfer to our tertiary care hospital.
- Notable labs: Transaminitis, CK of 1200, WBC of 26k and 41% bands, 2% atyp lymphs, Plats of 25,000 Creat of 3.9.
- BC at OSH with Coag Neg Staph x 1.

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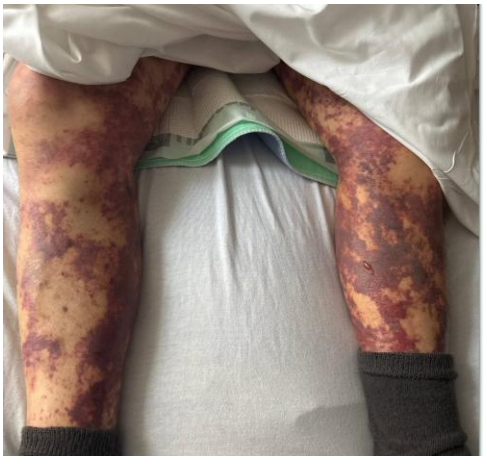
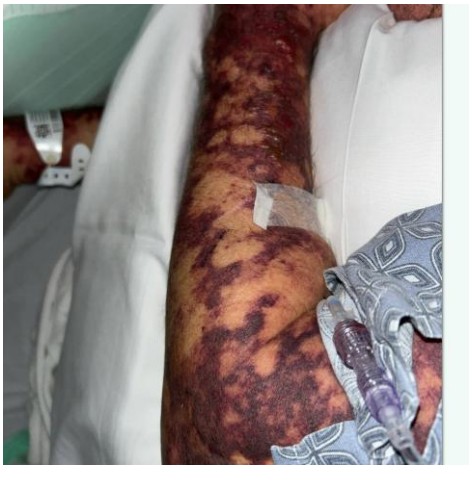
Profound Derm Findings on Admission: Purpura Fulminans





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Hospital Course

- In E.D., provider elicited that pt. had no other recent illnesses, lives in a rural area, reported numerous tick bites in prior weeks
- Started on Linezolid/Cefepime, aggressive IVF support – no pressor needs
- Anaplasma PCR ordered and was positive, and Doxycycline started day #1.
- Pt. developed progressive hepatic failure, and C.T. imaging c/w cirrhosis. Hep C was positive (not known to pt./untreated)
- On hosp day #4, deteriorated in ICU and passed.

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Purpura Fulminans and MOSF

- Multiple skin biopsies consistent with purpura fulminans.
- Seen with overwhelming infections , and associations with hereditary protein C deficiency and thrombotic DIC in skin.
- Hepatic failure/cirrhosis will exacerbate DIC picture.
- Classically can be seen with *Neisseria meningitidis, Strep. pneumoniae*, and *Capnocytophaga canimorsus* (animal bite).
- Nothing in the current literature reporting association with HGA (Anaplasmosis), but there are reports of TTP with HME (Ehrlichiosis). BMJ Case Reports doi: 10.1136/bcr-2018-226665

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Human Granulocytic Ehrlichiosis: Anaplasmosis

- Obligate intracellular bacteria that will grow as vacuoles in leukocytes (morulae).
- Transmitted by the *Ixodes scapularis tick* in the Northeast and Midwest U.S., with escalating cases in New England (12-fold rise in past decade per CDC reporting).
- Classically, will have fever, malaise, NO rash.
- Lab features are very consistent: Leukopenia/Bandemia/ Thrombocytopenia/ ATYPICAL LYMPHS, and transaminitis.
- Rapid recovery with doxycycline; mortality less than 1%.

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Illustrative Case #4

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Case Presentation #3

- 63 y.o. healthy male began with fevers/chills/rigors on 8/19/24. Some N/V and loose stools. Recorded temp as high as 103F.
- Took home COVID tests and were negative.
- Went to PCP, on **Martha's Vineyard**, where he resides in the summer.
- Afeb/VSS in office, and provider prescribed doxycycline 100 bid for likely tick-borne illness. " Tick studies" sent.
- Pt. denied any tick bites, or much outdoor activity. Mows his own lawn. Minimal gardening.
- Labs: WBC 9.3, Hbg/crit 15/46%, Comp panel all normal.

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Four Days Later… 8/24/24

- Goes to MV Hospital ED with cough, persistent fevers/chills (but not as severe), on doxycycline. Pt describes difficulty getting comfortable on L side when trying to sleep.
- CXR reveals LUL infiltrate. WBC 8.0/ Plats 181/ AST 85, ALT 83
- From 8/22/24 Testing:
  - Lyme Ab's, Babesia smear/PCR, Anaplasma PCR all negative.
  - RMSF and Ehrlichia Ab's all returned negative.
- ED provider instructs pt to continue the doxycycline, and adds cefpodoxime 200 mg BID for CAP.

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Pt. Called Back to Hospital on 8/29/24 for Abnormal Test Results from 8/24/24

- Still coughing, some minimal hemoptysis, and fever is mostly resolved
- Very fatigued. Appetite poor. Compliant with abx for a week now.
- Afebrile/ VSS . WBC 7.66, H/H down to 12.7/37% , and ALT now up to 180 and AST 91.
- CT of Chest: Subsegmental P.E. in RLL , 5cm x 5cm LUL consolidation with surrounding GGO and a 6 mm cavity in center. 1.7 cm mediastinal LN's.
- U/S revealed a R peroneal vv. DVT,
- Apixaban started , told to continue both abx that he was on.

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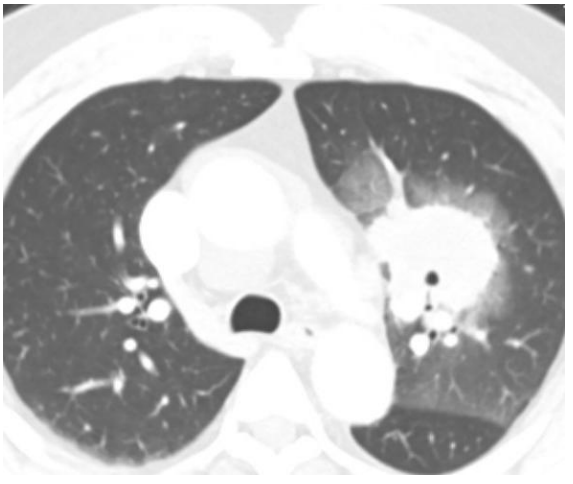
CT Chest 8/29/24



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Another Diagnostic Test Was Performed

Component Ref Range & Units	8/22/24 Comments
F. tularensis Ab, IgM Negative	**Borderline** Abnormal
F. tularensis Ab, IgG Negative	**Negative**

Ref Range & Units	8/29/24
F. tularensis Ab, IgM Negative	**Positive** Abnormal
F. tularensis Ab, IgG Negative	**Positive** Abnormal

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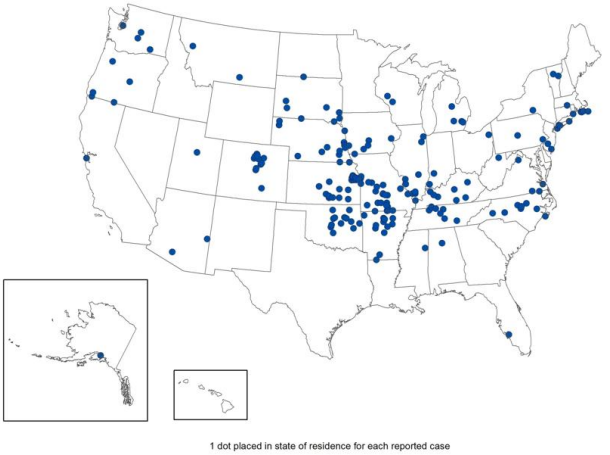
Tularemia Map of US 2023



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Tularemia Epidemiology

- Transmission to humans can occur from contact with infected animal (hunting/skinning)
- Contaminated carcass handling
- Ticks and other arthropods (mosquitos, fleas, lice, horse flies)
- Airborne form contaminated dust, hay, water and notably laboratory specimens

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Francisella Tularensis: Diagnosis

- Short incubation of 3–5-day range, with presentation based on inoculation route **ulceroglandular** or **pneumonic** – the most severe form with mortality of up to 60% -if untreated.
- May see lymphadenopathy, severe pharyngitis, conjunctivitis, severe febrile illness without focus (think Brucella).
- **Serologic diagnosis**: seroconversion about two weeks post exposure (acute) , but a paired serum (convalescent) at 2-4 weeks later (look for 4-fold rise)
- May see low-level, cross-reactive positivity with Brucella and Legionella
- Blood , pulmonary, LN's, skin, pharyngeal sampling for culture
- BUT ALERT MICRO LAB WHENEVER A CONCERN re: lab worker exposure risk

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Tularemia Treatment

- Mild to Moderate Disease: Doxycycline 100 bid for 14-21 days (higher rate of relapse) , or Ciprofloxacin 750 mg bid for 10-14 days (less relapse) – not unreasonable for pulmonic disease if not hospitalized
- Severe disease: Streptomycin or Gentamicin.
- No proven superiority of adding quinolone to aminoglycoside for severe disease
- No reliable comparison studies to favor efficacy of one oral agent over the other.
- Switched pt. to Ciprofloxacin to complete another 14 days of rx with follow up CT chest. Concern for hemoptysis risk of A/C for PE.
- Full clinical cure; and radiographic resolution in 3 mos.

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An Outbreak of Primary Pneumonic Tularemia on Martha's Vineyard

Katherine A. Feldman, D.V.M., M.P.H., Russell E. Enscore, M.S., Sarah L. Lathrop, D.V.M., Ph.D., Bela T. Matyas, M.D., M.P.H., Michael McGuill, D.V.M., M.P.H., Martin E. Schriefer, Ph.D., Donna Stiles-Enos, R.N., David T. Dennis, M.D., M.P.H., Lyle R. Petersen, M.D., M.P.H., and Edward B. Hayes, M.D. **November 29, 2001. N Engl J Med 2001;345:1601-1606**

- In both 1978 (7 cases) and 2000 (11 cases), clusters of primary pneumonic Tularemia, were reported in Martha's Vineyard.
- 1978 cluster, all seven (7) cases inhabited a single "cottage, with speculation that all infections occurred after a wet dog aerosolized *F. tularensis* while shaking itself off in the cottage.
- 2000 cluster of 15 patients total, 11 with pneumonic tularemia, reported between May 30 and late August.
- Of ten (10) pts who became ill with pulmonic tularemia, eight (8) had mowed and/weed whacked in two weeks before illness onset, half of these within 4-5 days of onset.

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Martha's Vineyard Risk for Tularemia

- Unique for much of the Northeast – most U.S. reported cases annually occur in Arkansas, Missouri and Oklahoma.
- Cottontail rabbits were introduced to both Cape Cod and Martha's Vineyard by game clubs for hunting in the 1930's.
- First locally reported case on M.V. soon thereafter.
- Two or fewer cases reported annually in M.V., outside the 1978 and 2000 clusters.

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