



Murine Typhus: A Re-emerging Threat in the United States

Clinician Outreach and Communication Activity (COCA) Call

Thursday, March 27, 2025

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- Content will not include any discussion of the unlabeled use of a product or a product under investigational use.
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Objectives

At the conclusion of today's session, the participant will be able to accomplish the following:

1. Discuss the epidemiology and ecology of murine typhus.
2. Describe diagnosis and treatment options for murine typhus.
3. Identify the best laboratory method to confirm acute infection with *Rickettsia typhi*.

To Ask a Question

- Using the Zoom Webinar System
 - Click on the “Q&A” button
 - Type your question in the “Q&A” box
 - Submit your question
- If you are a patient, please refer your question to your healthcare provider.
- If you are a member of the media, please direct your questions to CDC Media Relations at 404-639-3286 or email media@cdc.gov.

Today's Presenters

- **Johanna Salzer, DVM, PhD**
Veterinary Medical Officer
Lead, Epidemiology Team
National Center for Emerging and Zoonotic and Infectious Diseases
Centers for Disease Control and Prevention

- **Lucas Blanton, MD**
Associate Professor of Medicine
University of Texas Medical Branch

- **Christopher D. Paddock, MD, MPHTM**
Medical Officer
Lead, Microbiology and Diagnostic Team
National Center for Emerging and Zoonotic and Infectious Diseases
Centers for Disease Control and Prevention



Murine Typhus: A re-emerging threat in the United States

Johanna S. Salzer, DVM, PhD
Epidemiology Team Lead
Rickettsial Zoonoses Branch
Division of Vector-Borne Diseases
Jsalzer@cdc.gov

Murine Typhus Overview

- **Caused by *Rickettsia typhi***
 - Obligate intracellular organism
- **Spread through contact with infected fleas**
 - Oriental rat flea (*Xenopsylla cheopis*)
 - Cat flea (*Ctenocephalides felis*)
- **Transmitted through flea feces (flea dirt)**
- **Signs and symptoms begin up to 2 weeks after contact with infected fleas**
 - Acute febrile illness that can be fatal



Xenopsylla cheopis, the Oriental rat flea

Knowledge Check #1

Which arthropod serves as the vector for murine typhus?

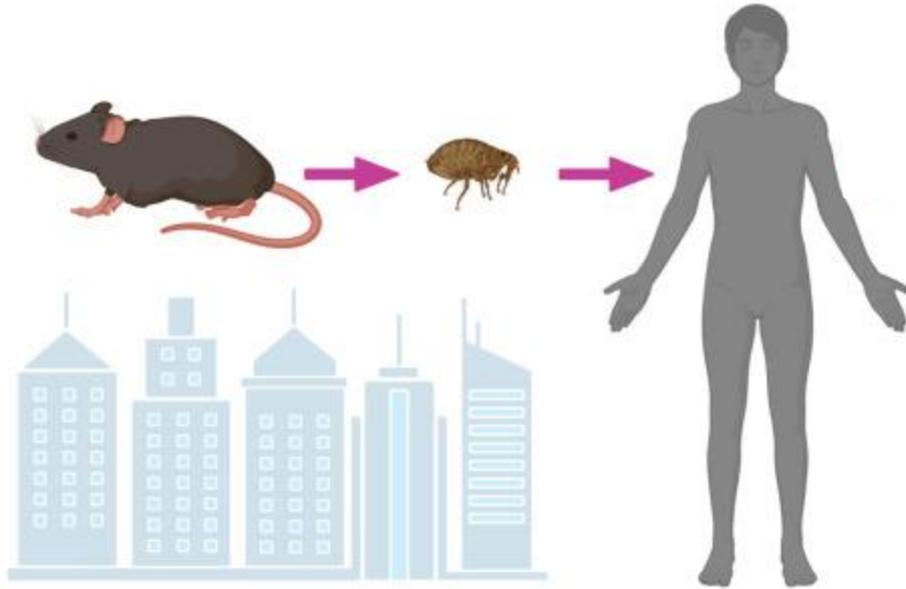
- A. Ticks
- B. Mosquitoes
- C. Fleas
- D. Lice

Knowledge Check #1 - Answer

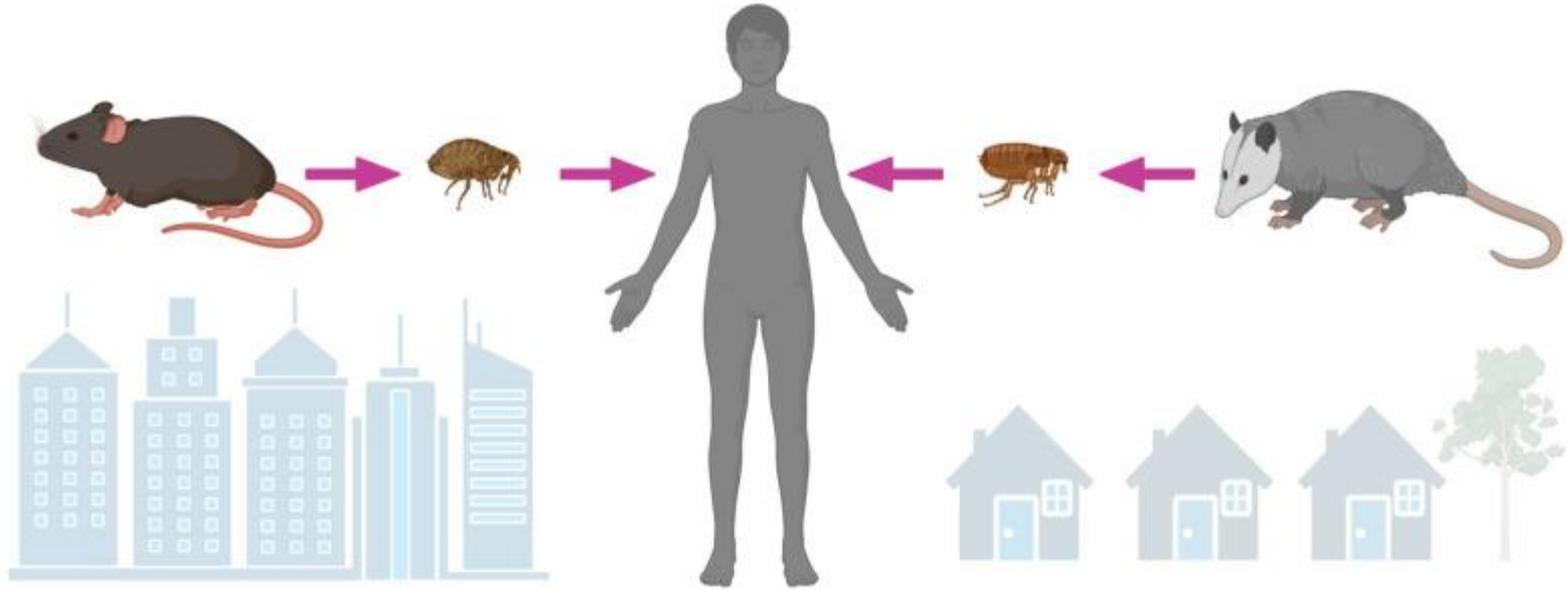
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Urban and Suburban Cycles



Urban and Suburban Cycles



Risk Factors for Infection

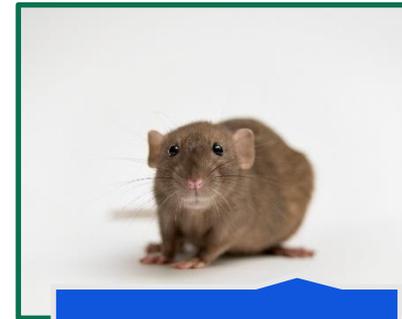
- **Contact with rats, opossums, and free-roaming cats**
 - Flea-preventative use
- **People living outdoors or in housing infested with rats or other rodents**
- **Increased risk among people experiencing homelessness**



Free-roaming cats



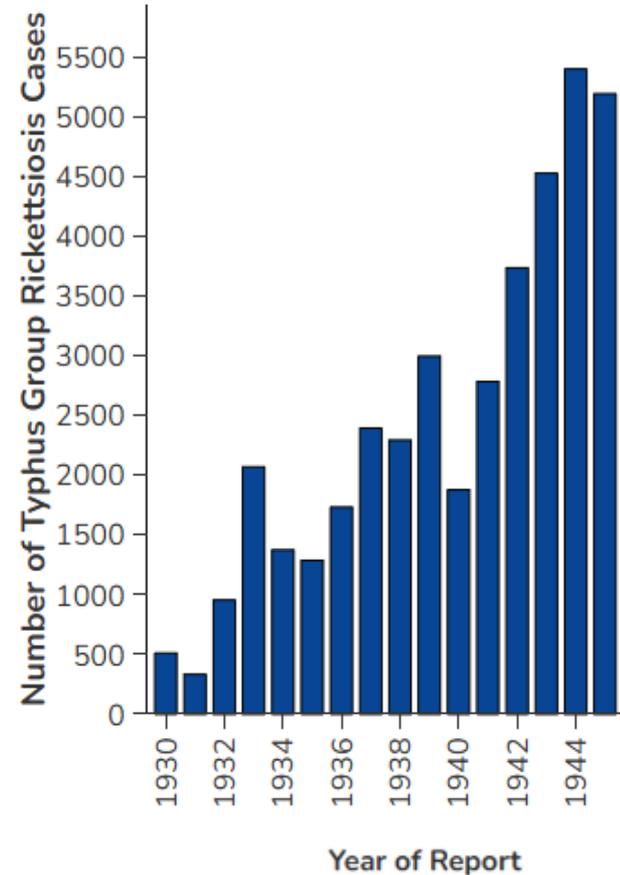
Opossums



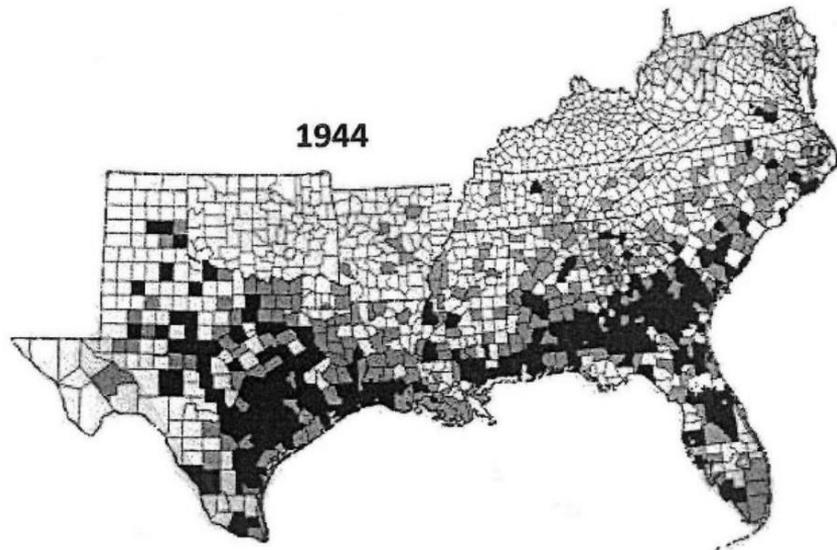
Rats

Historic Public Health Problem

- **Nationally Notifiable**
- **1931-1946:**
 - 42,000 cases reported



Incidence of murine typhus in the southeastern US



LEGEND

 20 or more cases per 100,000 population

 Less than 20 cases per 100,000 population

 No cases reported

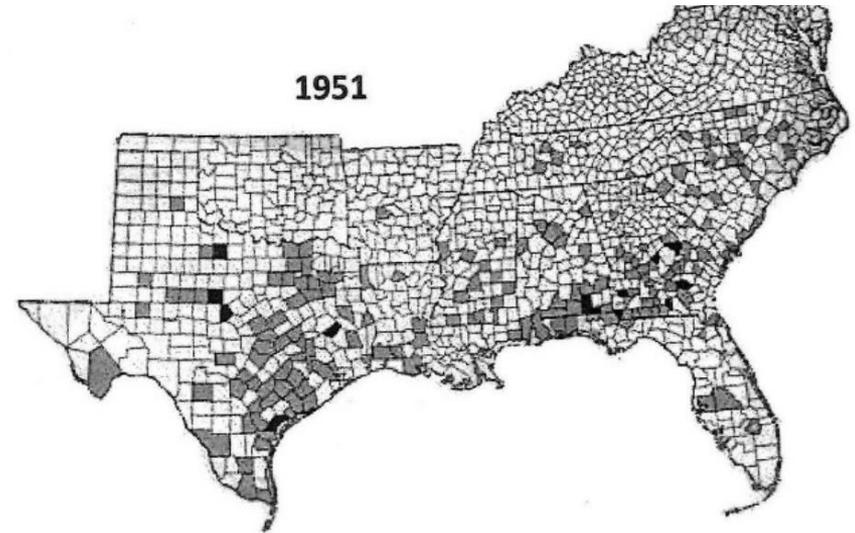
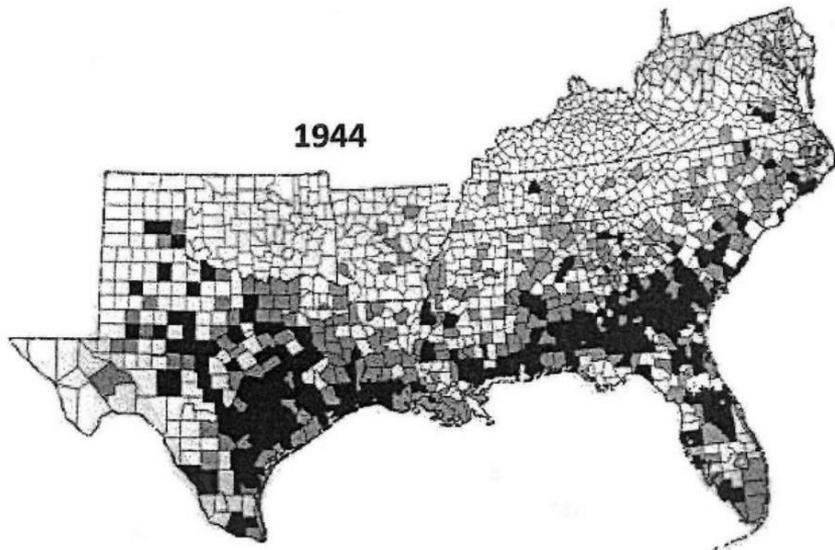
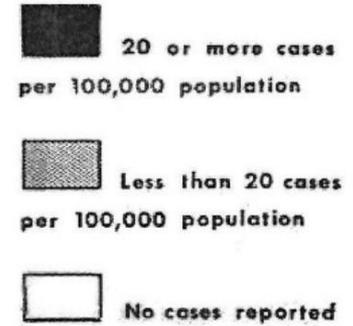
Figure re-drawn from [Sherman 1952](#), *Pub Hlth Rep* 67: 1249-1257. Snellgrove and Goddard 2024-

Public Health Intervention: Rodent and Flea Control

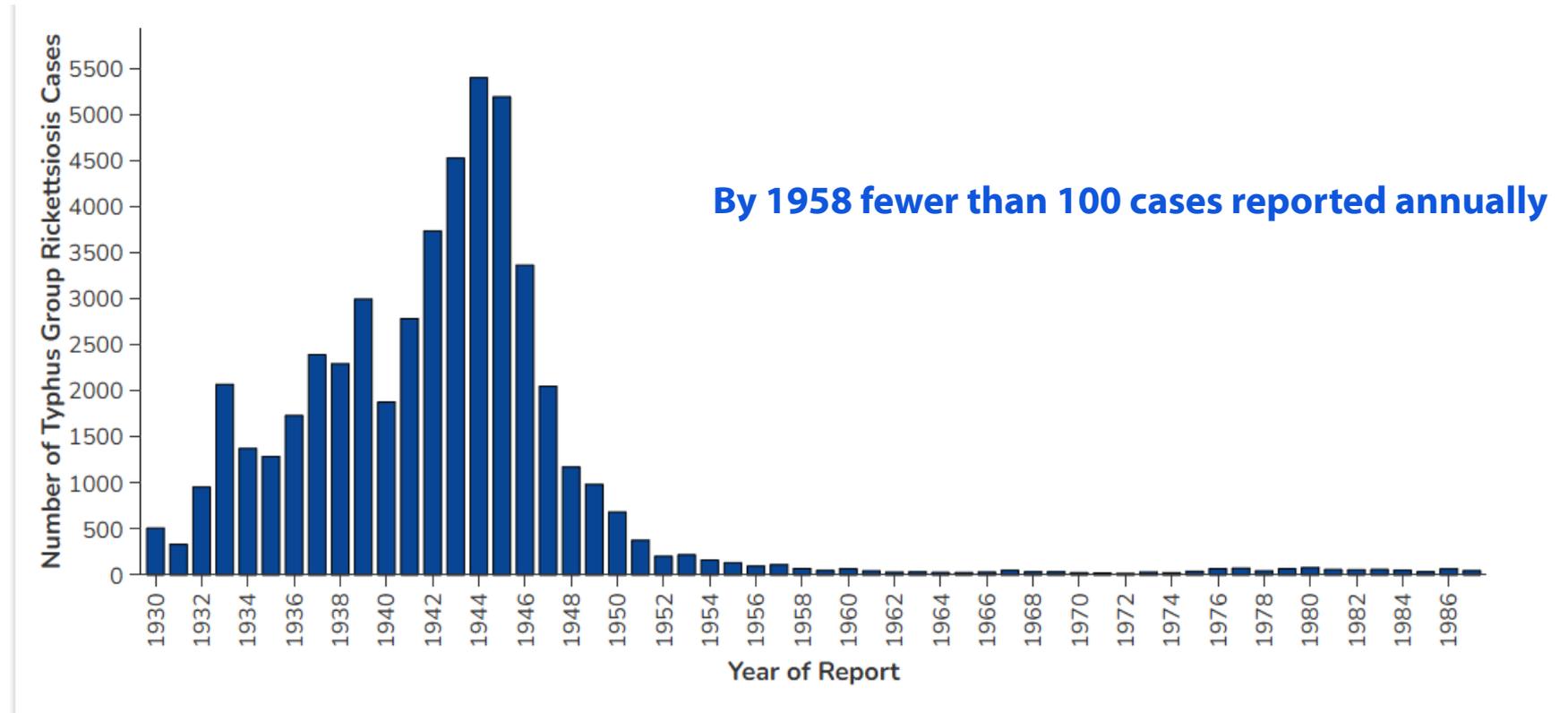


Incidence of murine typhus in the southeastern US

LEGEND



Historic Public Health Problem



Nationally Notifiable until 1987

“These three diseases are so rare and of such minimal current importance to make routine reporting unnecessary.”

Smallpox

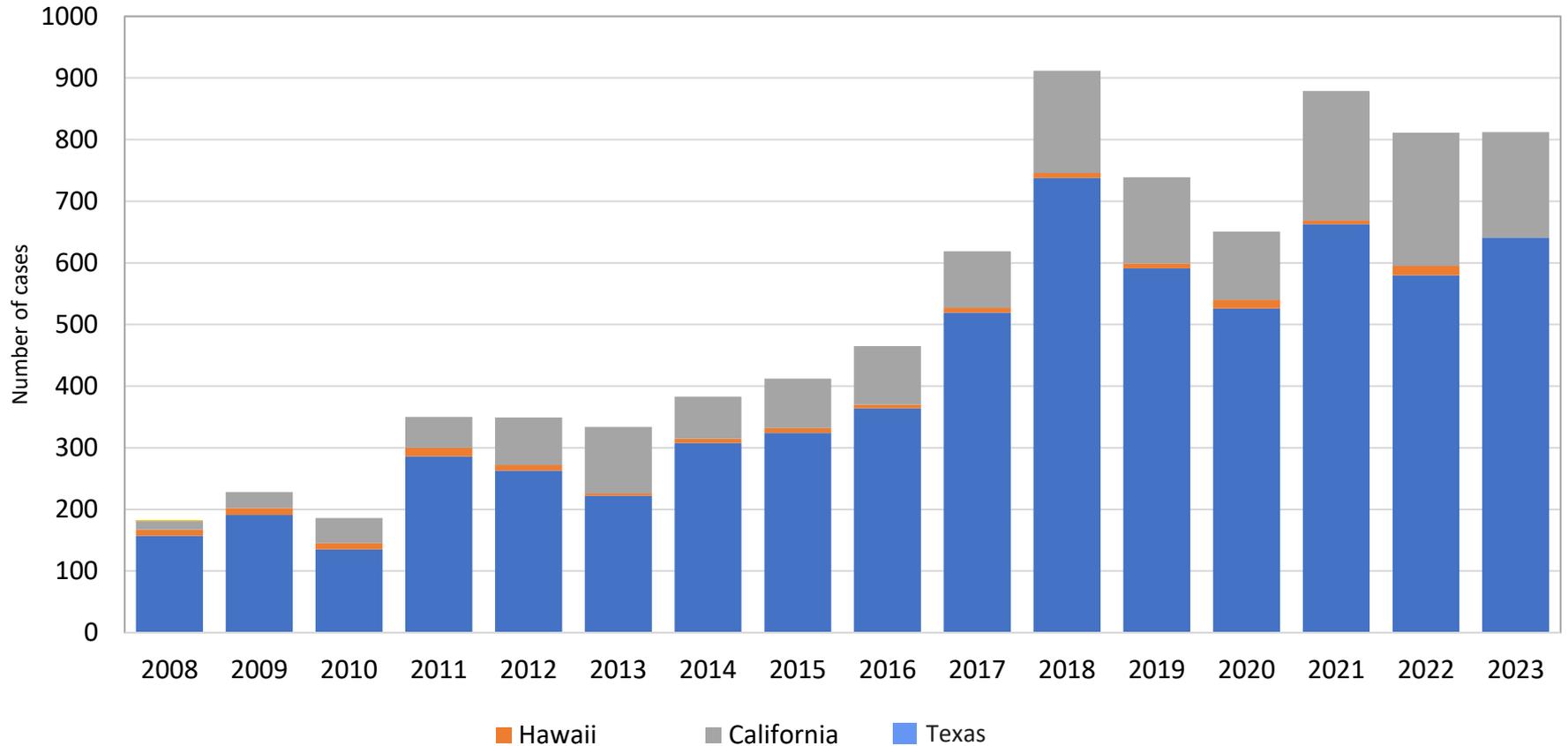
Murine
Typhus

Relapsing
Fever

In States Where Murine Typhus is Reportable, Those Reporting the Greatest Number of Murine Typhus Cases



Murine Typhus Case Count, 2008–2023



Knowledge Check #2

In the last 5 years, which two US states have reported the most cases of murine typhus?

- A. California and Texas
- B. Texas and Louisiana
- C. California and Arizona
- D. Texas and Georgia

Knowledge Check #2 - Answer

In the last 5 years, which two US states have reported the most cases of murine typhus?

- A. California and Texas
- B. Texas and Louisiana
- C. California and Arizona
- D. Texas and Georgia

Fleaborne Typhus–Associated Deaths — Los Angeles County, California, 2022

Jemma Alarcón, MD^{1,2}; Armine Sanosyan, MPH²; Zuelma A. Contreras, PhD²; Van P. Ngo, MPH²; Ann Carpenter, DVM¹; Jill K. Hacker, PhD³; William S. Probert, PhD³; Dawn Terashita, MD²; Sharon Balter, MD²; Umme-Aiman Halai, MD²

Abstract**Fleaborne Typhus-**

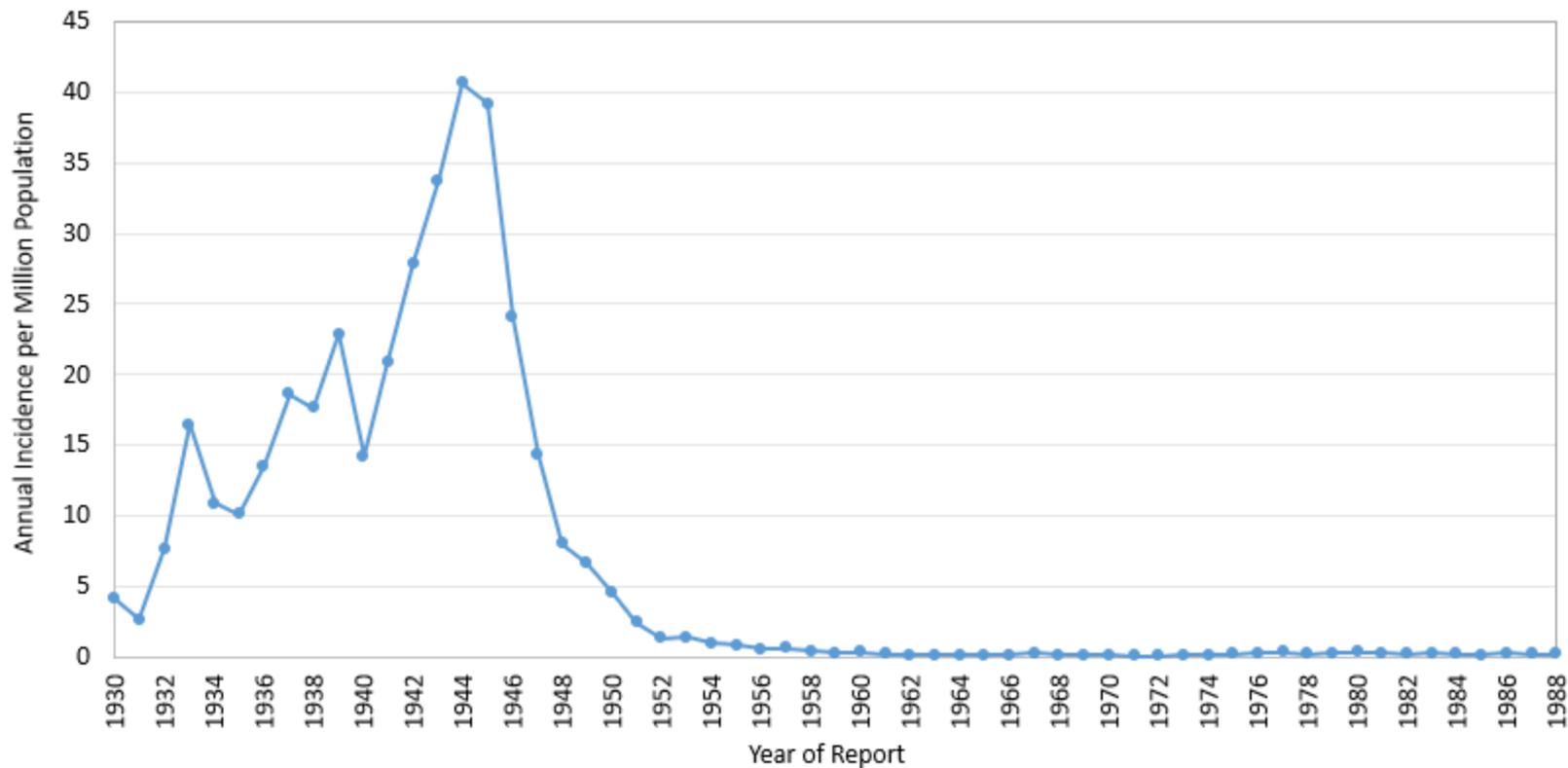
Jemma Alarcón, MD^{1,2}; Armine S
William S

Fleaborne typhus (also known as murine typhus), a widely distributed vectorborne zoonosis caused by *Rickettsia typhi*, is a moderately severe, but infrequently fatal illness; among patients who receive doxycycline, the case-fatality rate is <1%. Fleaborne typhus is a mandated reportable condition in California. Reported fleaborne typhus cases in Los Angeles County have been increasing since 2010, with the highest number (171) reported during 2022. During June–October 2022, Los Angeles County Department of Public Health learned of three fleaborne typhus–associated deaths. This report describes the clinical presentation, illness course, and methods used to diagnose fleaborne typhus in these three cases. Severe fleaborne typhus manifestations among these cases included hemophagocytic lymphohistiocytosis, a rare immune hyperactivation syndrome that can occur in the infection setting; myocarditis; and septic shock with disseminated intravascular coagulation. Increased health care provider and public health awareness of the prevalence and severity of fleaborne typhus and of the importance of early doxycycline therapy is essential for prevention and treatment efforts.

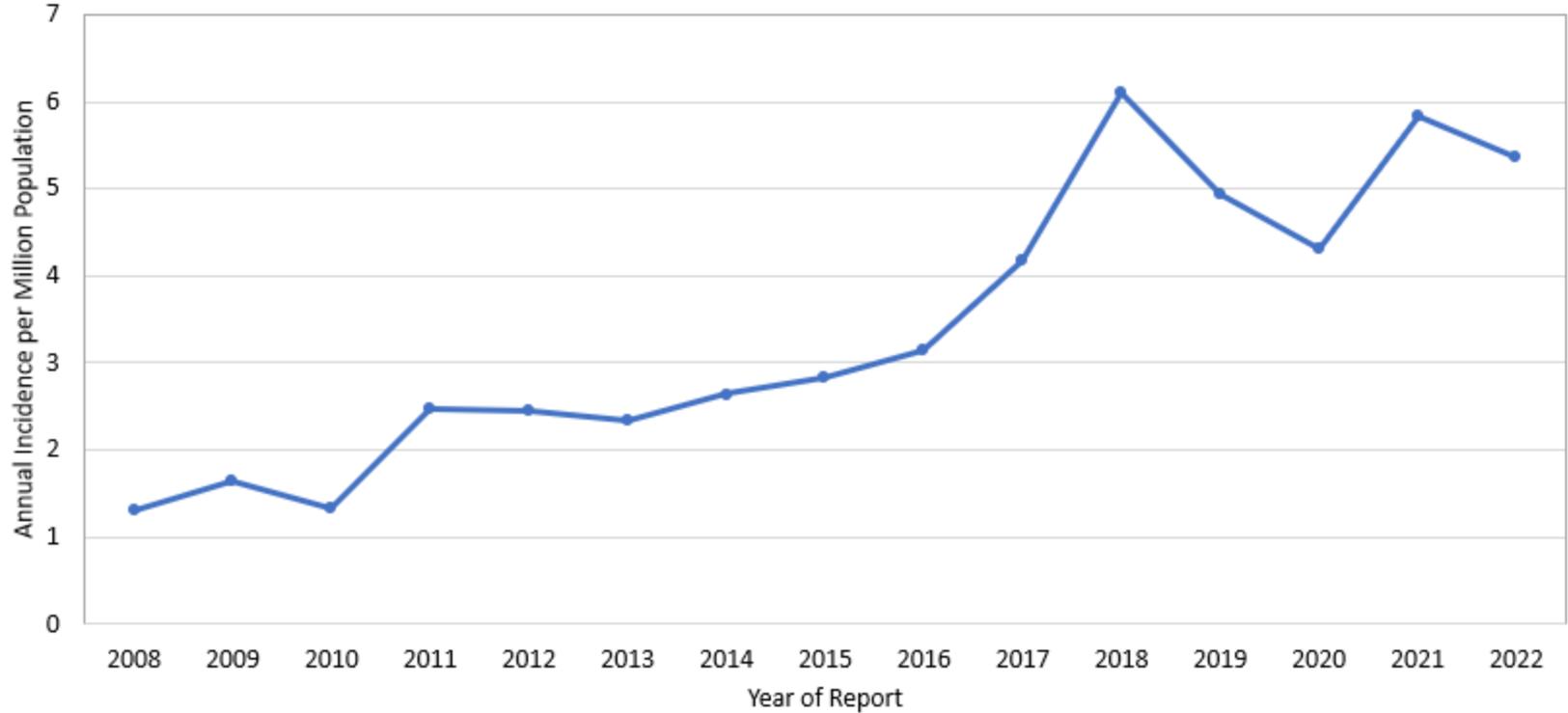
, California, 2022

r, DVM¹; Jill K. Hacker, PhD³;
i, MD²

Annual Incidence of Murine Typhus, United States, 1930–1988



Annual incidence of murine typhus in reportable states, 2008-2022



Murine Typhus: Clinical Manifestations and Treatment

March 27, 2025

Lucas Blanton, MD

Associate Professor of Medicine

University of Texas Medical Branch

Murine Typhus – An Acute Undifferentiated Febrile Illness

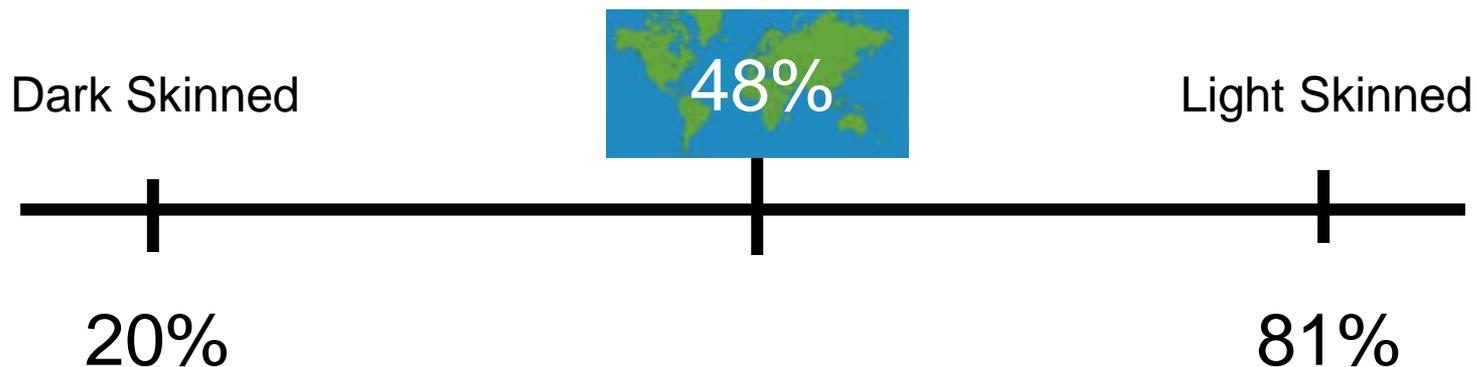
Signs and symptoms

| | | | |
|------------|-----|-------------------|-----|
| • Headache | 81% | • Rash | 48% |
| • Malaise | 67% | • Anorexia | 48% |
| • Chills | 63% | • Cough | 28% |
| • Myalgias | 52% | • Nausea/vomiting | 28% |

Rash of Murine Typhus – Usually Macular and/or Papular



Murine Typhus – Frequency of Rash



Stuart et al. Endemic (murine) typhus fever: Clinical observations of 180 cases. *Ann Int Med.* 1945;23:520-536.

Tsioutis C, et al. Clinical and laboratory characteristics, epidemiology, and outcomes of murine typhus: A systematic review. *Acta Tropica.* 2017;166:16-24.

Rash of Murine Typhus



Faint macular rash on the feet and ankles noticed only by the patient



Macules difficult to see when skin is darkly pigmented.



A rash that did not appear until several days were spent in the hospital



Petechial rash – easy to see but seldom occurs

Knowledge Check #3

What percentage of adult patients with murine typhus will have a rash at some point during illness?

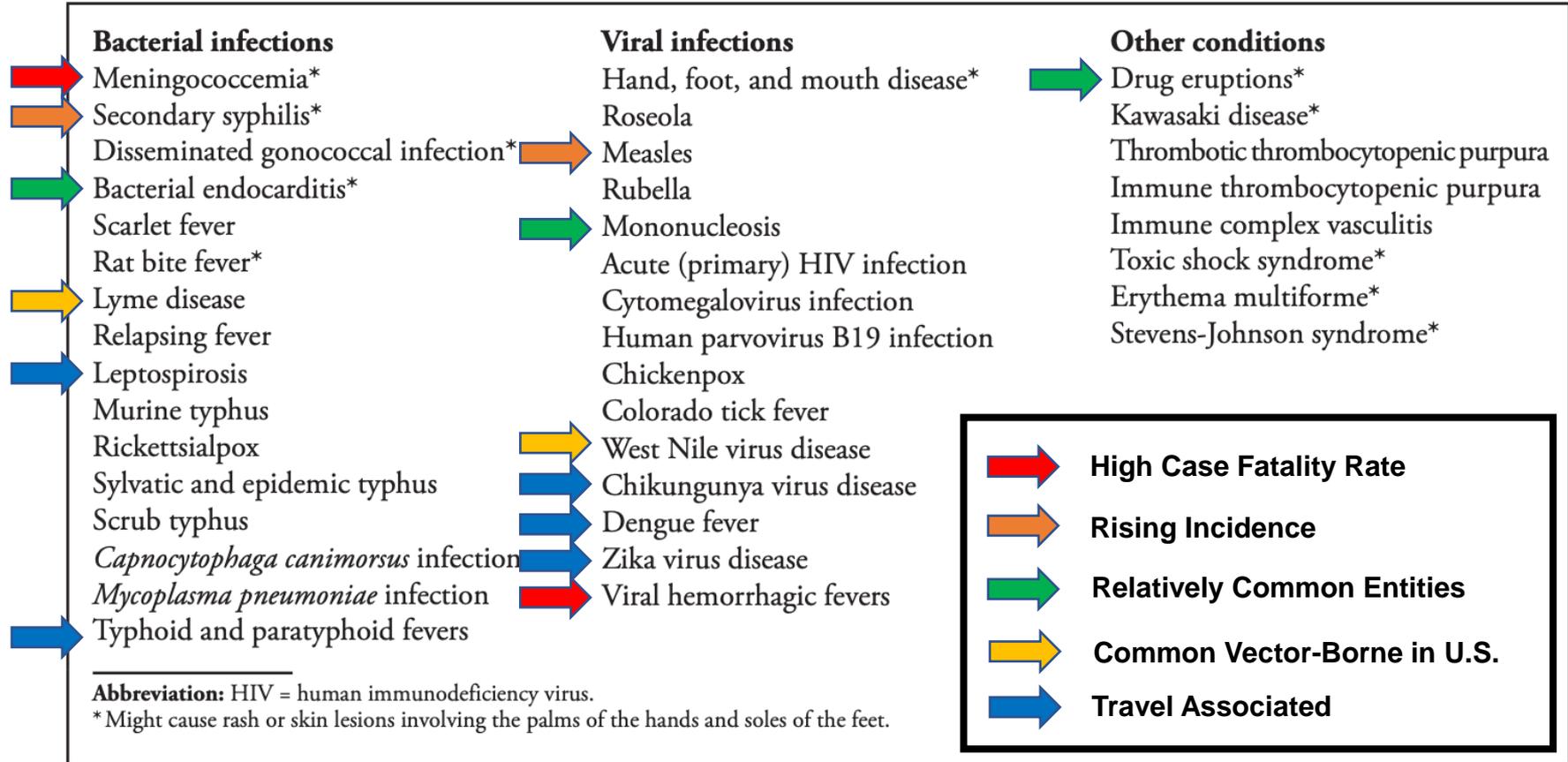
- A. 28%
- B. 89%
- C. 100%
- D. 48%

Knowledge Check #3 - Answer

What percentage of adult patients with murine typhus will have a rash at some point during illness?

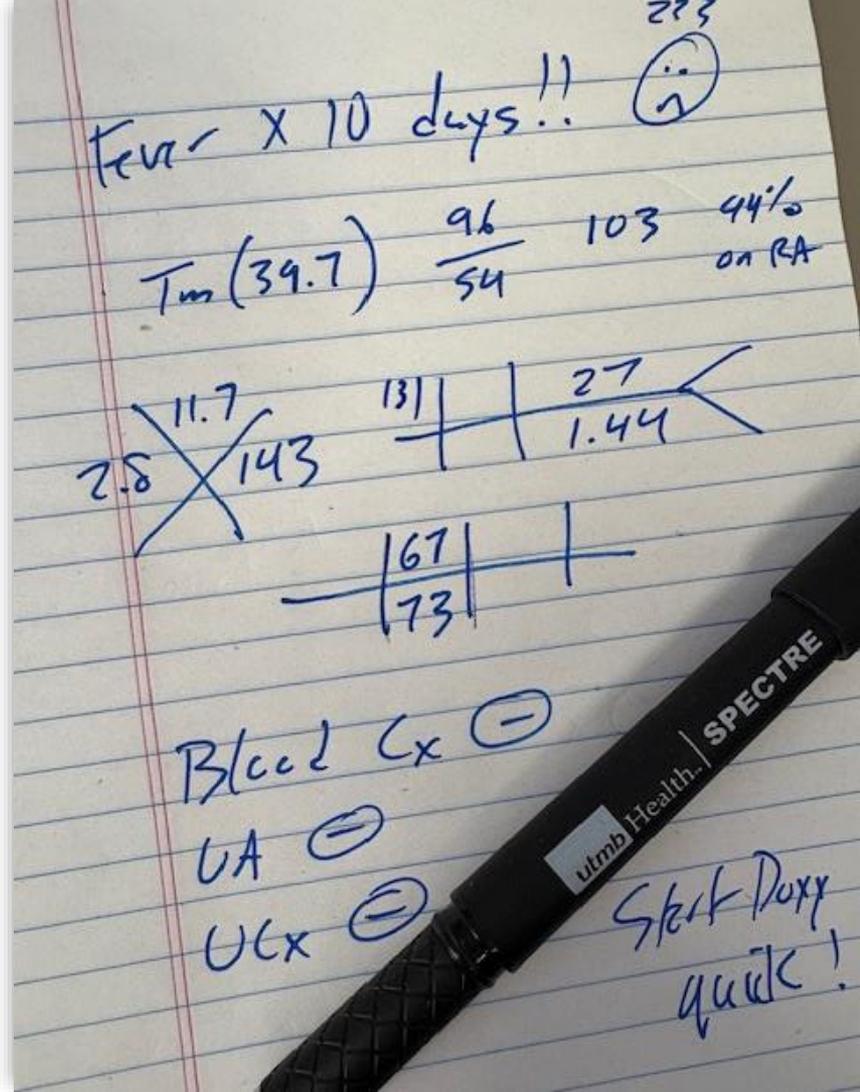
- A. 28%
- B. 89%
- C. 100%
- D. 48%

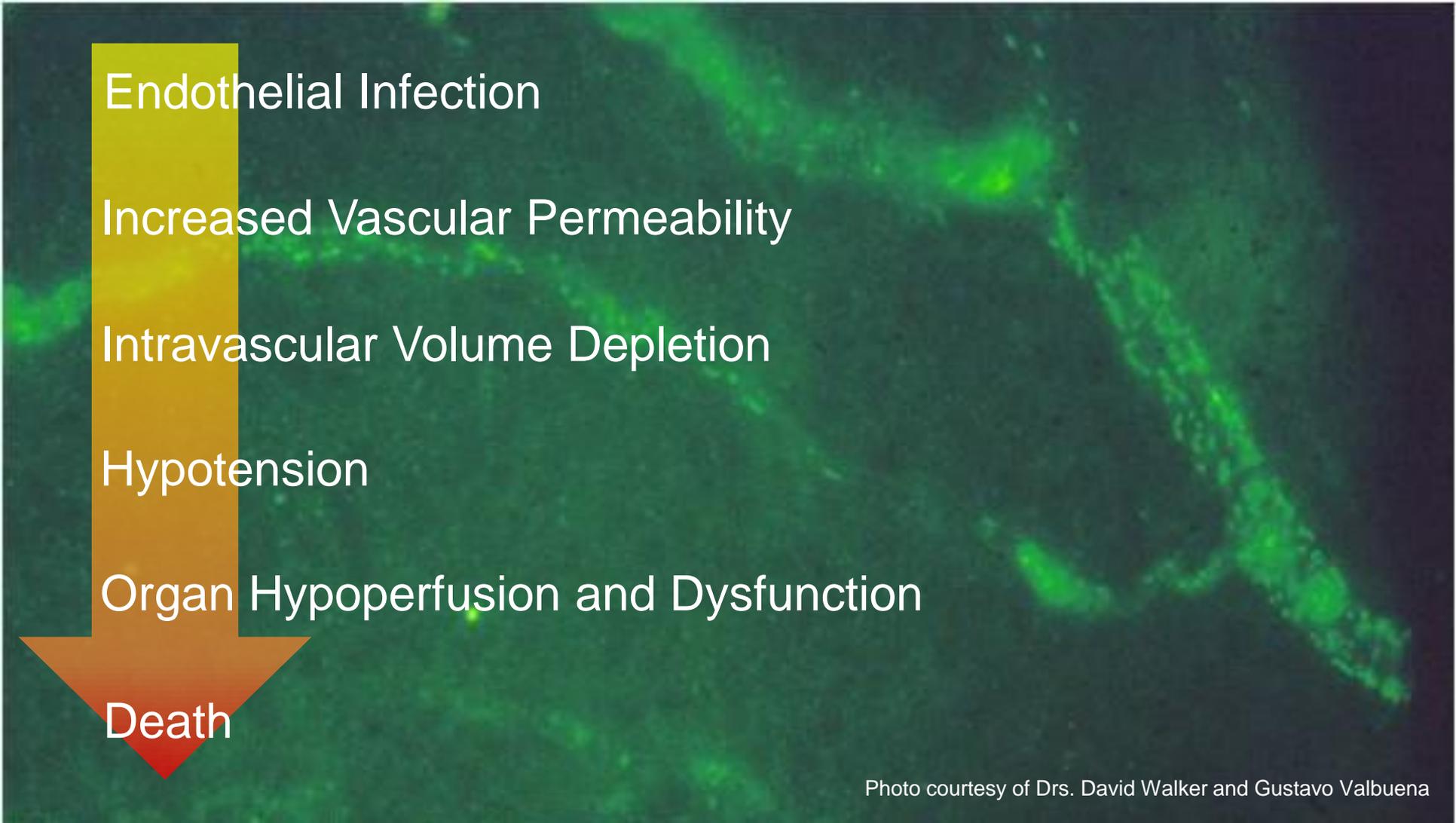
BOX 6. Selected conditions other than tickborne rickettsial diseases that can result in acute illness with fever and rash



Murine Typhus – Laboratory Abnormalities

- ↑ Liver enzymes 79%
- ↑ LDH 73%
- ↓ Albumin 60%
- ↑ ESR 60%
- ↓ Platelets 42%
- ↓ Hemoglobin 38%
- ↓ Sodium 35%
- ↓ WBC 24%





Endothelial Infection

Increased Vascular Permeability

Intravascular Volume Depletion

Hypotension

Organ Hypoperfusion and Dysfunction

Death

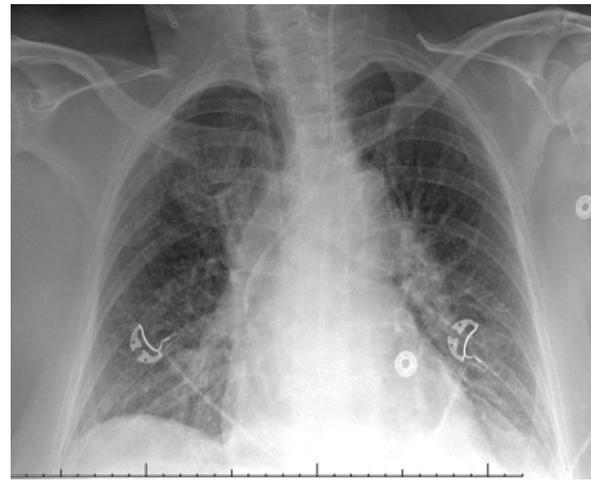
Severe Manifestations of Skin / Extremities



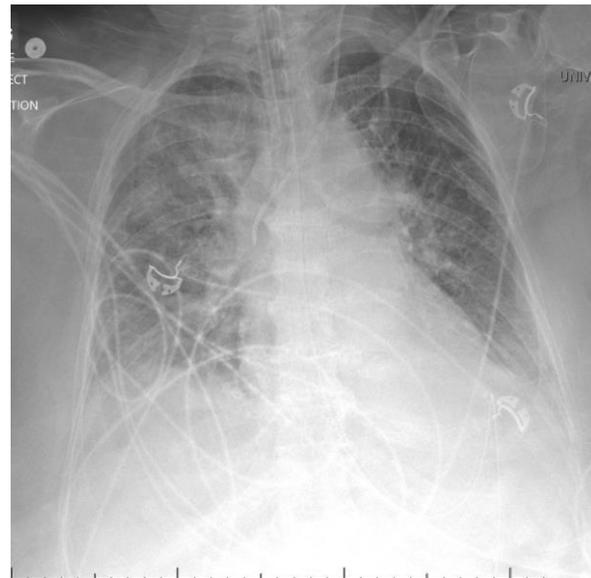
Severe Manifestations

- Renal
 - Acute kidney injury
 - May need hemodialysis
- Pulmonary
 - Cough in ~ 30%
 - CXR abnormalities in 17%
 - ARDS can occur
- Neurologic
 - Severe headache
 - Meningoencephalitis
 - Cranial nerve palsies, seizures, coma

Hernandez-Cabrera et al. Murine typhus with renal involvement in Canary Islands. *EID*. 2004; 150: 740-743.
Van der Vaart et al. Severe murine pulmonary system involvement. *EID*. 2014; 20: 1375-1377.
Silpapojakul S, et al. Rickettsial meningitis and encephalitis. *Arch Intern Med*. 1991; 151: 1753-1757.



2/11/2022



2/13/2022

Case Fatality Rate

- In Texas, 11 deaths occurred from 1985 – 2015
- Case fatality ~ 0.4%
- Case fatality in hospitalized ~2%
- Case fatality 1.8% In Los Angeles County, California in 2022

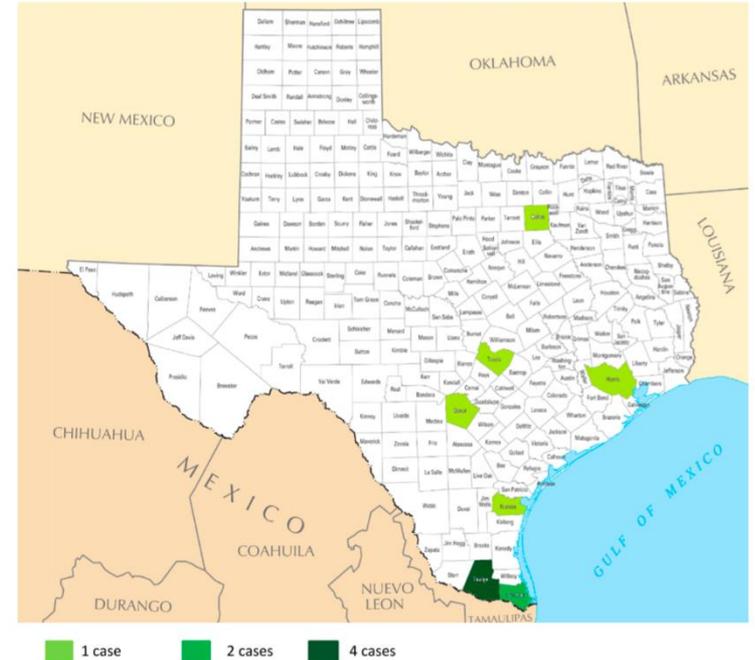


FIGURE 1. Texas counties with fatal flea-borne typhus by case count, 1985–2015.

Pieracci EG, et al. Fatal flea-borne typhus in Texas: a retrospective case series, 1985 – 2015. *AJTMH*. 2016; 96:1088-1093.

Dumler JS, et al. Clinical and laboratory features of murine typhus in South Texas, 1980 through 1987. *JAMA*. 1991; 266:1365-1370.

Alarcon J et al. Fleaborne typhus-associated deaths - Los Angeles County, California, 2022. *MMWR Morb Mortal Wkly Rep*. 2023;72:838-43.

Treatment

- Treatment should not be withheld while awaiting diagnostic tests
- Tetracyclines are the antibiotics of choice
 - Adults: Doxycycline 100 mg PO or IV twice daily
 - Children < 45 kg (100 lbs): Doxycycline 2.2 mg/kg PO or IV twice daily
- Doxycycline is orally bioavailable, but intravenous form may be needed in those hospitalized with nausea/vomiting or critical illness
- Treatment duration is ~ 7 days

Blanton, Dumler, Walker. "*Rickettsia typhi* (murine typhus)." Mandell's Principles and Practice of Infectious Diseases, 9th edition. Philadelphia, PA: Elsevier, Chapter 190, pgs. 2372-2376.

Newton et al. A prospective open-label, randomized trial of doxycycline versus azithromycin for the treatment of uncomplicated murine typhus. *CID*. 2019;68:738-747.

"Murine typhus (endemic or flea-borne typhus)." Red Book: 2024 – 2027 Report of the Committee on Infectious Diseases, 33rd edition. American Academy of Pediatrics.

Knowledge Check #4

What antibiotic should be the first choice to treat suspected murine typhus?

- A. Amoxicillin
- B. Doxycycline
- C. Ceftriaxone
- D. Ciprofloxacin

Knowledge Check #4 - Answer

What antibiotic should be the first choice to treat suspected murine typhus?

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- B. Doxycycline
- C. Ceftriaxone
- D. Ciprofloxacin

Treatment: Pearls and Possible Alternatives

- In those with severe illness, consider a 200 mg loading dose of doxycycline
- Patients usually improve within 24 to 48 hours after initiation of doxycycline
- Minocycline seems to be as effective as doxycycline
- Chloramphenicol is an alternative agent, but it is not available in the U.S.
- Azithromycin and fluoroquinolones have been used as alternative agents, but...
 - Success is based on limited observational studies
 - Time to defervesce is slower when compared to tetracyclines
 - In an RCT, azithromycin deemed not effective compared to doxycycline

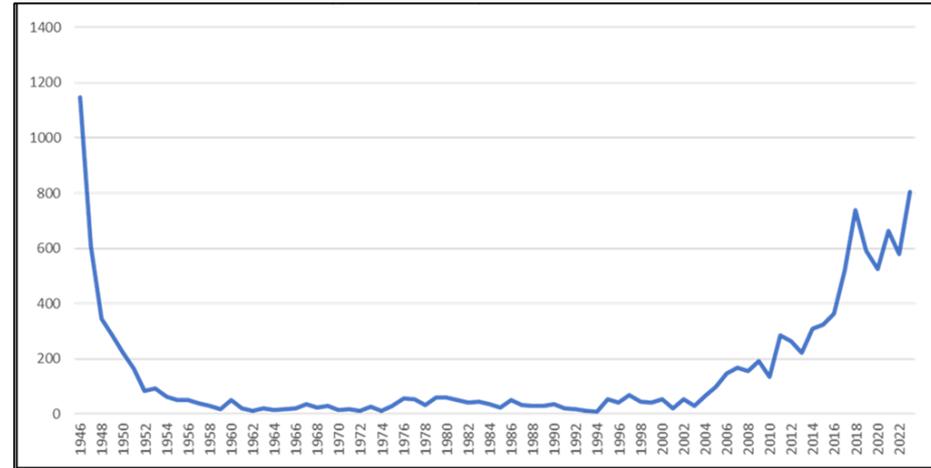
Caravedo Martinez et al. Manifestations and Management of Flea-Borne Rickettsioses. *Research and Reports in Trop Med.* 2021;12:1-14.

Newton et al. A prospective open-label, randomized trial of doxycycline versus azithromycin for the treatment of uncomplicated murine typhus. *CID.* 2019;68:738-747.



Forgotten, but not gone—murine typhus in the United States, 2025

Christopher Paddock, MD, MPHTM
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cpaddock@cdc.gov

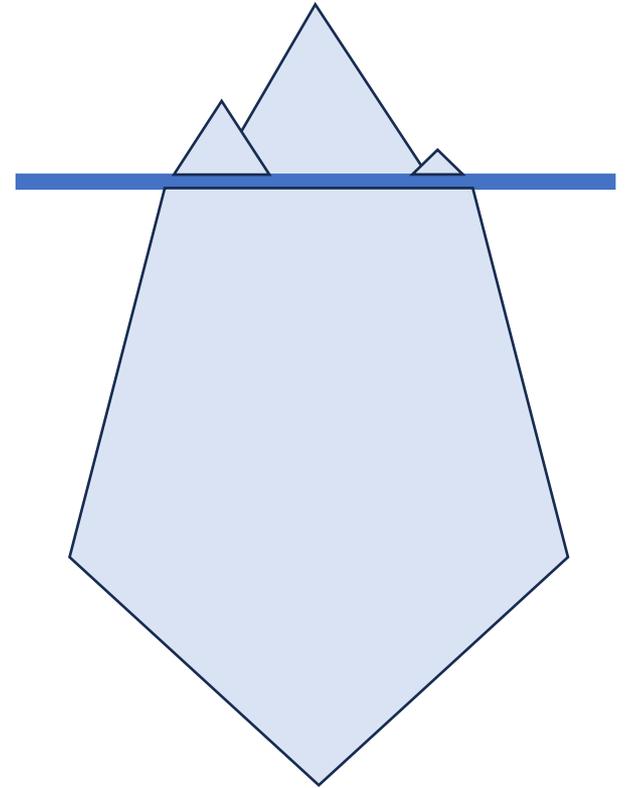


March 27, 2025

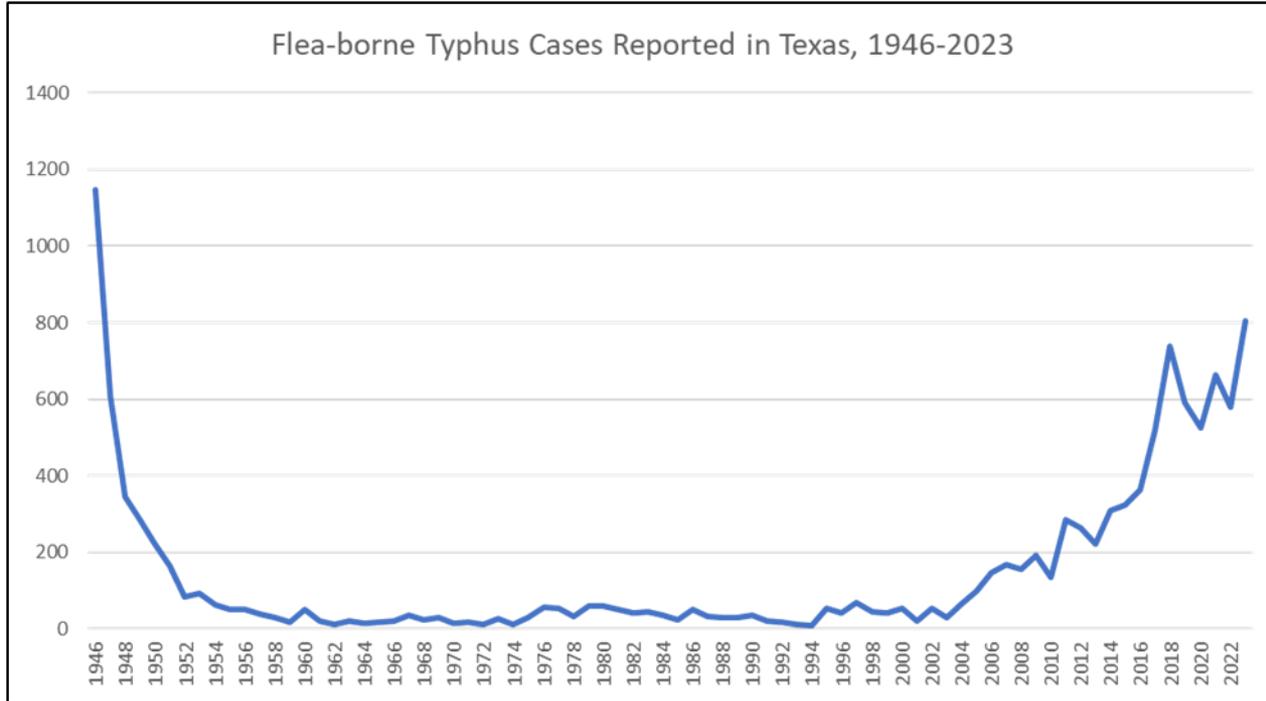
October 2024

- CDC notified by an organ procurement organization (OPO) in Texas of a hospitalized organ recipient diagnosed with murine typhus
- Further investigation reveals that the recipient of another organ from the same donor died 11 days following transplantation; testing at outside lab confirms murine typhus
- Donor died following a brief illness attributed to a noninfectious etiology

- CDC laboratories receive residual blood and tissue specimens from the donor
- DNA of *Rickettsia typhi* detected by PCR in all residual specimens
- Antigens of *R. typhi* detected by immunohistochemical stain in both pre-transplant allograft biopsies

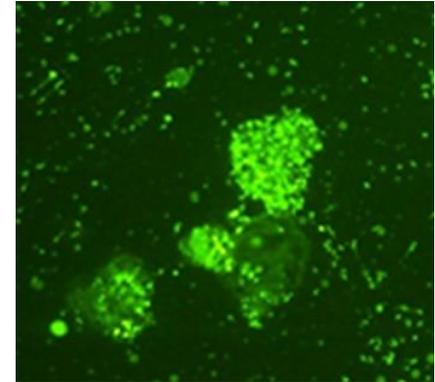
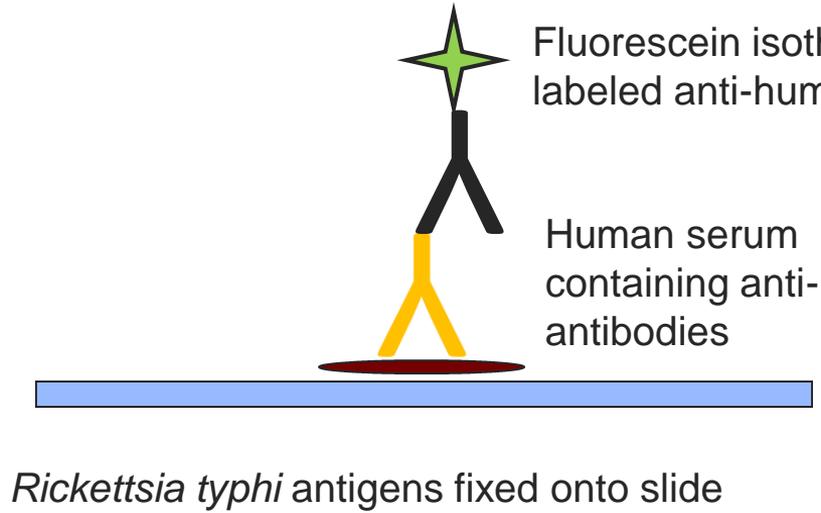
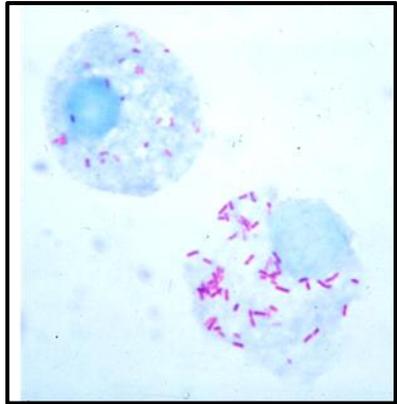


Return of murine typhus in Texas: a sleeping giant awakens



Sources: 1946-1993 Texas Department of State Health Services (TDH) Statistics of Communicable and Infectious Diseases; 1994-2007 TDH/DSHS Epi Annual Reports; 2008-2023 Finalized & Provisional (2023) NEDSS Data (courtesy of Bonny Mayes (TDSS))

Indirect immunofluorescence antibody (IFA) assay



1/32 1/64 1/128 1/256...

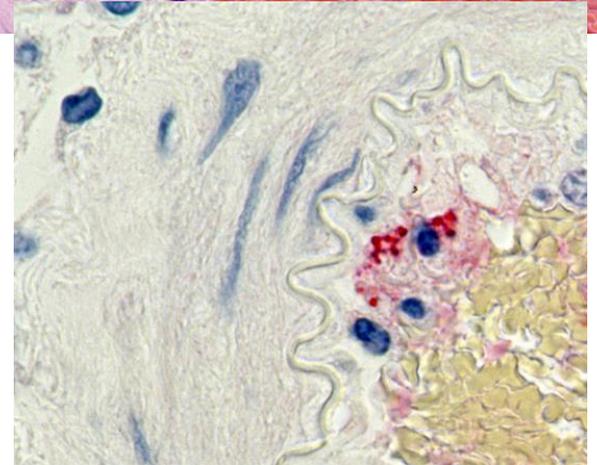
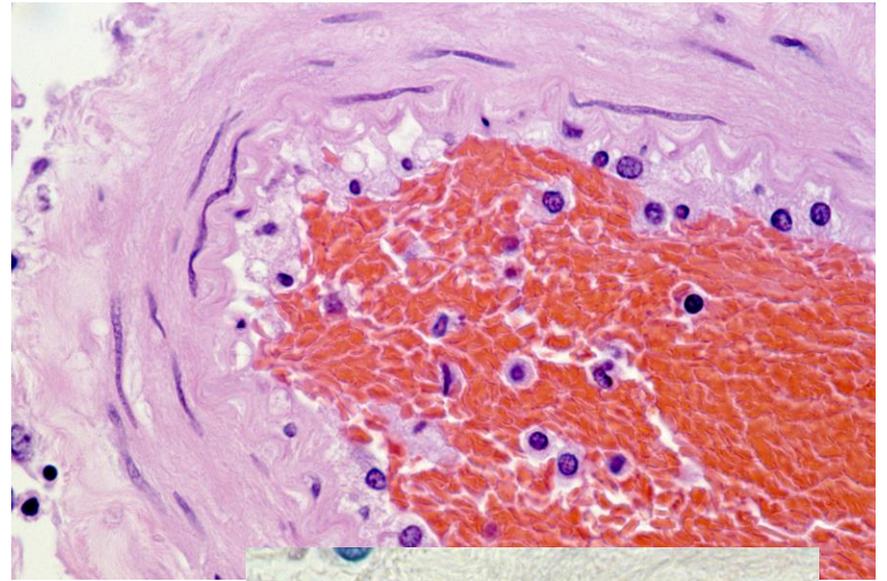


Limitations of IFA

- Diagnostic levels of antibody generally not detectable during first week of illness
- Background seroprevalence in the United States is unknown
- Confirmation of infection requires paired serum (acute and convalescent specimens)
- Early IgM antibodies relatively non-specific; antibodies elicited by other gram-negative bacteria can cross react with *Rickettsia* spp.
- Cross-reactivity with antigens of spotted fever group *Rickettsia* described in ~20-40%

Molecular methods: Strengths and limitations

- Direct evidence of infection
- Confirmatory result achievable with a single specimen
- Expensive relative to IFA
- Pathophysiology of infection limits sensitivity of conventional PCR limited during early stages of disease



Diagnostic assays for murine typhus

- IgG IFA for *Rickettsia typhi* (*serum*)
 - e.g., ARUP, LabCorp, Quest Diagnostics
 - CDC and some state health departments
- PCR for *Rickettsia* spp. (*whole blood*)
 - e.g., Quest Diagnostics
 - CDC and some state health departments
- Metagenomic DNA sequencing (*plasma*)
 - e.g., Karius[®]

BRIEF REPORT

Characteristics of *Rickettsia typhi* Infections Detected with Next-Generation Sequencing of Microbial Cell-Free Deoxyribonucleic Acid in a Tertiary Care Hospital

Fernando H. Centeno,¹ Todd Lasco,^{2,3} Asim A. Ahmed,⁴ and Mayar Al Mohajer^{1,3}

¹Department of Medicine, Baylor College of Medicine, Houston, Texas, USA, ²Department of Pathology and Immunology, Baylor College of Medicine, Houston, Texas, USA, ³Baylor St. Luke's Medical Center, Houston, Texas, USA, ⁴Medical Affairs, Karius, Redwood City, California, USA

10 patients diagnosed with murine typhus at one medical center in Houston

Karius[®] Test

Case Report

Successful Detection of Unrecognized *Rickettsia typhi* in Pregnancy Using Cell-Free Next-Generation Sequencing

Irene A. Stafford,¹ Fernando H. Centeno,² Mayar Al Mohajer,³ George Parkerson,³ Laila Woc-Colburn,^{3,4} Angelica Janice Burgos-Lee,⁵ Martha Rac,¹ James Dunn,⁶ and Kenneth Muldrew⁶

Murine typhus diagnosed in 2 pregnant women at one tertiary care hospital in Houston

Centers for Disease Control and Prevention

MMWR

Weekly / Vol. 72 / No. 31

Morbidity and Mortality Weekly Report

August 4, 2023

Fleaborne Typhus–Associated Deaths — Los Angeles County, California, 2022

Jemma Alarcón, MD^{1,2}; Armine Sanosyan, MPH²; Zuelma A. Contreras, PhD²; Van P. Ngo, MPH²; Ann Carpenter, DVM¹; Jill K. Hacker, PhD³; William S. Probert, PhD³; Dawn Terashita, MD²; Sharon Balter, MD²; Umme-Aiman Halai, MD²

Unsuspected fatal murine typhus diagnosed in LA County

Knowledge Check #5

The best laboratory test to confirm acute infection with *Rickettsia typhi* is:

- A. IgM IFA of serum.
- B. IgG IFA of serum.
- C. Molecular testing (e.g., nucleic acid amplification or metagenomic sequencing) of whole blood.
- D. Cell culture isolation of whole blood.

Knowledge Check #5 - Answer

The best laboratory test to confirm acute infection with *Rickettsia typhi* is:

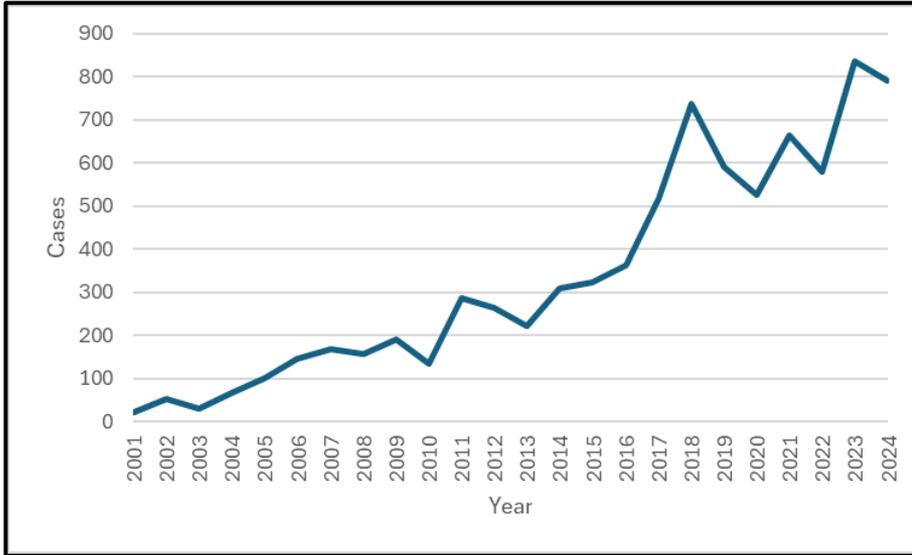
- A. IgM IFA of serum.
- B. IgG IFA of serum.
- C. **Molecular testing (e.g., nucleic acid amplification or metagenomic sequencing) of whole blood.**
- D. Cell culture isolation of whole blood.

Activity of doxycycline (continued)

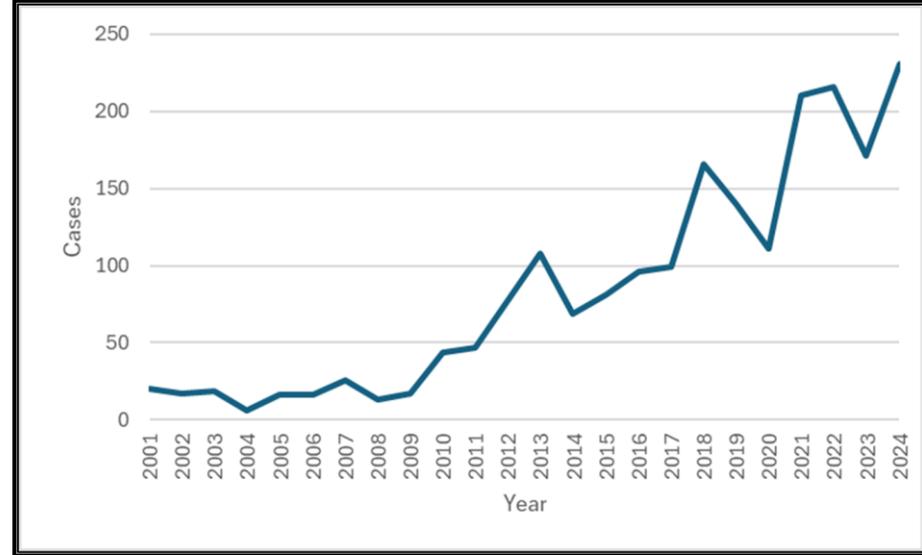
Actinomyces israelii
Anaplasma spp.
Bacillus anthracis
Balantidium coli
Bartonella spp.
Borrelia burgdorferi
Borrelia recurrentis
Brucella melitensis
Brucella suis
Brucella abortus
Burkholderia pseudomallei
Burkholderia mallei
Calymmatobacterium granulomatis
Campylobacter fetus
Chlamydia pneumoniae
Chlamydia psittaci
Chlamydia trachomatis
Coxiella burnetii
Dientamoeba fragilis
Ehrlichia spp.
Eikenella corrodens

Francisella tularensis
Leptospira spp.
Mycoplasma pneumoniae
Mycobacterium marinum
Mycobacterium fortuitum
Neisseria gonorrhoeae
Neisseria meningitidis
Nocardia asteroides
Orientia spp.
Pasturella multocida
Plasmodium falciparum
***Rickettsia* spp.**
Staphylococcus aureus
Streptobacillus moniliformis
Spirillum minus
Treponema pallidum
Treponema pertenue
Tropheryma whipplei
Ureaplasma urealyticum
Vibrio cholerae
Vibrio vulnificus
Yersinia pestis

Murine typhus, Texas and California, 2001-2024



Data courtesy of Bonny Mayes, M.A.,
Zoonoses Control Branch, Texas
Department of State Health Services



Data courtesy of Anne Kjemtrup, D.V.M., PhD,
Vector Borne Disease Section, California
Department of Public Health

Murine Typhus Outbreak Presenting as Multisystem Inflammatory Syndrome in Children During SARS-CoV-2 Pandemic

Zain Alamarat, MD, Norma Pérez, DO, Susan Wootton, MD, Ankur Kamdar, MD, Keely Smith, MD, Gloria P. Heresi, MD, and Michael Chang, MD

Review Article

Typhus group Rickettsia community-acquired bacterial central nervous system infections: We must think outside the box!

Pauline B. Roxas^a, Justice Cruz^b, Nicole Rae Horelka^c, Cesar Burgos^d, Jana Radwanski^e, Fernando Baires^f, Miguel Sierra-Hoffman^{g,h}, Heike Hesse^{i,*}, Amy C. Madril^l



Case Report: Renal Failure due to Focal Segmental Glomerulosclerosis in a Patient with Murine Typhus

Lucas S. Blanton,^{1*} Megan A. Berman,² and Marjan Afrouzian^{3,2}

¹Division of Infectious Diseases, Department of Internal Medicine, University of Texas Medical Branch, Galveston, Texas; ²Division of General Medicine, Department of Internal Medicine, University of Texas Medical Branch, Galveston, Texas; ³Department of Pathology, University of Texas Medical Branch, Galveston, Texas

Ischemic Hepatitis and Septic Shock Secondary to Murine Typhus Infection in Pregnancy

Marissa Berry, MD¹ , Amanda M. Wang, MD², Rana F. Lahham, MD², Xue Zhang, MD², Luis D. Pacheco, MD²

¹ Division of Maternal Fetal Medicine, The Ohio State University, Columbus, Ohio

² Division of Maternal-Fetal Medicine, The University of Texas Medical Branch, Galveston, Texas

Address for correspondence: Marissa Berry, MD, Division of Maternal Fetal Medicine, The Ohio State University, 395 W 12th Ave, Columbus, OH 43210 (e-mail: Marissa.Berry@osumc.edu).

AJP Rep 2024;14:e185–e187.

Case Report: Early Doxycycline Therapy for Potential Rickettsiosis in Critically Ill Patients in Flea-Borne Typhus-Endemic Areas

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LOCALIZED MYOSITIS AND TRANSIENT ENCEPHALOPATHY AS PRESENTING SYMPTOMS IN MURINE TYPHUS

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MAJOR ARTICLE



Distinguishing Multisystem Inflammatory Syndrome in Children From Typhus Using Artificial Intelligence: MIS-C Versus Endemic Typhus (AI-MET)

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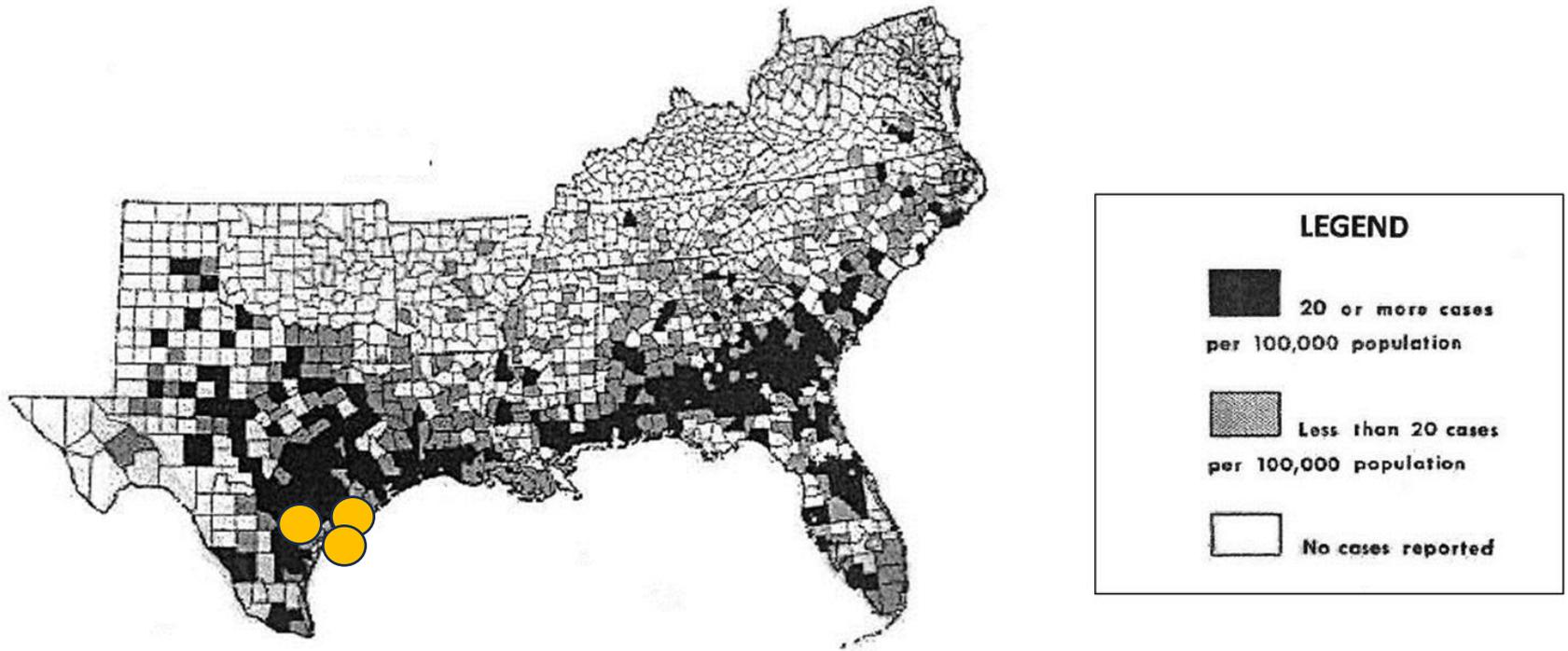
Murine Typhus Presenting as Septic Acute Cholangitis in a Young Woman From South Texas

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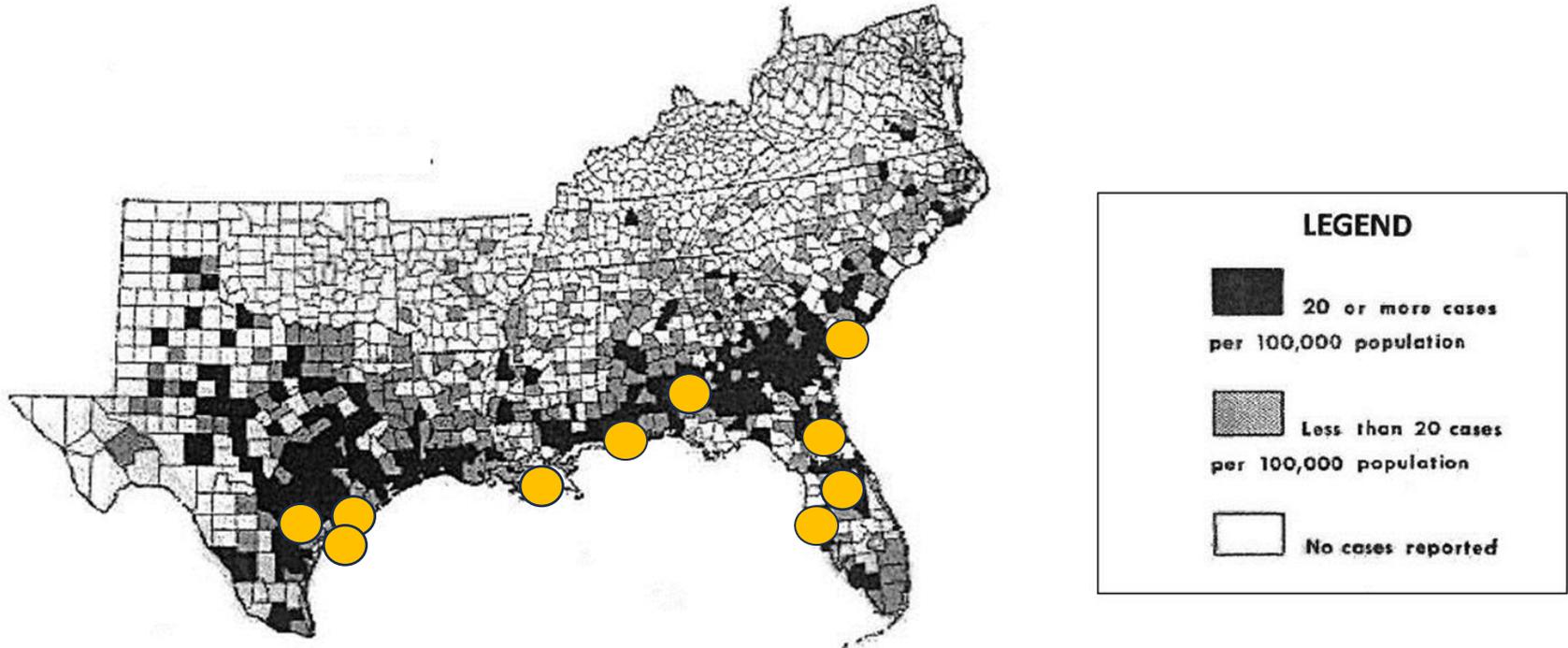
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Incidence of murine typhus in the southeastern United States, 1944



Publ Hlth Rep 1952; 67: 1249-57

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Publ Hlth Rep 1952; 67: 1249-57

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