



Ticks, Mites, Lice, and The Diseases They Transmit

Paul G. Auwaerter, MD

Johns Hopkins University School of Medicine

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Disclosures of Financial Relationships with Relevant Commercial Interests

- Research: Pfizer (investigational Lyme disease vaccine)
- Consulting: medical-legal, Tonix Pharmaceuticals, Tarsus Pharmaceuticals

Why the Board Exam Loves These Infections Play The Match Game

Condition

- Scrub typhus
- Louse-borne relapsing fever
- Tick-borne relapsing fever
- Boutonneuse (Mediterranean) fever
- Louse-borne epidemic typhus
- Endemic (murine) typhus

Pathogen

- *Rickettsia conorii*
- *Rickettsia prowazekii*
- *Borrelia recurrentis*
- *Borrelia hermsii*
- *Borrelia turicatae*
- *Rickettsia typhi*
- *Orientia tsutsugamushi*

Tick-borne Diseases of North America General Principles I

- Initial, early presentation non-specific:
 - "Flu-like illness" (e.g., fever, headache, myalgia)
- Diagnosis is clinical
 - Treatment is empiric—must start prior to return of diagnostic testing
- Rash/lesion +/- especially early
- Asymptomatic:symptomatic ratio is high

Ref: Diagnosis and Management of Tickborne Rickettsial Diseases: Rocky Mountain Spotted Fever and Other Spotted Fever Group Rickettsioses, Ehrlichioses, and Anaplasmosis — United States. A Practical Guide for Health Care and Public Health Professionals. MMWR May 13, 2016 / 65(2):1–44

Tick-borne Diseases of North America General Principles II

Seasonal but not always

Geography informs etiology, but it is evolving for many

Lab tip-offs:

- Thrombocytopenia
- Leukocytosis or leukopenia
- Elevated LFTs

Doxycycline is preferred therapy for most

- (All ages including children, e.g., RMSF, ehrlichiosis...ex. Lyme < 8 yrs)

Prognosis is worse at age extremes < 10 and > 60 yrs

Tick vectors

- Ticks cause 95% of vector-borne disease in the US
- Co-infections in some patients

The Major Tick-borne Diseases of North America

- **Lyme disease (separate talk)**
- Rocky Mountain spotted fever (RMSF)
- Ehrlichiosis
- Anaplasmosis
- Babesia spp.
- Relapsing fever (Borrelia spp.)

Other Tick-borne Diseases of North America

- Tick paralysis
- Southern tick associated rash illness (STARI)
- Viruses:
 - Powassan (Deer Tick Virus Lineage II, flavivirus)
 - Colorado tick fever (coltivirus)
 - Heartland virus (phlebovirus)
 - Bourbon virus (thogotovirus)
- Spotted Fever Group Rickettsia (partial)
 - *R. parkeri*
 - *R. rickettsii* subsp. californica
- Coxiella burnetii (rarely from ticks)
- Tularemia
 - (< 10% tickborne)
- Other Borrelia
 - *B. miyamotoi*
 - *B. mayonii*

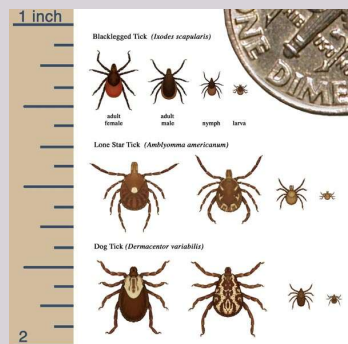
Ticks: Arachnids, Not Insects

- Number of species
 - >900 species or subspecies worldwide
 - 90 species in North America, handful cause most human infections
- Hematophagous arthropods
 - Parasitize every class vertebrates $\equiv$ entire world
- Two major families
 - Ixodidae, >700 species (hard ticks, attach & engorge)
 - Argasidae, >190 species (soft ticks, bite multiply & briefly)
- Four basic life stages
 - egg $\rightarrow$ larva $\rightarrow$ nymph $\rightarrow$ adult
- Vectors of human disease
 - #1 mosquitos
 - #2 ticks

Parola, Raoult. CID 2001; 32:997-928
Guglielmone, Zootaxa 2010;2528:1-28
Eisen. Ticks Tick Borne Dis 2022;12(6):102025

Top Ticks in North American that Transmit Human Pathogens (Ixodidae)

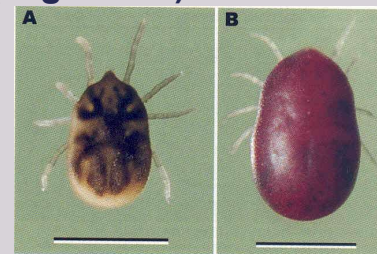
- #1 *Ixodes scapularis*
Black-legged tick
- #2 *Amblyomma americanum*
Lone star tick
- #3 *Dermacentor variabilis*
Dog tick
- #4 *Ixodes pacificus*
Western black-legged tick
- #5 *Dermacentor andersoni*
Rocky Mt wood tick



SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

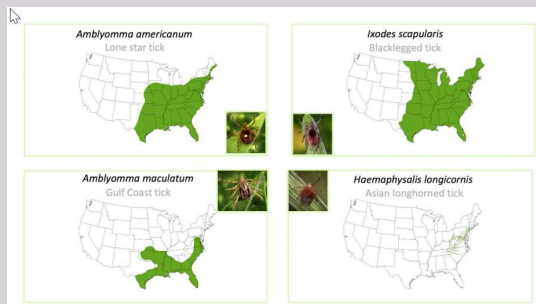
Eisen, Ticks Tick Borne Dis 2022;12(6):102025

Ornithodoros hermsii nymphal Tick Soft tick (Argasidae)



- A: shows the nymph before its infective blood meal (vector of tick-borne relapsing fever)
- B: shows it after feeding
- These are soft ticks that feed briefly at multiple spots—DO NOT remain attached
- Scale bars = 2 mm

Expanding Range and Ticks New to the US



I. Scapularis
Ticks that carry B. burgdorferi and bite humans mostly northern tick populations

H. Longicornis
May carry multiple pathogens, participation in transmitting to Humans occurs but uncertain to what degree

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Molaei, JID 2022;226(3):370-373

Selected Tickborne Diseases in the US

Home

Data Summary

Cases by Year

Cases by Month

Tickborne Disease Surveillance Data Summary

Total Reported Cases by Tickborne Disease, 2019-2022

Disease	2019	2020	2021	2022
Lyme disease	34,945	18,010	24,611	62,551
Anaplasmosis	5,655	3,639	6,744	5,633
Spotted fever rickettsioses	5,207	1,175	1,278	1,271
Ehrlichia chaffeensis ehrlichiosis	2,093	1,180	1,347	1,557
Babesiosis	2,418	1,827	1,915	
Tularemia	274	150	162	167
Undetermined ehrlichiosis/anaplasmosis	185	50	77	95
Powassan virus disease	43	21	24	47
Ehrlichia ewingii ehrlichiosis	43	21	19	25
Total	50,863	26,073	36,177	71,346

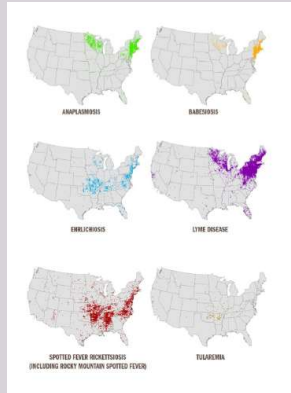
New 2022 CDC Surveillance Definition for Lyme disease

New 2022 CDC Surveillance Definition for Lyme disease

CDC, <https://www.cdc.gov/ticks/data-research/facts-stats/tickborne-disease-surveillance-data-summary.html#:~:text=During%202019%202022%2C%20state%20and,to%20CDC%20over%20the%20years.,> (accessed 5/15/23)

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

New Regions for Common Tickborne Infections



Range expanding for:

- Lyme disease
 - Upper Midwest
 - South along Appalachians
- Babesiosis
 - Expanding w/ Lyme disease range
- Ehrlichiosis
 - *E. chaffeensis*, northward

CDC, <https://www.cdc.gov/ticks/tickbornediseases/overview.html>
Accessed 1/16/23

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Question #1

62-year-old M, living in an exurb of Phoenix, Arizona, presents in early September with a three-day history of fever, myalgia, headache and rash. He works as an electrical lineman for a utility company. He lives with his family in an older adobe home with dogs. There is a faint maculopapular rash on the extremities. No tick bite recalled.

Which of the following is the most likely diagnosis?

- A. Human Monocytic Ehrlichiosis (HME)
- B. Human Granulocytic Anaplasmosis (HGA)
- C. Babesiosis
- D. Rocky Mountain Spotted Fever (RMSF)
- E. Tularemia

Question #1

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Rickettsial Species: Two Major Groups (Not a Comprehensive Rickettsial List)

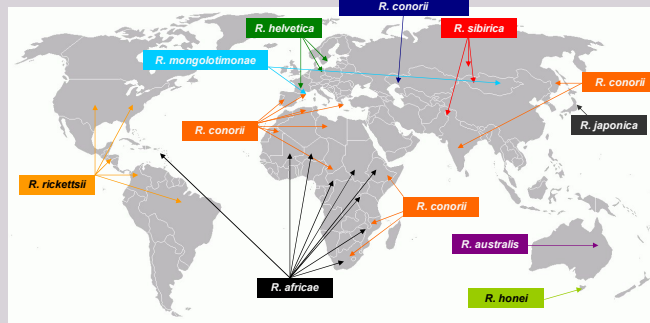
Spotted Fever Group (SFG)

- RMSF (*R. rickettsii*)
 - *R. rickettsii* subsp californica (prev 364D)
- *R. parkeri*
- *Rickettsia* sp.
- Rickettsialpox (*R. akari*)
- *R. conorii*
- *R. africae*
- *R. japonica*
- *R. australis*
- ...many more

Typhus Group

- Epidemic typhus
 - *R. prowazekii*
 - Body louse
 - Worldwide
- Murine/endemic typhus
 - *R. typhi*
 - Rat flea
 - Temperate--tropical, usually
- *R. felis*

Tick-borne Rickettsia Worldwide: Many Species

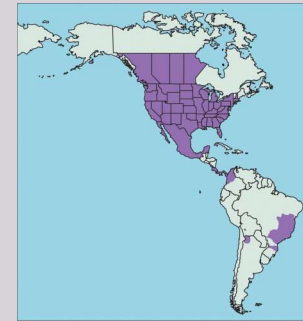


➤ 24 species causing human disease. List continues to grow.

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Parola, Clin Microbiol Rev 2013;26(4):657-702

Approximate Geographic Distribution of *R. rickettsii* in the American Continents



- Seen in all lower 48 states
- Mexico
- Parts of Canada
- Central and South America

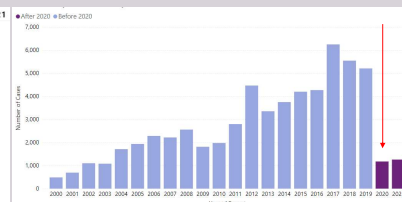
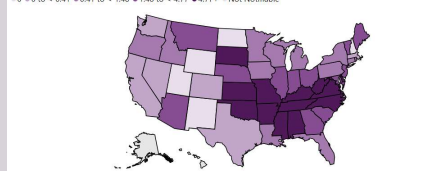
Ongoing epidemic in Northern Mexico (2015-present)

Alvarez-Hernandez, Lancet ID 2017;17(6):e189-196
Tinoco-Gracia, EID 2018;24(9):1723-25

CDC Changes:

- 2010: RMSF to "spotted fever rickettsioses" 2010 due to lack of serologic specificity includes RMSF, *R. parkeri*, Pacific Coast tick fever, Rickettsialpox, and others
- 2020: SFG criteria changes w/ IFA titer raise to $\geq 1:128$ from 1:64 to raise specificity, elimination of IFA IgM ELISA

Annual incidence (per million population) of reported spotted fever rickettsiosis—United States for 2021



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Source: CDC <https://www.cdc.gov/rocky-mountain-spotted-fever/data-research/facts-stats/index.html>

SFR in the United States

Incidence/Case Fatality 1920-2019



<https://www.cdc.gov/rocky-mountain-spotted-fever/data-research/facts-stats/index.html> (accessed 7/19/26)

Risk Factors for Fatal RMSF ('99-'07)

- Native Americans
- Age extremes: 5-9, 70+
- Alcoholism, chronic lung dz
- Delay in doxycycline:
 - Treatment after 5 days illness
- Immunosuppression

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Regan JJ, CID 2015; 60(11):1659-1666

Rocky Mountain Spotted Fever Signs and Symptoms

• Fever	99%
• Headache	91%
• Rash	88% (49% first 3 days)
• Myalgia	83%
• Nausea/vomiting	60%
• Abdominal pain	52%
• Conjunctivitis	30%
• Stupor	26%
• Edema	18%
• Meningismus	18%
• Coma	9%

Adapted from Helnick CG et al. J Infect Dis 150:480, 1984

Rocky Mountain Spotted Fever

Early: Rash Absent or Maculopapular
Starts On Extremities



Later Rash: Petechial



Fulminant RMSF Gangrenous Features (Usually Seen with Multi-organ Failure)



RMSF Diagnosis and Treatment

Start treatment upon suspicion: DON'T WAIT

- Mortality 4% if doxycycline w/i 5d of symptom onset; 35% if > 5d.

Labs: leukocytosis, thrombocytopenia, transaminitis, hyponatremia

Dx:

- Preferred:
 - Skin bxp immunohistochemistry (DFA): timely diagnosis, ~70% sensitive.
 - PCR: *R. rickettsii*-specific (blood less sensitive)
 - Skin bxp or swab (more sensitive, contact local health department → CDC)
- Acute/convalescent serology

Jay R. J Vector Borne Dis 2020;57(2):114-120

Outcome: RMSF According to Day Doxycycline Started after Sx Onset

	<u>% mortality</u>
• Day 1-5	0
• Day 6	33
• Day 7-9	27-50

Most lethal of Rickettsial infections: "Black measles"

In the US, mortality with treatment is ~2-5% (higher with delay in starting doxycycline)

Clin Infect Dis 2015; 60:1659-66

RMSF Diagnosis and Treatment

Other diagnostic issues

• Serology:

- Acute/convalescent samples
 - Not usually of timely clinical value
- IFA : gold standard; cross-reacts w/ other SFG species
 - May be helpful in confusing cases
 - IgG is best to confirm
 - IgM with low specificity

• False positives (especially IgM) common

- GA blood donor study: 11.1% IgG > 1:64, but only 28% fit case definition for hx SFGR
- Background seroprevalence up to 20% in some regions, e.g., Carolinas

• Asx infection common

- Single IgG titer insufficient for reliable diagnosis
- Both RMSF IgM & IGG can persist
- May mislead, result in unnecessary treatment

Straily A, JID 2020;221:1371
Ursery L, PLOS One May 2025

Pacific Coast Tick Fever

New Name:

Rickettsia rickettsii subsp *californica* (proposed)
(previously *Rickettsia* 364D/R. *philipii*)

Described in 1966

Transmitted by
Pacific Coast tick
(*Dermacentor occidentalis*)

Southern Oregon → Northern Baja

Common symptoms:

- Eschar
- Fever
- Headache
- Usually mild infection



Dermacentor occidentalis

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Padgett K PLOS Neg Trop Dis 2016
Paddock CF JID 2025;231(4):849-858

Question #2

31-year-old M from the Tidewater (SE) region of Virginia presents in June with a 3-day history of fever and rash.

Exam: unremarkable, but T39.2°C, discrete black eschar on leg, scattered maculopapular rash elsewhere

Which of the following is the most likely etiologic agent?

- Rickettsia rickettsii*
- Ehrlichia chaffeensis*
- Rickettsia parkeri*
- Anaplasma phagocytophilum*
- Rickettsia akari*

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“American Bouton-neuse Fever” *Rickettsia parkeri*

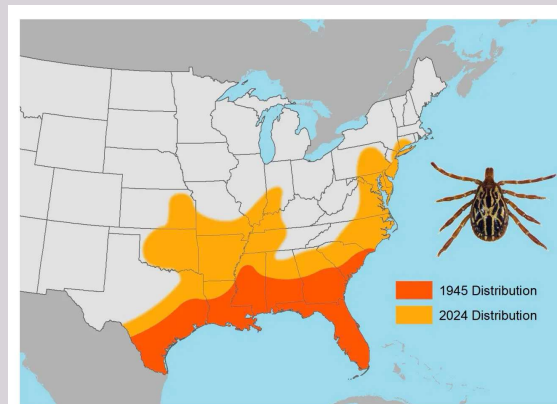
- Transmission: Gulf Coast ticks (*A. maculatum*) transmit most
 - Southeastern US, Gulf Coast
- AKA “Maculatum fever”
 - Also seen in Central and South America, including Argentina, Uruguay, parts of Brazil
- Symptoms 2-10 d post-bite
 - Headache, myalgia
 - Skin
 - Faint salmon-colored rash
 - Single or multiple eschars
- Diagnosis
 - Spotted fever group serology,
 - Immunohistochemistry
 - PCR or culture from skin bxp or swab of eschar

MMWR Morb Mortal Wkly Rep 2016; 65(28): 718-9
Kelman, Infection 2018;46(4):559-563
Scott, Trends in Micro 2022;30(5):511-512

Examples of *R. parkeri*- associated Rashes



Source: CDC



A. maculatum (Gulf Coast Tick range); first human case of *R. parkeri* in CT (2024)
Connecticut Agricultural Experimental Research Station, 2024

Question #3

22-year-old M upstate NY July c/o HA and fever x 3d now confused. No known tick bite but an outdoorsman. Exam without meningism or rash. Labs normal.
Admitted, doxycycline, CTX, vancomycin started. Head CT: normal
LP: WBC 130 60%P, 40%L, glucose: nl, protein 65 mg/dL (elevated).

Which of the following is the most likely etiologic agent?

- A. Anaplasma phagocytophilum
- B. Ehrlichia chaffeensis
- C. Heartland virus
- D. Powassan virus
- E. Borrelia miyamotoi

Question #3

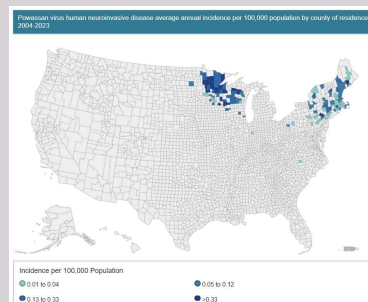
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- C. Heartland virus
- D. Powassan virus***
- E. Borrelia miyamotoi

POWV: Reported cases mostly neuroinvasive Tick-borne flavivirus infection

- Mostly present in Spring-Summer
 - But can be year-round
 - Related to nymphal Ixodes scapularis
- All ages, median 62 years, 72% male, incubation 1-5 weeks
- Clinical Syndromes
 - Neuroinvasive (90%)
 - Encephalitis (72%)
 - Meningitis (16%)
 - Other neurologic (2%)
 - Non-Neuroinvasive (10%)



- Hospitalized (90%)
- Death (11%, most > 50 years)
- Neurologic sequelae ~50%

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Krow-Lucal ER. Vect Borne Zoo Dis 2018; 18(6):286-290
<https://www.cdc.gov/powassan/data-maps/historic-data.html>

Powassan Virus Diagnosis & Care

- Antibody testing best sensitivity
 - CT or MRI may be normal; severe cases often with cerebellar changes (70%)
- CSF: IgM POWV
 - Commercial, State Public Health labs & CDC
 - Needs confirmation by plaque-reduction neutralizing test to r/o cross-reactivity with other flaviviruses
- Other:
 - Viral RNA serum, CSF, tissue
 - Performs best early in illness
 - Immunohistochemistry, fixed tissue
- Treatment: supportive care
- Prognosis: mortality ~ 10%, neurologic sequelae 50%

Plantadosi A. Inf Dis Clin N Am 2022;36(3):671-688

Question #4

- 28-year-old F presents 8d after from a safari in Tanzania
- Fever, mild headache, fatigue x 5d
- Prior to travel, immunized against yellow fever
- Took malaria prophylaxis: atovaquone/proguanil
- Temperature is 38.6°, P76, R14, BP 116/70
- Exam is unremarkable except for four punctuate eschars on the legs and bilateral inguinal lymph node enlargement
- Lab: Thick and thin blood smears (x 2) negative

Question #4

**Four
Inoculation
Eschars
(Arrows)**



Question #4

Which of the following is the most likely etiologic agent?

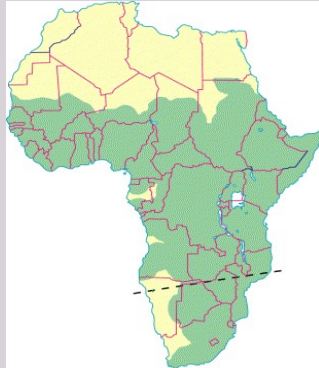
- A. *Rickettsia conorii*
- B. *Rickettsia africae*
- C. *Rickettsia rickettsii*
- D. *Anaplasma phagocytophilum*
- E. *Ehrlichia chaffeensis*

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- E. *Ehrlichia chaffeensis*

Range of *R. africae* African Tick Bite Fever (green)



Range of *R. conorii* Mediterranean Spotted Fever

Figure 4

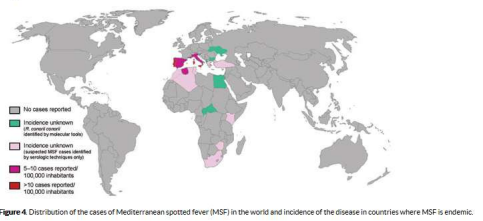


Figure 4. Distribution of the cases of Mediterranean spotted fever (MSF) in the world and incidence of the disease in countries where MSF is endemic.

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Roveri, EID 2008;14(9)

Clinical Characteristics of *R. africae* Infection

	%
Fever $\geq 38.5^{\circ}$	88
Neck muscle myalgia	81
Inoculation eschars	95
Multiple eschars	54
Lymphadenopathy	43
Rash (vesicular)	46 (45)
Death	0

Racuit D, et al. N Engl J Med 2001; 344:1504-10

African Tick Bite Fever

- Seroprevalence:
 - High in residents, *R. africae*, 30-56%
- Amblyomma ticks (cattle, ungulates)
 - Clusters of cases, multiple eschars
- Incubation period 6-7d
- Dx:
 - Biopsy or swab: PCR or MIFA
 - Serology
- Rx: doxycycline
- Complications unusual

Rickettsioses and The Returning Traveler Common Cause of Fever After Malaria, Typhoid

- Most common: 280 travelers (1996-2008)
 - Spotted fever group (83.5%)
 - 87.5% acquired in sub-Saharan Africa
- Others
 - Scrub typhus (5.7%)
 - Q fever (3.6%)
 - Typhus group (2.5%)
 - Human granulocytic ehrlichiosis (0.4%)

Jensenius M, EID 2009;15(11)

Question #5

- 48-year-old M presents in October with fever and rash
- Supervisor for apartment building in Queens, NY. Lives in cellar apartment
- Exam: T 39°C
- Brown-black 8mm eschar on RLE
- ~30 papulovesicular lesions on trunk



Question #5

Which of the following is the most likely etiologic agent?

- A. *R. rickettsii*
- B. *R. parkeri*
- C. *R. akari*
- D. *R. conorii*
- E. *Borrelia recurrentis*

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- D. *R. conorii*
- E. *Borrelia recurrentis*

Rickettsialpox

Organism

- *R. akari*

Reservoir

- House mouse

Vector

- Mouse mites

Clinical

- Single eschar
- Rash: papulovesicular (20-40) or maculopapular

Diagnosis

- PCR swab eschar/vesicle

Treatment

- Doxycycline



Maculopapular rash due to *R. akari* (CDC)

Partial DDx of Vesicular Rash

- HSV
- VZV
- Poxviruses
 - Mpox
- Rickettsialpox
- African tick bite fever
- Queensland tick typhus

Scrub Typhus

“Scrub typhus is probably the single most prevalent, under-recognized, neglected, and severe but easily treatable disease in the world”

Paris DH et al. Am J Trop Med Hyg 2013;89:301-7

Scrub Typhus

Organism

- *O. tsutsugamushi* (> 70 strains)

Vector

- Trombiculid mite (chiggers)

Geography

- Triangle from Japan to Eastern Australia to Southern Russia (rural)
 - Southern China an endemic focus (Yunnan province)

Clinical

- ~1 million cases/yr
- Severe (~ 35%) high fever
- Eschar, painful/draining lymph nodes, rash, delirium
 - Meningitis and meningoencephalitis with progressive infection
 - Development of multiorgan system failure
 - Case fatality rates up to 70% in severe/untreated infection

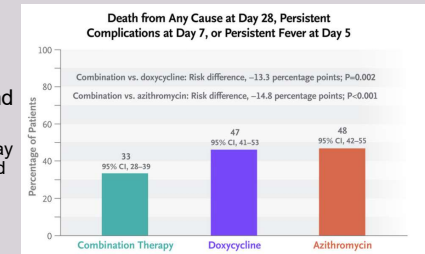


Eschar is often associated with regional lymphadenitis



Scrub Typhus Treatment

- Treatment
- Doxycycline 100 mg PO BID x 7d
 - Alt: azithromycin
- Combination: appears superior and safe
 - Doxycycline 200 mg IV twice daily day 1 (load), then 100 mg twice daily x 6d
 - PLUS
 - Azithromycin 500 mg IV twice daily d1, then 500 mg daily x 6d
- Benefits severe scrub typhus w/ organ involvement



Jang MO, AAC 2014;58(3):1488-93
Varghese GM, NEJM 2023;388:792-803

Question #6

- 31M presents in January with 3d fever, HA, malaise, and myalgia
- Works as counselor at wilderness camp in Pennsylvania
- Flying squirrels common at camp, including residing in the walls of his cabin
- Exam is notable only for fever (39.60; no rash), tachycardia (P110)

For which of the following is a diagnostic test most likely to be positive?

- A. Murine typhus
- B. Epidemic typhus
- C. RMSF
- D. Tularemia
- E. Relapsing fever

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If You Read a Question with “Flying Squirrel” You Say “Epidemic typhus” or “*R. prowazekii*”

- Rare infection in the US
 - 1976-2001, 39 cases
- Generally East Coast
- None with louse exposure (the classic vector) in N. America
 - Not “epidemic” but sporadic
 - Most with flying squirrel exposure (*Glaucomys volans*)



Lewisboro Field Guide, phot Steve Geller

MMWR 2003; 9 (10); Lancet ID 2008;8(7):417

Louse-borne Relapsing Fever (LBRF)

Organism

- *Borrelia recurrentis*

Vector

- Human body louse

Geography

- Worldwide, but now seen in Sudan, Ethiopia, Somalia, Bolivia...
- (Refugee camps, famine, natural disasters)

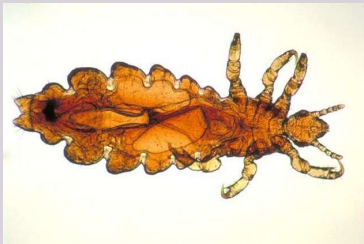
Clinical Illness

- More severe than TBRF, (incl. jaundice)

Therapy

- Doxycycline
- Jarisch-Herxheimer risk ~37-100%

Vectors of Diseases (In this Module)



Body louse infestation = pediculosis
Pediculus humanus humanus



Human flea infestations
Oriental rat flea (*Xenopsylla cheopsis*) and
the cat flea (*Ctenocephalides felis*)

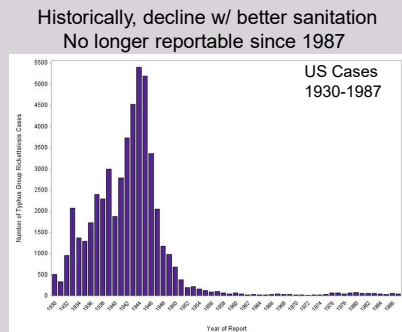
Typhus: Two Forms

	Epidemic	Endemic
Organism	<i>R. prowazekii</i>	<i>R. typhi</i>
Vector	Louse (body>>head)	Flea (rat, cat)
Who	War refugees, crowded conditions/poor hygiene	Worldwide (U.S. Southern California, Texas, Hawaii)
Severity	Lethal	Usually milder, some fatalities
Treatment	Tetracycline Doxycycline (preferred) Chloramphenicol	Tetracycline Doxycycline
Prevention	Boil clothes; delouse (malathion, permethrin)	Flea prevention (cats, domestic animals) Reduce rodent population
Recrudesce	Brill-Zinsser Disease (years-decades)	None known

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Murine (or Endemic) Typhus

- In the US, mostly seen in California, Hawaii, and Texas
- Agent: *Rickettsia typhi*
- Infected cat/rat flea feces → skin
- Most don't recall a flea bite
- Usually non-specific febrile infection
 - Underdiagnosed
 - ~50% with rash
- Occasional severe disease:
 - Meningoencephalitis
 - Pneumonitis
 - Shock



Dittrich, Lancet Global Health 2015;3:e104; Blanton Am J Trop Med 2017;96(1):53
CDC, accessed 7/6/2026 <https://www.cdc.gov/typhus/about/murine.html>

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™

Morbidity and Mortality Weekly Report (MMWR)

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

Weekly / August 4, 2023 / 72(31);838-843

Incidence:
2010: 1
2022: 171

- Deaths 3 (autopsies)
- HLH
- Myocarditis
- Septic shock
- Late or no doxycycline

Case fatality usually < 1.0%
LA Series: 1.8%

Suspect: exposure to rodents, cats
Homeless

→ Doxycycline

Murine (or Endemic) Typhus

Consider especially febrile illness:

- CA, TX, Gulf coast

Dx:

- Serology *R. typhi* (IFA)
- Acute/convalescent, 4x rise
- Cross-reacts with *R. prowazekii* and SFG rickettsia

PCR

- Blood, often negative

Treatment:

- No RCTs
- Doxycycline (preferred)
 - Azithromycin: open-label trial found azithromycin inferior to doxy
- Alternatives: limited data
 - Chloramphenicol
 - Levofloxacin
 - Ciprofloxacin

Dittrich, Lancet Global Health 2015;3:e104; Blanton Am J Trop Med 2017;96(1):53
Newton, CID 2019;68(1 March):739

Flea-borne Spotted Fever/rickettsiosis *R. felis*



Found globally; underdiagnosed
Discovered in 1990

- Cat fleas

Often lumped in with murine typhus

Usually mild illness but can be severe

- Fever, headache
- Rash variable (macular)
- Eschar in 12%

Dx:

- RMSF serology is often reactive
 - Acute/convalescent *R. typhi* serology
- PCR (tissue)

Treatment: doxycycline

Martinez MAC, Resp Rep Trop Med 2021;12:1-15

Other Location-specific Tick-borne Rickettsioses: Partial

Queensland tick typhus, *R. australis*

- Australia-Queensland, New South Wales, Tasmania, coastal areas of eastern Victoria

North Asian tick fever, *R. sibirica*

- North China; Mongolia; Asiatic areas of Russia

Tick-borne lymphadenopathy (TIBOLA) or *Dermacentor*-borne necrosis erythema and lymphadenopathy (DEBONEL)

- Ascribed to *R. slovaca* or *R. raoultii*:
 - Europe and Asia

Far-Eastern tick-borne rickettsiosis, *R. heilongjiangensis*:

- Far East Russia and northern China

Oriental spotted fever, *R. japonica*:

- Japan

Thai tick typhus, *R. honei*:

- Thailand, Australia, Tasmania, Flinders Island

Australian spotted fever:

- *R. marmionii*

Question #7

- 43F visited southern Missouri on vacation, returns 7d later with fever, headache and diffuse myalgia x 3d
- Physical examination: no findings
- Laboratory evaluation
- WBC: 2.1/mm³ (80% PMNs, 10% lymphocytes, 8% monocytes)
- Hemoglobin: 13 g/dL, hematocrit: 38%
- Platelets: 105,000/mm³
- AST: 364 U/L, ALT: 289 U/L Tbili 2.7
- Renal function: normal

Question #7

Which of the following is the most likely etiologic agent?

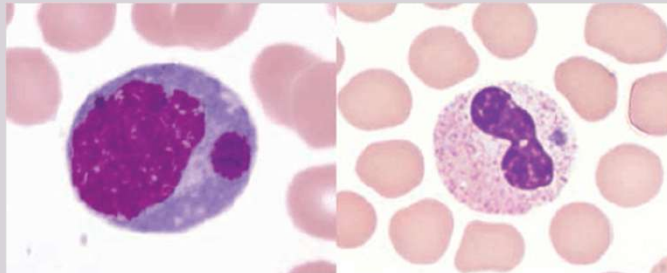
- A. *Anaplasma phagocytophilum*
- B. *Ehrlichia chaffeensis*
- C. *Borrelia hermsii*
- D. *Babesia divergens*
- E. *Borrelia burgdorferi*

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Which of the following is the most likely etiologic agent?

- A. *Anaplasma phagocytophilum*
- B. *Ehrlichia chaffeensis**
- C. *Borrelia hermsii*
- D. *Babesia divergens*
- E. *Borrelia burgdorferi*

Morulae



HME

HGA

Seen 2%-38 Monocytes / Seen 20%-75% PMNs/Bands

Human Monocytic Ehrlichiosis (HME)

E. chaffeensis

Vector: Lone star tick

Rash: ~30%

- Maculopapular or petechial

Labs: LFTs ↑, leukopenia, thrombocytopenia

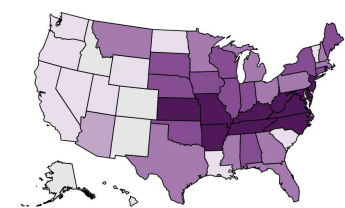
Mortality: 2.7%

Diagnosis

- PCR
- Morulae (2-38%)
- Serology: acute/convalescent
- Treatment: doxycycline

Annual incidence (per million population) of reported *Ehrlichia chaffeensis* ehrlichiosis—United States for 2021

0 0.0 to < 0.2 0.2 to < 2.2 2.2 to < 8.4 8.4+ Not Notifiable



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Source: CDC <https://www.cdc.gov/ehrlichiosis/data-research/facts-stats/index.html> (accessed 6/22/24)

Other Ehrlichia (Less Common)

Organism	Vector	Geography	Risk	Mortality
<i>E. ewingii</i> (aka canine Ehrlichia)	Amblyomma americanum (Lone star tick)	Most cases in Southcentral US	Immune compromised	Low
<i>Ehrlichia muris euclairensis</i> (former Ehrlichia muris-like [EML] agent)	Ixodes scapularis (black-legged tick)	Wisconsin, Minnesota	Elderly, immune compromised	Low

Human Granulocytic Anaplasmosis

Anaplasma phagocytophilum

Vector: *Ixodes scapularis*

Rash: rare

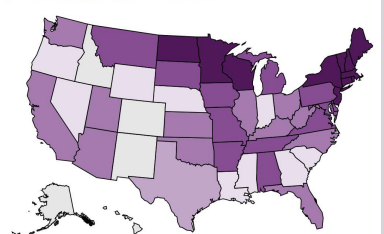
Labs: LFTs, leukopenia, thrombocytopenia

Mortality: 0.3-0.7% (immunosuppressed ↑ 16 x)

Diagnosis: same as HME (but morulae seen > 25%)

Annual incidence (per million population) of reported anaplasmosis—United States for 2017

0 0.0 to < 0.13 0.13 to < 1.1 1.1 to < 9.4 9.4+ Not Notifiable



Geography: cross-reactivity with *E. chaffeensis* may account for much of Southern state representation

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Source: CDC <https://www.cdc.gov/anaplasmosis/hcp/statistics/index.html> (accessed 6/22/24)

Borrelia miyamotoi (AKA Hard Tick Relapsing Fever HTRF)

Unusual vector: Ixodes ticks

- Epidemiology = Lyme disease
- Appears similar to HGA (rash infrequent)
- Severe infection may be sepsis-like
- Meningoencephalitis in immunocompromised
- ↓ WBC, ↓ PLT, ↑ LFTs

Diagnosis: PCR, blood smear (observing spirochetes), serology

Treatment: similar to Lyme disease

Telford, Clin Microbiol Infect 2015
<https://www.cdc.gov/relapsing-fever/about/about-htrf.html> (accessed 7/19/26)

Tickborne Relapsing Fever US

Borrelia spp. (mainly *B. hermsii*)

- Ornithodoros soft ticks (brief, painless)

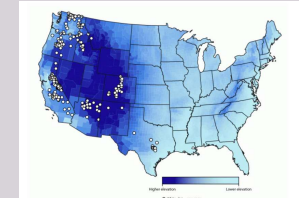
Epidemiology

- Western states; 14-45 cases/yr
- Rustic housing and rodents
- Elevation 1500-8000 feet

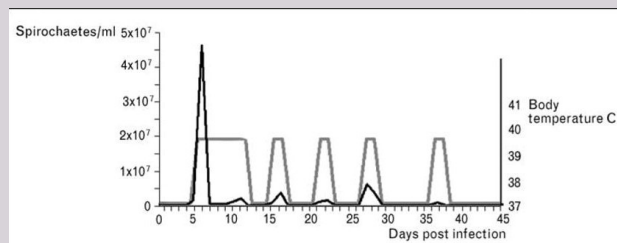
Clinical Manifestations

- Fever (relapsing), HA, myalgia, N/V
 - Can be severe: ARDS
- Laboratory
 - AKI, ↓ platelets,
 - Dx: blood microscopic exam, PCR
- Rx: PCN, doxycycline
 - Jarisch Herxheimer reaction in 54%

FIGURE: Cases* of soft tick relapsing fever (n=210), by county of exposure – United States, 2012-2021

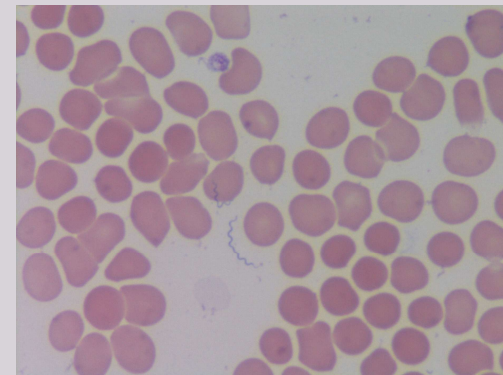


Beeson AM MMWR 2023;72(23):777-781



Relapsing Fever: recurrent bacteremia (black line) correlates with sudden fever (grey).

After initial bacteremia, relapses are lower and fever duration somewhat shorter.



Diagnosis: observation of spirochetes in blood film

Question #8

- 48F c/o headache and fatigue worsening over 2 months since May tick bite
 - PMH: negative
 - SH: Married, works from home, has a dog, resides in suburban eastern PA
 - Treated with doxycycline for Lyme disease, no benefit
- Physical examination: afebrile, normal vital signs, no findings
- Laboratory evaluation :
 - WBC: 7.0 cells/mm³ (70% PMNs, 18% lymphocytes, 12% monocytes)
 - Hemoglobin: 11.8 g/dL, hematocrit: 35%
 - Platelets: 145,000/mm³
 - ALT: 22 U/L
 - Babesia IgG 1:128 (positive ≥ 1:64)
 - Blood smear: no parasites

Question #8

What is the best recommended next step?

- A. Check Babesia duncani serology
- B. Check Babesia PCR
- C. Repeat blood smear
- D. Azithromycin + atovaquone for 7-10 days
- E. None of the above

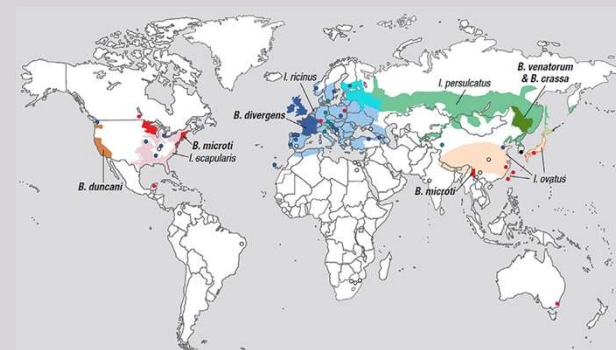
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- A. Check Babesia duncani serology
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- C. Repeat blood smear
- D. Azithromycin + atovaquone for 7-10 days
- E. None of the above***

Low Babesia microti IgG titer + negative smear + nonspecific chronic symptoms should not trigger treatment

Babesia spp: Global

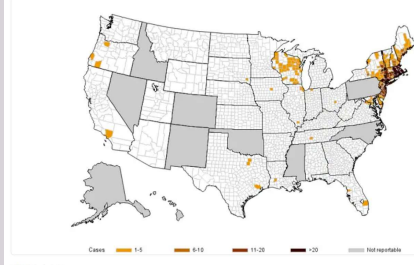


SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Vannier et al. NEJM 2012 366:2397

Babesia in the US

Number* of reported cases of babesiosis, by county of residence — 40 states, 2020†, ‡



SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

<https://www.cdc.gov/babesiosis/maps-graphs> (accessed 7/20/26)

- Not reportable in all states
- Occurs within Lyme disease geography, but is more limited
- Vector:
 - *B. microti* → *Ixodes scapularis*
 - *B. duncani* → *Dermacentor albipictus*
 - (likely, west coast only)
 - < 20 documented cases
- 1500-2500 cases/yr

Babesia Species

- Malaria-like parasite, resides in RBCs
- Geography: *Babesia microti* (most cases in U.S.)
 - Nantucket, Martha's Vineyard, Long Island, Mid-Atlantic/New England, upper Midwest (similar to Lyme disease)
- Range of illness: Asx to “flu-like” to fatal
- **Was a** common cause of blood transfusion-related infection in US
 - Though decreasing through screening
 - But question may still appear on the boards

Severe Babesiosis

- n=34, Long Island NY
- Clinical manifestations
 - 41% Multi-organ failure
 - ARDS, DIC, CHF, ARF
- Risk factors:
 - age >60
 - splenectomy,
 - immunosuppression (e.g., HIV, rituximab)
- Labs
 - increased LTFs,
 - thrombocytopenia
 - anemia (Hb<10),
 - parasitemia (>10%)
- Immunocompromised mortality
- > 20%

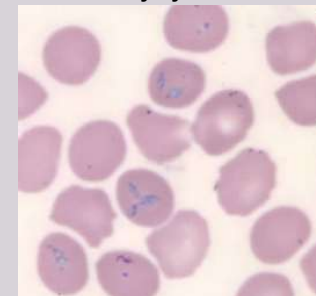
Hatcher JC, et al. Clin Infect Dis 2001; 32:1117-25

Babesiosis: Smear Diagnosis

Maltese Cross Tetrads



Species Level Identification only by PCR



Diagnosis of Babesiosis

- May observe hemolysis
- Wright-Giemsa-stained thin blood smears
 - 1-3 μ intraerythrocytic merozoites
 - Parasitemia range: 0-80% (may be confused with malaria)
 - Maltese cross: diagnostic (not seen w/ malaria)
 - Quick, if technical expertise available
- PCR: now widely available
 - Highly specific, but often send-out test = delay
- Serology (IFA)
 - High titer or acute/convalescent c/w active or recent infection
 - Low titer, negative smear: don't treat!

Treatment of Babesiosis

- Severe (2020 IDSA guidelines)
 - Atovaquone 750 mg PO q12h + Azithromycin 500-1000 mg IV q24h
 - Step down with improvement to lower dose azithromycin
 - Previous: quinine + clindamycin (now an alternative)
 - Duration: 7-10d (may require longer for persistent parasitemia or immunosuppressed)
- Blood exchange transfusion: severe hemolysis, > 10% parasitemia or 5-10% + organ compromise
 - *B. divergens*, many require
 - *B. microti*, some cases
 - Evidence for benefit, observational w/ 78% lower adjusted odds of death/readmission^a
- Mild-moderate severity
 - Azithromycin PO plus atovaquone PO

Krause et al CID 2021; 72 (2) e49-65; ^aSTOP-BABESIOSIS
JAMA Internal Medicine. 2020;186(5):597-607

Colorado Tick Fever

Transmission *D. andersoni*

- 4,000-10,000 feet

Agent: Coltivirus

Sx: range from

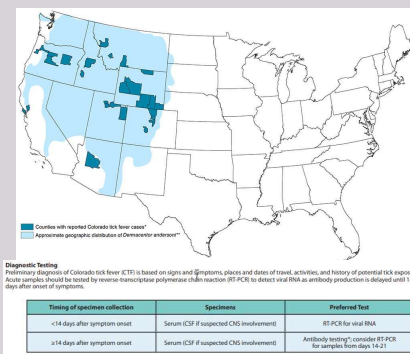
- Mild febrile flu-like illness
 - May include rash: maculopapular or petechial
- Rare: severe illness multi-system, neuroinvasive disease

Labs:

- $\downarrow$ WBC, atypical lymphocytes
- $\downarrow$ plt

Dx: samples to state lab, some commercial lab testing

- Not a reportable illness



SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Cluster of Tick Paralysis Cases

- Four cases within 20 miles of each other
 - Ages 6, 58, 78, 86 years
- Ticks on neck or back
 - Usually dog ticks or Rocky Mt wood ticks
- Ascending motor paralysis without sensory loss
- Treatment: remove tick = cure
- Pathogenesis: neurotoxin in tick saliva

MMWR 2006; 55: 933-5

Question #9

- A 59-year-old man from Missouri presents with fever (390), headache, myalgia, anorexia, nausea, one week after removing an engorged tick from his groin. No travel
- Exam: unremarkable except ill appearing, no rash
- Lab: WBC 2300, PLT 42,000, ALT 111
- Suspect ehrlichiosis (but no morulae on blood smear)

Question #9

After sending appropriate diagnostic tests the patient has not improved after three days of doxycycline.

Which of the following is the most likely etiologic agent?

- A. *R. rickettsii*
- B. *B. burgdorferi*
- C. *R. parkeri*
- D. Heartland virus
- E. Severe fever with thrombocytopenia syndrome virus

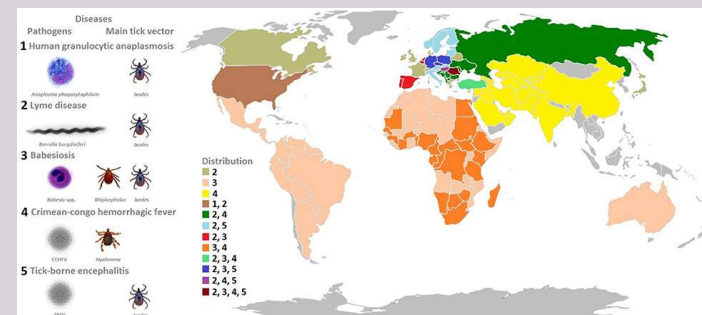
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- D. Heartland virus***
- E. Severe fever with thrombocytopenia syndrome virus

But Wait: There's More (#4) and More (#5)



SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Front Cell Infect Microbiol, 2017;7:114

Tick-borne Infections: Some Testable Points

- Rash: RMSF rash appears after several days of fever and viral-like prodrome
 - Meningococcal rash is earlier
 - No bite site (no tache noire)
 - Give doxycycline, even for kids
- Blood smear may be helpful
 - Morulae: PMNs = Anaplasma, Monocytes = Ehrlichia
 - Spirochete: relapsing fever Borrelia or *B. miyamotoi*
 - Erythrocyte inclusions: Babesia

Tick-borne Infections: Some Testable Points

Babesia:

- No longer a common cause of blood transfusion infection in the US
- Splenectomy or immunocompromise = severe infection risk

Co-infections in the US: may complicate some infections, especially after a black-legged tick (*I. scapularis*) bite

- Lyme disease + Babesia OR Lyme disease + HGA mostly

Flying squirrels: epidemic typhus

Rodent-infested urban house: Rickettsialpox

- Mouse mites.
- Tache noire first → > dozen papules/vesicles

Key Features of Select Tick, Louse, and Mite-borne Diseases

Disease	Usual Organism	Geography	Eschar	Rash	High Fever	Comment
Tick-borne						
Rmsf	<i>R. Rickettsii</i>	N.C.S. America	No	Yes	Yes	Serious
Stari	Unknown	S. Sc, Ma	No	Yes (Em-like)	No	Mild
<i>R. Parkeri</i>	<i>R. Parkeri</i>	Gulf, South, Atlantic	Yes (≥1)	Yes	No	
African Tick Bite Fever	<i>R. Africae</i>	Sub-saharan Africa	Yes (≥1)	Yes	No	Mild
Hme	<i>E. Chaffeensis</i>	S. Sc, Ma	No	Yes (+/-)	Yes	Cytopenias Transaminitis
Hga	<i>A. Phagocytophilum</i>	Ne, Ny, Ma, Mw	No	Yes (Rare)	Yes	Cytopenias Transaminitis
Babesiosis	<i>B. Microti</i>	Ne, Ny, Ma, Mw	No	No	Yes	
Tbrf	<i>B. Hermsii</i>	W Mountains	No	No	Yes	Spirochetes In Blood Smear
Louse-borne						
Epidemic Typhus	<i>R. Prowazekii</i>	Worldwide	No	Yes	Yes	War, Refugee Camps Serious
Mite-borne						
Rickettsialpox	<i>R. Akari</i>	Worldwide	Yes (Single)	Yes (V)	No	Mouse Exposure
Scrub Typhus	<i>O. Tsutsugamushi</i>	India, Asia, N. Australia	Yes	Yes	Yes	Serious

C	Central	NY	New York
EM	Erythema Migrans	RMSF	Rocky Mountain Spotted Fever
HGA	Human Granulocytic Anaplasmosis	S	South
HME	Human Monocytic Ehrlichiosis	SC	South Central
MA	MidAtlantic	SE	Southeast
MW	Mid-West	STAR	Southern Tick Associated Rash Illness
N	North	TBRF	Tick-borne Relapsing Fever
NE	New England	V	Vesicular
		W	West

SEE ENLARGED SLIDE FOLLOWING ENTIRE PRESENTATION

Condition

- Scrub typhus
- Louse-borne relapsing fever
- Tick-borne relapsing fever
- Boutonneuse (Mediterranean) fever
- Louse-borne epidemic typhus
- Endemic (murine) typhus

Match to the Pathogen

- *Rickettsia conorii*
- *Rickettsia prowazekii*
- *Borrelia recurrentis*
- *Borrelia hermsii*
- *Borrelia turicatae*
- *Rickettsia typhi*
- *Orientia tsutsugamushi*