


# 51 - Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul Auwaerter, MD


**INFECTIONOUS DISEASE BOARD REVIEW** **AUGUST 20-24 2022**

**Ticks, Mites, Lice, and The Diseases They Transmit**

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7/21/2022

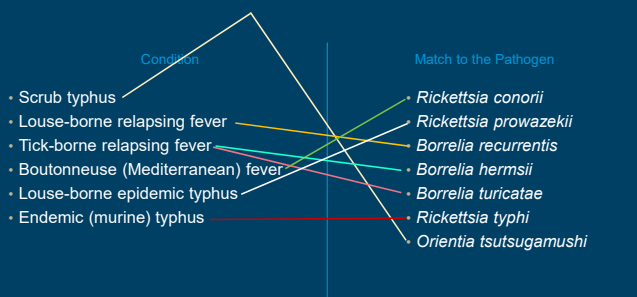

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**Disclosures of Financial Relationships with Relevant Commercial Interests**

- **Consultant:** EMD Serono, Humanigen
- **Ownership Interest:** Johnson & Johnson, Wellstat

Why the board exam loves these infections  
PLAY THE MATCH GAME

Condition	Pathogen
• Scrub typhus	• <i>Rickettsia conorii</i>
• Louse-borne relapsing fever	• <i>Rickettsia prowazekii</i>
• Tick-borne relapsing fever	• <i>Borrelia recurrentis</i>
• Boutonneuse (Mediterranean) fever	• <i>Borrelia hermsii</i>
• Louse-borne epidemic typhus	• <i>Borrelia turicatae</i>
• Endemic (murine) typhus	• <i>Rickettsia typhi</i>
	• <i>Orientia tsutsugamushi</i>



**Condition** | **Match to the Pathogen**

- Scrub typhus → *Rickettsia conorii*
- Louse-borne relapsing fever → *Rickettsia prowazekii*
- Tick-borne relapsing fever → *Borrelia recurrentis*
- Boutonneuse (Mediterranean) fever → *Borrelia hermsii*
- Louse-borne epidemic typhus → *Borrelia turicatae*
- Endemic (murine) typhus → *Rickettsia typhi*
- Endemic (murine) typhus → *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
- Characteristic 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 often changes over time  
 Lab tip-offs:

- Thrombocytopenia
- Leukocytosis or leukopenia
- Elevated LFTs

Doxycycline is preferred therapy for most  
 (all ages including children, e.g., Lyme, RMSF, ehrlichiosis...)

Prognosis is worse at age extremes < 10 and > 60 yrs  
 Convergence in tick vectors  
 Co-infection probably underestimated

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## The Major Tick-borne Diseases of North America

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

## Other Tick-borne Diseases of North America

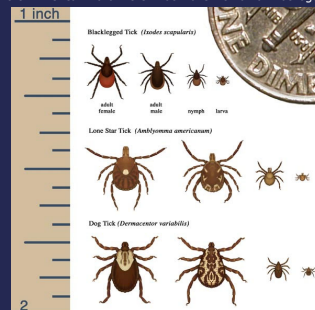
- Tick paralysis
- Southern tick associated rash illness (STAR!)
- Viruses:
  - Powassan (Deer Tick Virus Lineage II, flavivirus)
  - Colorado tick fever (coltivirus)
  - Heartland virus (phlebovirus)
  - Bourbon virus (thogotovirus)
- Spotted Fever Group Rickettsia (partial)
  - *R. parkeri*
  - Rickettsia 364D aka *R. philippii* (Pacific Coast tick fever)
- Coxiella burnetii
- Tularemia
  - (< 10% tickborne)
- Other Borrelia
  - *B. miyamotoi*
  - *B. mayonii*

## Ticks: arachnids, not insects

- Number of species
  - 896 species or subspecies
- Hematophagous arthropods
  - parasitize every class vertebrates  $\approx$  entire world
- Two major families
  - Ixodidae, 702 species (hard ticks, attach & engorge)
  - Argasidae, 193 species (soft ticks, bite multiply & briefly)
- Four basic life stages
  - egg  $\rightarrow$  larva  $\rightarrow$  nymph  $\rightarrow$  adult
- Vectors of human disease
  - #1 mosquitoes
  - #2 ticks

Parola, Raoult CID 2001; 32:897-928  
Guglielme, Zoolaxa 2010;2528:1-28

Common North American Hard Ticks That Transmit Human Pathogens (Ixodidae) 1



Common North American Hard Ticks (Ixodidae) 2



Amblyomma americanum (Lone star tick)

Common North American Hard Ticks (Ixodidae) 3  
Dog ticks



*D. variabilis*

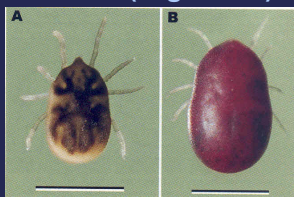
*D. andersoni*

*R. sanguineus*

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## *Ornithodoros Hermsi* nymphal Tick Soft tick (Argasidae)



A: shows the nymph before its infective blood meal (from California)  
B: shows it after feeding  
These are soft ticks that feed briefly at multiple spots  
Scale bars = 2 mm

### Question #1:

62M 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 a lineman for a utility company. He lives with his family in an older adobe home with dogs. He has beginnings of petechial features on the wrists and ankles.

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

## Rickettsial species: two major groups (not a comprehensive pathogen list)

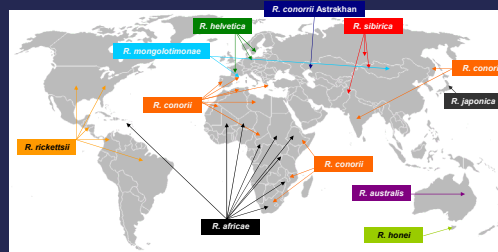
### Spotted Fever Group (SFG)

- RMSF (*R. rickettsii*)
- *R. parkeri*
- *Rickettsia* sp. 364D
- 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

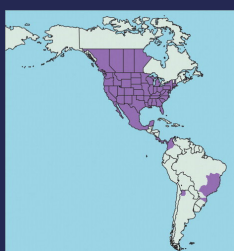
## Tick-borne Rickettsia World Wide: many species



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

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

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



See 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  
Tosco-Garcia, EID 2018;24(9):1722-25

Figure 1 - Number of reported cases of spotted fever rickettsiosis - United States, 2000 - 2019

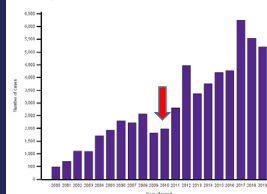
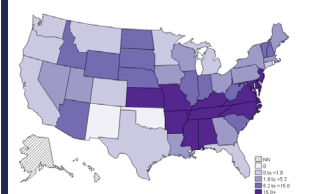


Figure 4 - Annual incidence (per million population) of reported spotted fever rickettsiosis - United States, 2019. (NN: Not notifiable)



Source: CDC (accessed 7/17/22)

Δ category from RMSF to "spotted fever rickettsioses" 2010  
Includes RMSF, *R. parkeri*, Pacific Coast tick fever, and Rickettsialpox.

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## RMSF in the United States

### Incidence/Case Fatality 1920-2015

CDC, <https://www.cdc.gov/rmsf/stats/index.html> (accessed 6/21/21)

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

- Native Americans
- Age extremes: 5-9, 70+
- Use of chloramphenicol (not doxycycline)
- Delay in diagnosis:
  - Treatment after 5 days illness
- Immunosuppression

Am J Trop Med Hyg 2012;86:713-9

## 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 Helmick 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**
- Labs: leukocytosis, thrombocytopenia, transaminitis
- Dx:
  - Preferred:
    - Skin bxp immunohistochemistry (DFA): timely diagnosis, ~70% sensitive.
    - PCR: *R. rickettsii*-specific
    - Skin bxp or swab (not routinely available, contact local health department → CDC)

## RMSF diagnosis and treatment

- Other diagnostics
- Culture: cell culture-based (BSL3 agent)
- Serology: obtain acute/convalescent samples
  - Not usually of timely clinical value.
  - IFA: gold standard; cross reacts w/ other SFG species.
    - May be helpful in confusing cases.
- Caveats: **DON'T USE AS SCREENING TEST**
  - False positives (especially IgM) common
    - Georgia blood donor study 11.1% IgG > 1:64, but of these only 28% fit case definition for Spotted Fever Group rickettsiosis [Straily A, *JID* 2020;221:1371]
    - Single IgG titer insufficient for reliable diagnosis
  - Background seroprevalence up to 20% in some regions, e.g., Carolinas
    - Asx infection likely common
  - Both RMSF IgM & IGG can persist
    - May mislead diagnosis, cause necessary treatment

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## OUTCOME: RMSF ACCORDING TO THE DAY DOXYCYCLINE STARTED

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

Most lethal of Rickettsial infections: "Black measles"  
In US mortality with treatment ~2-5% (higher with delays)

Clin Infect Dis 2015; 60:1659-66

## Question #2:

31M from Tidewater region of Virginia presents in June with three days 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?

- A. *Rickettsia rickettsii*
- B. *Ehrlichia chaffeensis*
- C. *Rickettsia parkeri*
- D. *Anaplasma phagocytophilum*
- E. *Rickettsia akari*



## "American Bouton-neuse Fever" *Rickettsia parkeri*

- Transmission: Lone Star or Gulf Coast ticks (*A. maculatum*)
  - Southeastern US, Gulf Coast
- AKA "Maculatum fever"
  - Also seen in Southern South America including Argentina, Uruguay, parts of Brazil
- Symptoms
  - 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

## Examples of *R. parkeri*-associated rashes



Source: CDC



Darker color: Gulf Coast tick range; lighter color: Lone star tick; Red dots: *R. parkeri*

## Pacific Coast Tick Fever

*Rickettsia philippii* (Rickettsia 364D)  
Described in 2008

Transmitted by Pacific Coast tick (*Dermacentor occidentalis*)

Northern Baja → Southern Oregon, Most cases

Common symptoms:  
Eschar  
Fever  
Headache



*Dermacentor occidentalis*

Pladgett K  
PLOS Neg Trop Dis 2016

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## Question 3

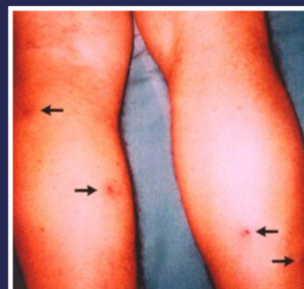
28F presents 8d after from a safari in Tanzania  
Fever, mild headache, fatigue x 5d  
Prior to travel, immunized against yellow fever  
Took malaria prophylaxis: atovaquone/proguanil

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

Four Inoculation  
Eschars (Arrows)

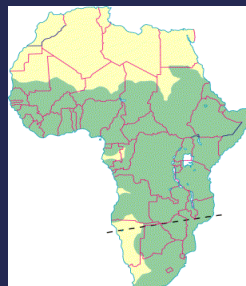


## Question #3 Continued:

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

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



Range of *R. conorii*  
Mediterranean Spotted Fever

Figure 4

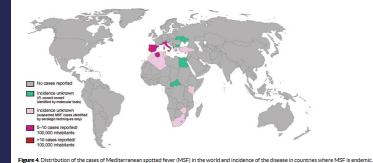


Figure 4. Distribution of the range of Mediterranean spotted fever (MSF) in the world and incidence of the disease in countries where MSF is endemic.

Roverly, EID 2006;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

Raoult 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

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

Most common

- *R. africae* (88%)

Others

- Murine typhus (~ 3%)
- Mediterranean spotted fever
- Scrub typhus

Occasional

- RMSF, epidemic typhus, N. Asian or Queensland tick typhus

Jensenius M. CID, 2004; 39: 1493-9  
Inter J Infect Dis 2004; 8: 139

## Question #4:

48M presents in October with fever and rash

Supervisor for apartment bldg in Queens, NY. Lives in cellar apt.

Exam: T 39°C

brown-black 8mm eschar on RLE  
~30 papulovesicular lesions on trunk



## Question #4:

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*

## 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

Pox viruses

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

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## 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/drainng lymph nodes, rash, delirium
    - Meningitis and meningoencephalitis with progressive infection
    - Development of multiorgan system failure
    - Case fatality rates up to 70%
- Treatment
  - Doxycycline x 7 days, relapses common
  - Alt: azithromycin (AAC 2014;58:1488-93)



Eschar is often associated with regional lymphadenitis



## Question #5:

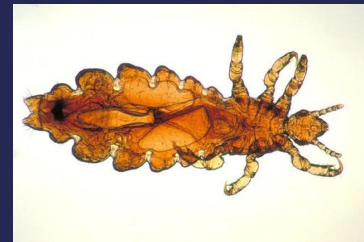
31M presents in January with 3d fever, HA, malaise, and myalgia. Works as counselor at wilderness camp in Pennsylvania. Flying squirrels common at camp including residing in the walls of his cabin. Exam is notable only for fever (39.6°; no rash), tachycardia (P110)

A diagnostic test for which of the following is most likely to be positive

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

If I say "flying squirrel"  
You say "epidemic typhus" or  
"R. prowazekii"

MMWR 2003; 9 (10); Lancet Infect Dis 2008;8(7):417  
Rare infection in US (1976-2001, 39 cases)  
Generally East Coast  
None with louse exposure (the classic vector), so not "epidemic" but sporadic  
Most with flying squirrel exposure (*Glaucomys volans*)



Body louse: infestation = pediculosis  
*Pediculus humanus humanus*



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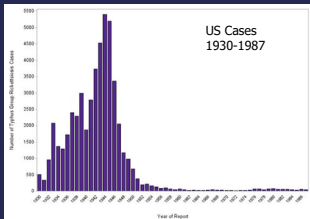
### Typhus: Two Forms

	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	Mild
Treatment	Tetracycline Doxycycline Chloramphenicol	Tetracycline Doxycycline Chloramphenicol
Prevention	Boil clothes, delouse (lindane, malathion, permethrin, DDT)	Flea prevention (cats, domestic animals) Reduce rodent population
Recrudescence	Brill-Zinsser Disease (years-decades)	None known

### Murine (or endemic) typhus



- In US, mostly seen in California, Hawaii, and Texas
- Historically, decline w/ better sanitation  
No longer reportable since 1987 (Outbreak LA County 2018)
- Infected flea feces → skin
- Most don't recall fleabite
- Usually non-specific febrile infection
  - Likely quite underdiagnosed
  - ~50% with rash
  - Occasional severe disease:
    - Meningoencephalitis
    - Pneumonitis
    - Shock



US Cases 1930-1987

Dittrich, Lancet Global Health 2015;3:e104; Blanton Am J Trop Med 2017;96(1):53 CDC, accessed 7/10/2020 <https://www.cdc.gov/typhus/murine/history.html>

### Murine (or endemic) typhus

- 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: recent 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

### 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. raoulti*:
  - Europe and Asia.
- Far-Eastern tick-borne rickettsiosis, *R. beilongjiangensis*:
  - Far East Russia and northern China.
- Oriental spotted fever, *R. japonica*:
  - Japan.
- Thai tick typhus, *R. bonoi*:
  - Thailand, Australia, Tasmania, Flinders Island
- Australian spotted fever:
  - R. marmorii*, Australia.

### Question #6:

- 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/mm<sup>3</sup> (80% PMNs, 10% lymphocytes, 8% monocytes)
  - Hemoglobin: 7.0 g/dL, hematocrit: 24%
  - Platelets: 105,000/mm<sup>3</sup>
  - AST: 364 U/L, ALT: 289 U/L
  - renal function: normal

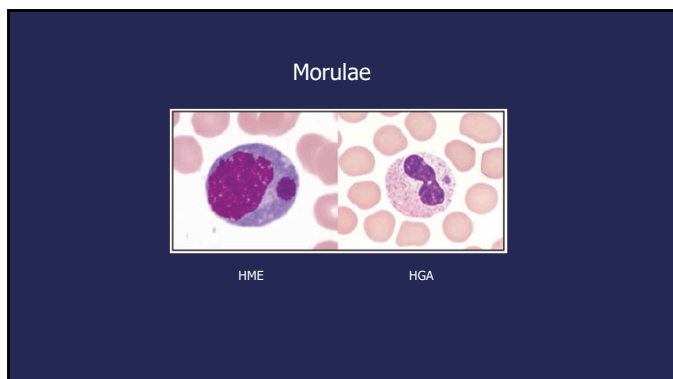
### Question #6

Which of the following is the most likely etiologic agent?

- Anaplasma phagocytophilum
- Ehrlichia chaffeensis
- Borrelia hermsii
- Babesia divergens
- Borrelia burgdorferi

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## 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

Figure 3 – Annual incidence (per million population) of reported Ehrlichia chaffeensis ehrlichiosis—United States, 2019. (NN= Not notifiable)

Source: CDC (accessed 7/10/22)

## 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%)

Figure 3 – Annual incidence (per million population) of reported anaplasmosis—United States, 2019. (NN= Not notifiable)

Geography: cross reactivity with HME accounts for most Southern state representation

Source: CDC (accessed 7/10/22)

## Other Ehrlichia (less common)

Organism	Vector	Geography	Risk	Mortality
<i>E. ewingii</i> (a canine ehrlichia)	Lone star	Most cases in Southcentral US	Immune compromised	Low
<i>E. muris</i>	<i>Ixodes persulcatus</i> <i>H. feva</i>	Europe, Russia, Japan, West Coast US	Older patients	Low
<i>Ehrlichia muris euclairensis</i> (former Ehrlichia muris-like agent)	Deer tick	Wisconsin, Minnesota	Elderly, immune compromised	Low

### Question #7:

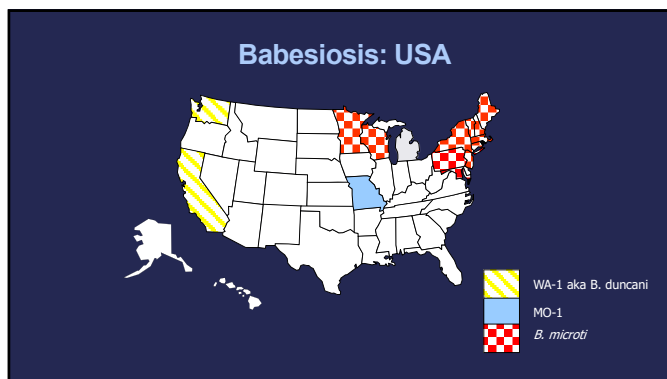
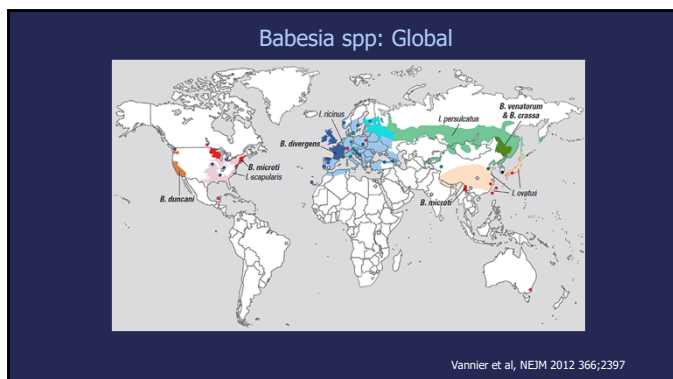
- 48F c/o headache and fatigue worsening over 2 months since May tick bite
  - PMH: negative
  - SH: Married, works from home, has a dog, resides in suburban eastern PA
  - Treated with doxycycline for Lyme disease, no benefit
- Physical examination: afebrile, normal vital signs, no findings
- Laboratory evaluation :
  - WBC: 7.0 cells/mm<sup>3</sup> (70% PMNs, 18% lymphocytes, 12% monocytes)
  - Hemoglobin: 11.8 g/dL, hematocrit: 35%
  - Platelets: 145,000/mm<sup>3</sup>
  - ALT: 22 U/L
  - Babesia IgG 1:128 (positive ≥ 1:64)
  - Blood smear: no parasites

### Question #7:

- 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

# 51 - Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul Auwaerter, MD



**Babesia species**

- Malaria-like parasite, resides in RBCs
- Geography: *Babesia microti* (most common in U.S.)
  - Nantucket, Martha's Vineyard, Long Island, Mid-Atlantic/New England, upper Midwest (similar to Lyme disease)
- > 1700 cases per year (2014 data)
  - Range of illness: "flu-like" to fatal
- Reservoir, vector
  - White-footed mouse;
  - Tick transmission: *Ixodes scapularis*
- Severe disease risks:
  - asplenic, HIV, chemotherapy, age >55, transplant
- **Pearl:** most common cause of blood transfusion-related infection in US
  - Though decreasing through screening

**Severe Babesiosis**

- n=34, Long Island NY
- Clinical manifestations
  - 41% Multi-organ failure
    - ARDS, DIC, CHF, ARF
  - 3 deaths
- Risk factors:
  - age >60
  - splenectomy,
  - immunosuppression (e.g., HIV, rituximab)
- Labs
  - increased LTFs,
  - thrombocytopenia
  - anemia (Hb<10),
  - parasitemia (>10%)
- Mortality in immunocompromised > 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
  - 1-3µ 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!

# 51 - Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul Auwaerter, MD

## Treatment of Babesiosis

- **Severe (2020 IDSA guidelines)**
  - Atovaquone 750 mg PO q12h + Azithromycin 500 mg IV q24h
    - Previous: quinine + clindamycin (now an alternative)
  - Duration: 7-10d (may require longer for persistent parasitemia or immunosuppressed)
- **Blood exchange transfusion: severe only**
  - B. divergens, many require
  - B. microti, some cases
  - Limited evidence for benefit
    - Severe hemolytic anemia or multi-organ failure
- **Mild-moderate severity**
  - Azithromycin PO plus atovaquone PO

Krause, et al CID 2021; 72 (2) e49-65

## 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, NV
- Can be severe: ARDS

### Laboratory

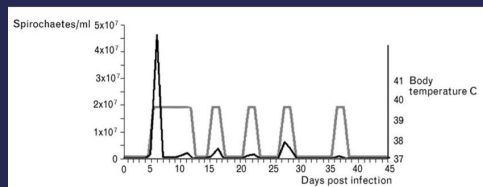
- AKI, ↓ platelets,

### Rx: PCN, doxycycline

- Jarisch Herxheimer reaction in 54%

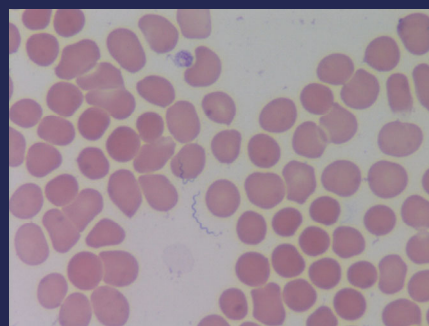


MMWR 2012;61:174-6



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

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



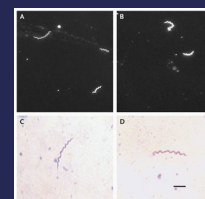
Diagnosis: observation of spirochetes in blood film, PCR

## 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

## Newer Borrelia species: *B. miyamotoi*

- Unusual vector: Ixodes ticks (larvae?)
- Epidemiology = Lyme disease
- Appears similar to HGA
  - Meningoencephalitis in immunocompromised
  - ↓ wbc, ↓ plt, ↑ LFTs
- Diagnosis: blood smear (observing spirochetes), PCR, serology
- Treatment: similar to Lyme disease



Spirochetes in CSF

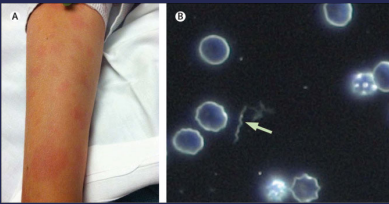
Gugliotta, NEJM 2013

Telford, Clin Microbiol Infect 2015

# 51 - Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul Auwaerter, MD

*Borrelia mayonii*



5 of 6: acute febrile illness with rash (macular)  
1 of 6: 1 months knee pain/swelling  
To date: only see in in Minnesota and Wisconsin

Pritt et al. Lancet ID 2016;16(5):556

### 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 #8:

A 59 y.o. man from Missouri presents with fever (39°), 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

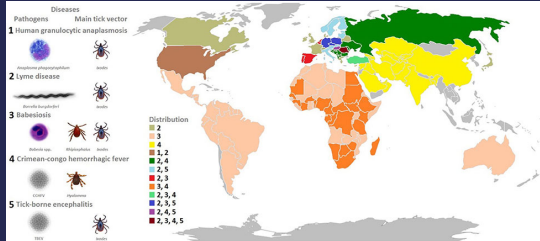
Suspect ehrlichiosis (but no morulae on blood smear)

### Question #8:

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

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



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 (tache noire)
  - Give doxycycline, even for kids
- Blood smear maybe helpful
  - Morulae: PMN = Anaplasma, Monocyte = Ehrlichia
  - Spirochete: relapsing fever Borrelia or *B. miyamotoi*
  - Erythrocyte inclusions: Babesia

# 51 - Ticks, Mites, Lice and The Diseases They Transmit

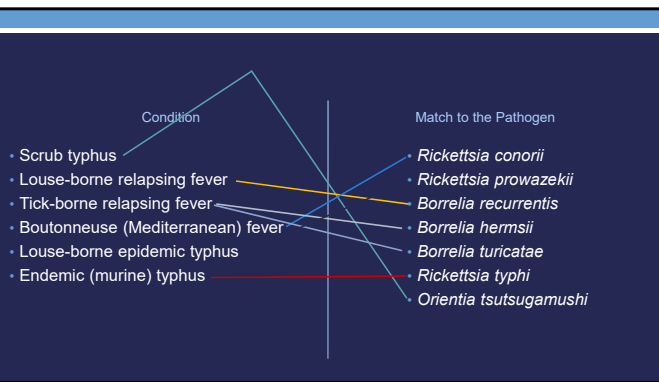
Speaker: Paul Auwaerter, MD

## Tick-borne infections: some testable points?

- Babesia:
  - Most common cause of blood transfusion infection in US
  - Splenectomy or immunocompromise = risk severe infection risk
- Co-infections in the US: may complicate some infections especially after 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
<b>TICK-BORNE</b>						
RMSF	<i>R. rickettsii</i>	N.C.S. America	No	Yes	Yes	Serious
STARI	Unknown	S, SC, MA	No	Yes (EM)	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 Transmits
HGA	<i>A. phagocytophylum</i>	NE, NY, MA, MW	No	Yes (+)	Yes	Cytopenias Transmits
Babesiosis	<i>B. microti</i>	NE, NY, MA, MW	No	Yes (+)	Yes	Spirochetes in blood smear
TBRF	<i>B. hermsii</i>	W Mountains	No	No	Yes	
<b>LOUSE-BORNE</b>						
Epidemic typhus	<i>R. prowazekii</i>	Worldwide	No	Yes	Yes	War, refugee camps serious
<b>MITE-BORNE</b>						
Rickettsialpox	<i>R. akari</i>	Worldwide	Yes (1)	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	Mid-Atlantic	SE	Southeast
MW	Mid-West	STARI	Southern Tick Associated Rash Illness
N	North	TBRF	Tick-borne Relapsing Fever
NE	New England	V	Vesicular
		W	West



**Thank You!  
and  
The End.**

*B. mayonii*  
Spirochete in Culture

Pitt, Clin Micro and Inf 2022