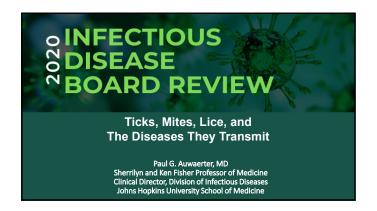
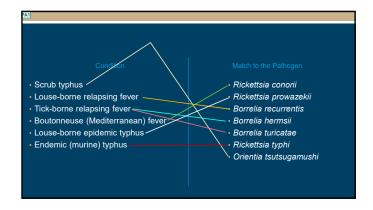
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Why the board exam loves these infections PLAY THE MATCH GAME Scrub typhus · Rickettsia conorii · Louse-borne relapsing Rickettsia prowazekii fever Borrelia recurrentis • Tick-borne relapsing fever Borrelia hermsii Boutonneuse Borrelia turicatae (Mediterranean) fever · Rickettsia typhi · Louse-borne epidemic Orientia tsutsugamushi typhus • Endemic (murine) typhus



## 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

## 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

### PA1 Please do not include this slide in the handout!

Paul Auwaerter, 6/29/2017

Speaker: Paul G. Auwaerter, MD

### The Major Tick-borne Diseases of North America

- · Lyme disease
- Rocky Mountain spotted fever (RMSF)
- Ehrlichioses
- Anaplasmosis

#2 ticks

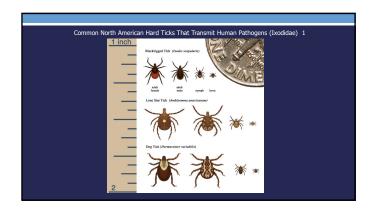
- · Relapsing fever (Borrelia spp.)
- Babesia

### Other Tick-borne Diseases of North America

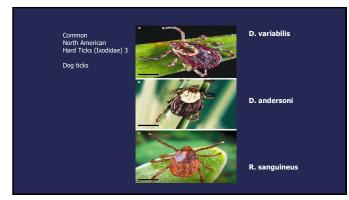
- Tick paralysis
- Southern tick associated rash illness (STARI)
- Viruses:
  - Powassan (Deer Tick Virus Lineage II, flavivirus)
  - Colorado tick fever (coltivirus)
  - Heartland virus (phlebovirus)
  - Bourbon virus (thogotovirus)
- Spotted Fever Group Rickettsia
- · R. parkeri
- Rickettsia 364D aka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

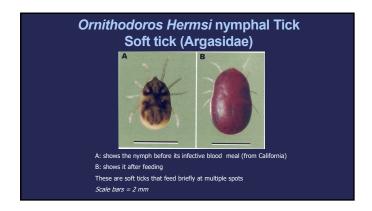
### Ticks: arachnids, not insects Number of species 986 species or subspecies Hematophagous arthropods parasitize every class vertebrates a entire world Two major families kodidae, 702 species (hard ticks, attach & engorge) Argasidae, 193 species (soft ticks, bite multiply & briefly) Four basic life stages egg → larva → nymph → adult Vectors of human disease ## mosquitos

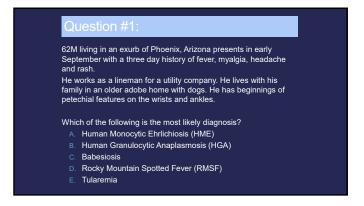
Parola, Raoult CID 2001; 32:897-928 Cupilelmone Zootaxa 2010:2528:1-28

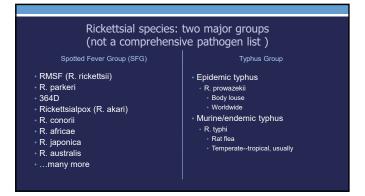




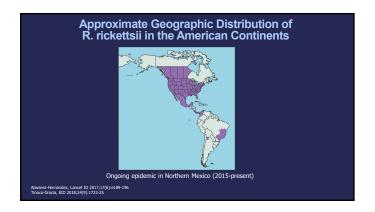


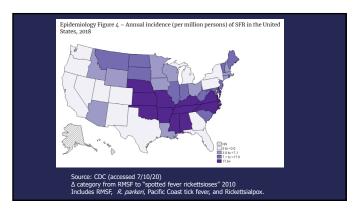




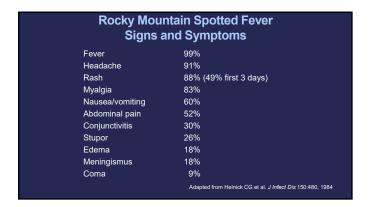


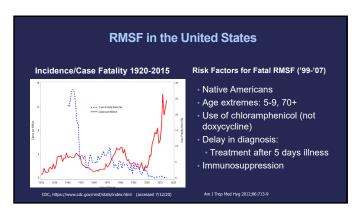






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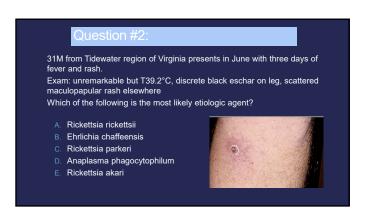




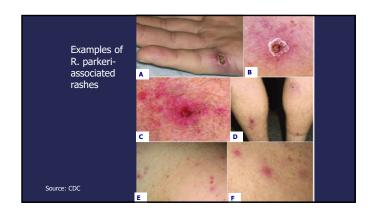
### RMSF diagnosis and treatment Start treatment upon suspicion: DON'T WAIT Labs: leukocytosis, thrombocytopenia, transaminitis Dx: Preferred: Skin bxp immunohistochemistry (DFA): timely diagnosis, ~70% sensitive. PCR: R. rickettsii-specific Skin bxp or swab (not routinely available, contact local health 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 rickettisoissi [Strally A, JID 2020;221:1371] Single IgG titer insufficient for reliable diagnosis Background seroprevalence up to 20% in some regions Ass infection likely common Both RMSF IgM & IgG can persist May mislead diagnosis, cause necessary treatment

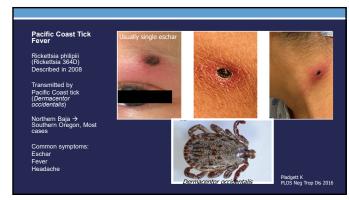




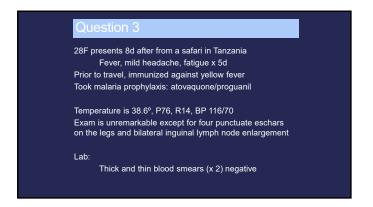


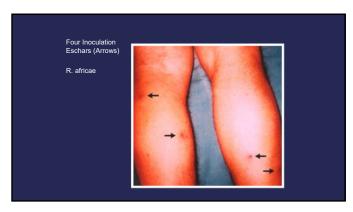




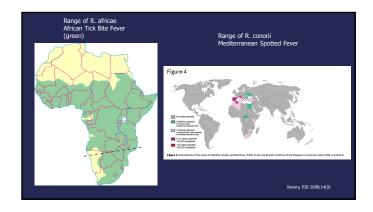


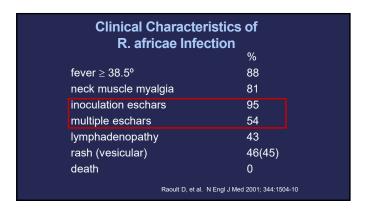
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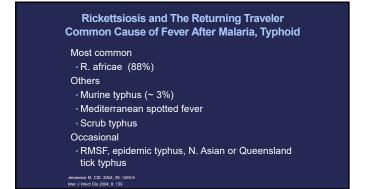
## Question #3 Continued: Which Of The Following Is The Most Likely Etiologic Agent? A. Rickettsia conorii B. Rickettsia africae C. Rickettsia rickettsii D. Anaplasma phagocytophilum E. Ehrlichia chaffeensis



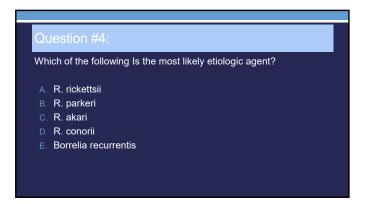


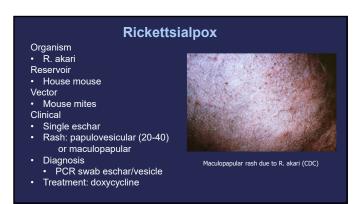
## African Tick Bite Fever Seroprevalence: High in residents, R. africae, 30-56% Amblyomma ticks (cattle, ungulates) Clusters of cases, multiple eschars Incubation period 6-7d Dx: Biopsy or swab: PCR or MIFA Serology Rx: doxycycline Complications unusual

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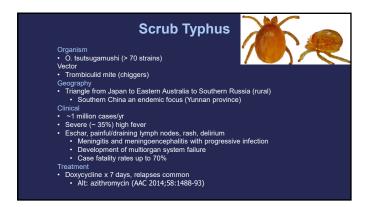




## Partial DDx of Vesicular Rash HSV VZV Pox viruses Rickettsialpox African tick bite fever Queensland tick typhus

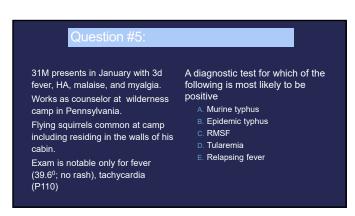


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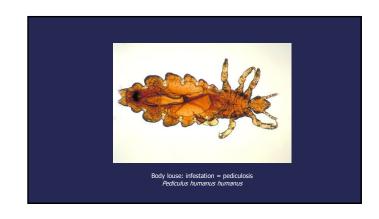




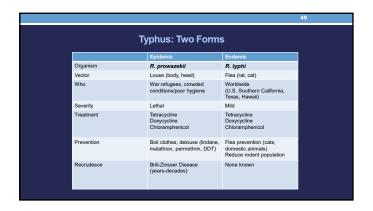


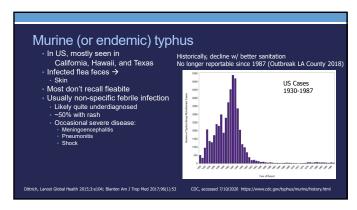
If I say "flying squirrel"
You say "epidemic typhus" or
"R. prowazekii"

MMWR 2003; 9 (10); Lancet Infec 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)



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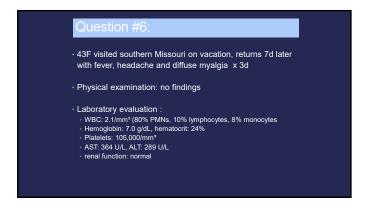




### Murine (or endemic) typhus • Dx: · Treatment: No RCTs · Serology R. typhi (IFA) Doxycycline (preferred) · Acute/convalescent, 4x rise Azithromycin: recent open label trial found azithromycin inferior to doxy · Cross-reacts with R. prowazekii and SEG rickettsia · Alternatives: limited data • PCR Chloramphenicol Blood, often negative 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

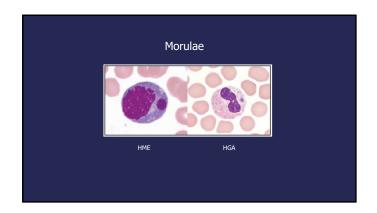
Other location-specific tick-borne Rickettsioses: partial

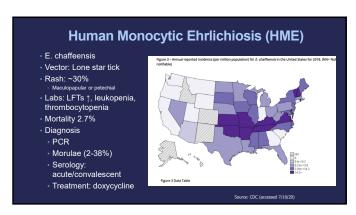
- Queensland tick typhus, R. australis
- Australia-Queensland, New South Wales, Tasmania, coastal areas of eastern Victoria
- North Asian tick fever, R. sibeirica
- North China; Mongolia; Asiatic areas of Russia
- Tick-borne lymphadenopathy (TIBOLA) or Dermacentor-borne necrosis erythema and lymphadenopathy (DEBONEL), ascribed to R. slovaca or R. raoulti:
- Europe and Asia.
- Far-Eastern tick-borne rickettsiosis, R. beilongijangensis:
- Far East Russia and northern China.
- Oriental spotted fever, R. japonica:
- Japan.
- Thai tick typhus, R. bonei:
- Thalland, Australia, Tasmania, Flinders Island
- Australian spotted fever:
- R. marmionii, Australia.

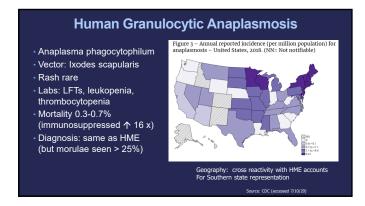


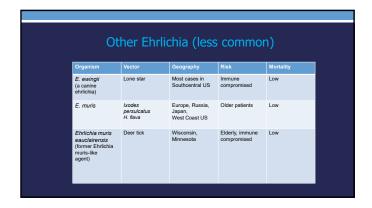
Which of the following is the most likely etiologic agent?

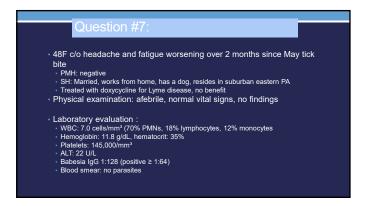
A. Anaplasma phagocytophilum
B. Ehrlichia chaffeensis
C. Borrelia hermsii
D. Babesia divergens
E. Borrelia burgdorferi

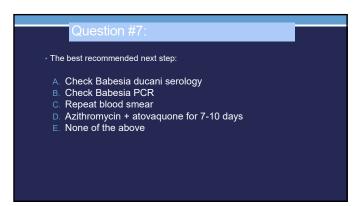




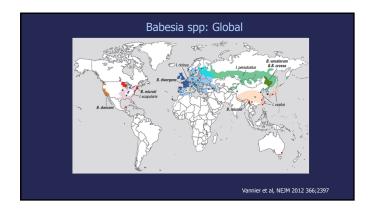








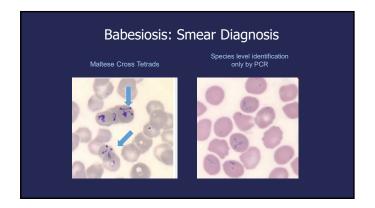
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### Babesia species Malaria-like parasite, resides in RBCs Geography: Babesia microti (most common in U.S.) Nantucket, Martha's Vineyard, Long Island, Mid-Atlantic/New England, upper Midwest (similar to Lyme disease) 1700 cases per year (2014 data) 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

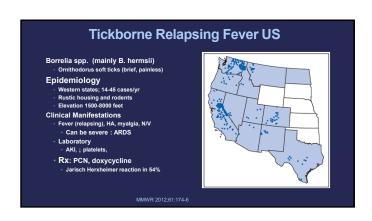
### Severe Babesiosis • n=34, Long Island NY Labs Clinical manifestations · increased LTFs, • 41% Multi-organ failure • thrombocytopenia · ARDS, DIC, CHF, ARF · anemia (Hb<10), 3 deaths · parasitemia (>10%) · Risk factors: • age >60 Mortality in · splenectomy, immunocompromised > 20% · immunosuppression (e.g., HIV, rituximab) Hatcher JC, et al. Clin Infect Dis 2001; 32:1117-25

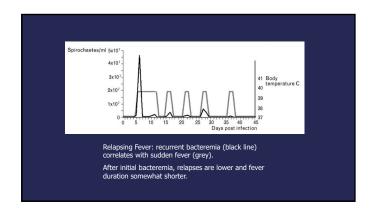


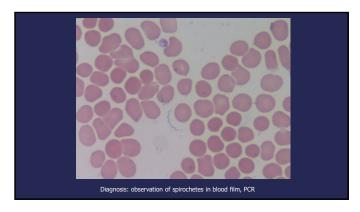
# Diagnosis of Babesiosis May observe hemolysis Wright-Giemsa stained thin blood smears 1-3μ intraerythrocytic merozoites Parasitemia range: 0-80% (may be confused with malaria) Maltese cross: diagnostic (not seen w/ malaria) Quick, if technical expertise available PCR: now widely available Highly specific, 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!

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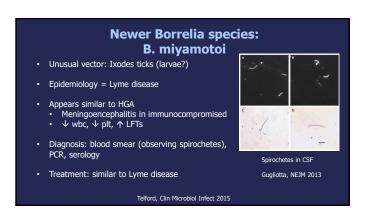
## Treatment of Babesiosis • Severe (new 2020 IDSA guidelines) • Atovaquone 750 mg PO q12h +Azithromycin 500 mg IV q24h • Previous: quinine/quinidine + clindamycin • Duration: 7-10d (may require longer for persistent parasitemia or immunosuppressed) • Blood exchange transfusion: severe only • B. divergens, many require • B. microti, some cases • Limited evidence for benefit • Mild-moderate severity • Azithromycin PO plus atovaquone PO







## 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



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### **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

### Duestion #8:

A 59 y.o. white male from Missouri presents with fever (39°), headache, myalgia, anorexia, nausea, one week after removing an engorged tick from his groin. No travel.

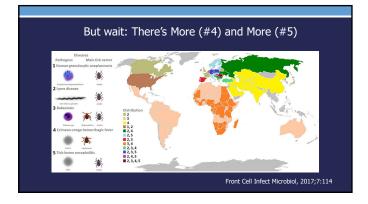
Exam: unremarkable except ill appearing, no rash. Lab: wbc 2300 plt 42,000 ALT 111

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



### 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

