46 – Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul G. Auwaerter, MD

Why the board exam loves these infections
PLAY THE MATCH GAME

<table>
<thead>
<tr>
<th>Condition</th>
<th>Pathogen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scrub typhus</td>
<td>Rickettsia conorii</td>
</tr>
<tr>
<td>Louse-borne relapsing fever</td>
<td>Rickettsia prowazekii</td>
</tr>
<tr>
<td>Tick-borne relapsing fever</td>
<td>Borrelia recurrentis</td>
</tr>
<tr>
<td>Boutonneuse (Mediterranean) fever</td>
<td>Borrelia hermsii</td>
</tr>
<tr>
<td>Louse-borne epidemic typhus</td>
<td>Borrelia turicatae</td>
</tr>
<tr>
<td>Endemic (murine) typhus</td>
<td>Rickettsia typhi</td>
</tr>
<tr>
<td>Orientia tsutsugamushi</td>
<td></td>
</tr>
</tbody>
</table>

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 Disease: 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

Disclosures of Financial Relationships with Relevant Commercial Interests

- Scientific Advisory Board – DiaSorin, Adaptive BioTherapeutics
- Grantee – MicroBplex, NIH/SBIR (Lyme disease diagnostics)
- Equity – JNJ
PA1  Please do not include this slide in the handout!
Paul Auwaerter, 6/29/2017
The Major Tick-borne Diseases of North America

- Lyme disease
- Rocky Mountain spotted fever (RMSF)
- Ehrlichioses
- Anaplasmosis
- 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 (cottivirus)
  - Heartland virus (phlebovirus)
  - Bourbon virus (thogotovirus)
- Spotted Fever Group Rickettsia (partial)
  - *R. parkeri*
  - *Rickettsia 364D aka R. philippi* (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 of vertebrates in 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 → larva → nymph → adult
- **Vectors of human disease**
  - #1 mosquitoes
  - #2 ticks

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

- *Amblyomma americanum* (Lone star tick)
- *D. variabilis*
- *D. andersoni*
- *R. sanguineus*
46 – Ticks, Mites, Lice and The Diseases They Transmit
Speaker: Paul G. Auwaerter, MD

Ornithodoros Hermi 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)

<table>
<thead>
<tr>
<th>Spotted Fever Group (SFG)</th>
<th>Typhus Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>- RMSF (R. rickettsii)</td>
<td>- Epidemic typhus</td>
</tr>
<tr>
<td>- R. parkeri</td>
<td>- R. prowazekii</td>
</tr>
<tr>
<td>- 364D</td>
<td>- Body louse</td>
</tr>
<tr>
<td>- Rickettsialpox (R. akari)</td>
<td>- Worldwide</td>
</tr>
<tr>
<td>- R. conorii</td>
<td>- Murine/endemic typhus</td>
</tr>
<tr>
<td>- R. africae</td>
<td>- R. typhi</td>
</tr>
<tr>
<td>- R. japonica</td>
<td>- Rat flea</td>
</tr>
<tr>
<td>- R. australis</td>
<td>- Temperate–tropical, usually</td>
</tr>
<tr>
<td>- ...many more</td>
<td></td>
</tr>
</tbody>
</table>

Tick-borne Rickettsia World Wide: many species

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

Approximate Geographic Distribution of R. rickettsii in the American Continents

Ongoing epidemic in Northern Mexico (2015-present)

Epidemiology/ Figure 1 – Annual incidence (per million persons) of RMSF in the United States, 2019

Source: CDC (accessed 7/10/20)
A category from RMSF is “spotted fever rickettsioses” 2010
Includes RMSF, R. parkeri, Pacific Coast tick fever, and Rickettsialpox.
Rocky Mountain Spotted Fever

**Signs and Symptoms**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>99%</td>
</tr>
<tr>
<td>Headache</td>
<td>91%</td>
</tr>
<tr>
<td>Rash</td>
<td>88% (49% first 3 days)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>83%</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>60%</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>52%</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>30%</td>
</tr>
<tr>
<td>Slpor</td>
<td>26%</td>
</tr>
<tr>
<td>Edema</td>
<td>18%</td>
</tr>
<tr>
<td>Meningismus</td>
<td>18%</td>
</tr>
<tr>
<td>Coma</td>
<td>9%</td>
</tr>
</tbody>
</table>

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

Incidence/Case Fatality 1920-2015

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

---

**RMSF in the United States**

Incidence/Case Fatality 1920-2015

<table>
<thead>
<tr>
<th>Year</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1920</td>
<td>300</td>
</tr>
<tr>
<td>1930</td>
<td>250</td>
</tr>
<tr>
<td>1940</td>
<td>200</td>
</tr>
<tr>
<td>1950</td>
<td>150</td>
</tr>
<tr>
<td>1960</td>
<td>100</td>
</tr>
<tr>
<td>1970</td>
<td>50</td>
</tr>
<tr>
<td>1980</td>
<td>25</td>
</tr>
<tr>
<td>1990</td>
<td>12</td>
</tr>
<tr>
<td>2000</td>
<td>8</td>
</tr>
<tr>
<td>2010</td>
<td>5</td>
</tr>
<tr>
<td>2015</td>
<td>3</td>
</tr>
</tbody>
</table>

---

**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)

---

**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)
- Other diagnostic:
  - 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; out of these only 28% fit case definition for Spotted Fever Group rickettsiosis (Straly A, JID 2020;221:1371)
  - Single IgG titer insufficient for reliable diagnosis
  - Background seroprevalence up to 20% in some regions
  - Ax infection likely common
  - Both RMSF IgM & IGG can persist
  - May mislead diagnosis, cause necessary treatment

---

©2020 Infectious Disease Board Review, LLC
**46 – Ticks, Mites, Lice and The Diseases They Transmit**

*Speaker: Paul G. Auwaerter, MD*

---

### OUTCOME: RMSF ACCORDING TO THE DAY DOXYCYCLINE STARTED

| 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 Boutonneuse 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 biopsy or swab of eschar

Kelman, Infection 2018; 46(4): 559-563
CID 2008; 47: 1188-96

---

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

Source: CDC

---

### Pacific Coast Tick Fever

*Rickettsia philipii* (*Rickettsia 364D*)
Described in 2008
Transmitted by Pacific Coast tick (*Dermacentor occidentalis*)
Northern Baja → Southern Oregon, Most cases
Common symptoms: Eschar, Fever, Headache

PLOS Neg Trop Dis 2016

---

Darker color: Gulf Coast tick range; lighter color: Lone star tick; Red dots: *R. parkeri*
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 38.6º, 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 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 38.6º, 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

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

Clinical Characteristics of R. africae Infection
<table>
<thead>
<tr>
<th></th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>fever ≥ 38.5º</td>
<td>88</td>
</tr>
<tr>
<td>neck muscle myalgia</td>
<td>81</td>
</tr>
<tr>
<td>inoculation eschars</td>
<td>95</td>
</tr>
<tr>
<td>multiple eschars</td>
<td>54</td>
</tr>
<tr>
<td>lymphadenopathy</td>
<td>43</td>
</tr>
<tr>
<td>rash (vesicular)</td>
<td>46(45)</td>
</tr>
<tr>
<td>death</td>
<td>0</td>
</tr>
</tbody>
</table>


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
46 – Ticks, Mites, Lice and The Diseases They Transmit

Speaker: Paul G. Auwaerter, MD

Rickettsiosis 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

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. Borreia 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”


©2020 Infectious Disease Board Review, LLC
46 – Ticks, Mites, Lice and The Diseases They Transmit
Speaker: Paul G. Auwaerter, MD

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%
Treatment
• Doxycycline x 7 days, relapses common
  • Alt: azithromycin (AAC 2014;58:1488-93)

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°C; 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 Infec Dis 2006; 6(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)
46 – Ticks, Mites, Lice and The Diseases They Transmit
Speaker: Paul G. Auwaerter, MD

Typhus: Two Forms

<table>
<thead>
<tr>
<th>Typhus</th>
<th>Endemic Typhus</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organism</strong></td>
<td>R. prowazekii</td>
</tr>
<tr>
<td><strong>Vector</strong></td>
<td>Louse (body, head)</td>
</tr>
<tr>
<td><strong>Misp</strong></td>
<td>War refugees, crowded conditions/ poor hygiene</td>
</tr>
<tr>
<td><strong>Severity</strong></td>
<td>Lethal</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Tetracycline</td>
</tr>
<tr>
<td><strong>Prevention</strong></td>
<td>Bol clothes, delouse (lindane, malathion, permethrin, DDT)</td>
</tr>
</tbody>
</table>

Murine (or endemic) typhus

- In US, mostly seen in California, Hawaii, and Texas
- Infected flea feces → Skin
- Most don’t recall fleabite
- Usually non-specific febrile infection
- Likely underdiagnosed
- ~70% with rash
- Occasional severe disease:
  - Meningoencephalitis
  - Pneumonitis
  - Shock

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

Other location-specific tick-borne Rickettsioses: partial

- Queensland tick typhus, R. australis
  - Australia-Queensland, New South Wales, Tasmanian 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 (DEBONE), ascribed to R. slovaca or R. ricketsiae
  - Europe and Asia
- Far-Eastern tick-borne rickettsiosis, R. beilongjiangensis
  - Far East Russia and northern China
- Orienta spotted fever, R. japonica
  - Japan
- Thai tick typhus, R. bonjani
  - Thailand, Australia, Tasmania, Flinders Island
- Australian spotted fever
  - R. marmionii
  - 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/mm³ (80% PMNs, 10% lymphocytes, 8% monocytes
  - Hemoglobin: 7.0 g/dL, hematocrit: 24%
  - Platelets: 105,000/mm³
  - AST: 384 U/L, ALT: 289 U/L
  - Renal function: normal

Question #6

- 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

©2020 Infectious Disease Board Review, LLC
Morulae

Human Monocytic Ehrlichiosis (HME)

- E. chaffeensis
- Vector: Lone star tick
- Rash: ~30%
- Labs: LFTs ↑, leukopenia, thrombocytopenia
- Mortality 2.7%
- Diagnosis
  - PCR
  - Morulae (2-38%)
  - Serology: acute/convalescent
  - Treatment: doxycycline

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%)

Other Ehrlichia (less common)

<table>
<thead>
<tr>
<th>Organism</th>
<th>Vector</th>
<th>Geography</th>
<th>Tick</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. ewingii (canine ehrlichia)</td>
<td>Lone star</td>
<td>Most cases in Southern US</td>
<td>Immune compromised</td>
<td>Low</td>
</tr>
<tr>
<td>E. muris</td>
<td>Ixodes persulcatus, R. Rebase</td>
<td>Europe, Russia, Japan, West Coast US</td>
<td>Older patients</td>
<td>Low</td>
</tr>
<tr>
<td>Ehrlichia muris, Ehrlichia equi, Anaplasma marginale (former Ehrlichia muris-like agent)</td>
<td>Deer tick</td>
<td>Wisconsin, Minnesota</td>
<td>Elderly, immune-compromised</td>
<td>Low</td>
</tr>
</tbody>
</table>

Organism Vector Geography Risk Mortality

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/mm³ (70% PMNs, 18% lymphocytes, 12% monocytes
    - Hemoglobin: 9.8 g/dL, hematocrit: 31%
    - Platelets: 145,000/mm³
    - ALT: 22 UL
    - Babesia IgG 1:128 (positive ≥ 1:64)
    - Blood smear: no parasites

The best recommended next step:

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

©2020 Infectious Disease Board Review, LLC
46 – Ticks, Mites, Lice and The Diseases They Transmit
Speaker: Paul G. Auwaerter, MD

Babesia spp: Global

Babesiosis: USA

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
- 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%

Diagnosis of Babesiosis
- May observe hemolysis
- Wright-Giemsa stained thin blood smears
  - 1-3 intraerythrocytic merozoites
  - Parasitemia range: 3-40% (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

Babesiosis: Smear Diagnosis
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

Borrelia spp. (mainly B. hermsii)
- Ornithodorous 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

Rx: PCN, doxycycline
- Jarisch Herxheimer reaction in 54%

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
46 – Ticks, Mites, Lice and The Diseases They Transmit
Speaker: Paul G. Auwaerter, MD

**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. white male 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 #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)**

- 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

©2020 Infectious Disease Board Review, LLC
Tick-borne infections: some testable points?

- Babesia:
  - Most common cause of blood transfusion infection in US
  - Splenectomy = risk severe infection
- 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

---

**Tick-borne infections: some testable points?**

- Babesia:
  - Most common cause of blood transfusion infection in US
  - Splenectomy = risk severe infection
- 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**

<table>
<thead>
<tr>
<th>Disease</th>
<th>Usual Organism</th>
<th>Geography</th>
<th>Eschar</th>
<th>Rash</th>
<th>High fever</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>TICK-BORNE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMSF</td>
<td><em>R. rickettsii</em></td>
<td>N,C,S, America</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Serious</td>
</tr>
<tr>
<td>STARI</td>
<td>Unknown</td>
<td>S, SC, MA</td>
<td>No</td>
<td>Yes (EM)</td>
<td>No</td>
<td>Mild</td>
</tr>
<tr>
<td>R. parkeri</td>
<td><em>R. parkeri</em></td>
<td>Gulf, South Atlantic</td>
<td>Yes (&gt;1)</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>African tick bite fever</td>
<td><em>R. africae</em></td>
<td>Sub-Saharan Africa</td>
<td>Yes (&gt;1)</td>
<td>Yes</td>
<td>No</td>
<td>Mild</td>
</tr>
<tr>
<td>HME</td>
<td><em>E. chaffeensis</em></td>
<td>S, SC, MA</td>
<td>No</td>
<td>Yes (+/-)</td>
<td>Yes</td>
<td>Cytopenias, Transaminitis</td>
</tr>
<tr>
<td>HGA</td>
<td><em>A. phagocytophilum</em></td>
<td>NE, NY, MA, MW</td>
<td>No</td>
<td>Yes (+/-)</td>
<td>Yes</td>
<td>Cytopenias, Transaminitis</td>
</tr>
<tr>
<td>Babesiosis</td>
<td><em>B. microti</em></td>
<td>NE, NY, MA, MW</td>
<td>No</td>
<td>Yes (+/-)</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>TBRF</td>
<td><em>B. hermsii</em></td>
<td>W Mountains</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
</tbody>
</table>

**LOUSE-BORNE**

- Epidemic typhus: *R. prowazekii*
  - Worldwide
  - No
  - Yes
  - Yes
  - Serious
  - War, refugee camps

**MITE-BORNE**

- Rickettsialpox: *R. akari*
  - Worldwide
  - Yes (1)
  - Yes (V)
  - No
  - Mouse exposure
- Scrub typhus: *O. tsutsugamushi*
  - India, Asia, N. Australia
  - Yes
  - Yes
  - Yes
  - Serious
- Louse-borne relapsing fever: *Borrelia recurrentis*

**Match to the Pathogen**

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

**Thank You! and The End.**