Tick-Borne Illnesses

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Ticks

Arachnids (e.g. spiders & mites)

Adult females leave host to lay eggs

https://www.cdc.gov/ticks/life_cycle_and_hosts.html
FIGURE 19. Sizes of the larva, nymph, and adult stages of *Rhipicephalus sanguineus* (brown dog tick) compared with a human finger.

Photo/CDC
Tick-Borne Illnesses

Ehrlichiosis

Rocky Mountain Spotted Fever

Tularemia

Lyme
  - B. burgdorferi
  - B. mayoni

STARI

Heartland Virus

Bourbon virus

Babesiosis

Colorado Tick Fever

Tick Borne Relapsing Fever
<table>
<thead>
<tr>
<th>Disease</th>
<th>Kansas Case Count by Classification</th>
<th>Incidence Rate per 100,000</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Confirmed</td>
<td>Probable</td>
</tr>
<tr>
<td>RMSF</td>
<td>1</td>
<td>145*</td>
</tr>
<tr>
<td>Ehrlichiosis (E. chaffeensis)</td>
<td>25</td>
<td>21</td>
</tr>
<tr>
<td>Tularemia</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>Lyme</td>
<td>11</td>
<td>12</td>
</tr>
</tbody>
</table>

http://www.kdheks.gov/
Human Monocytic Ehrlichiosis

- Canine ehrlichiosis described 1935
  - *E. canis* (later identified)
  - fever + clusters of intracellular organisms in peripheral monocytes
- 1937 - genus *Ehrlichia* named after Paul Ehrlich (German)

April 1986
- 51 y.o. man, Arkansas, Ft Chaffee
- ill 12 – 14 days after tick bite
- fever, ↓ BP, confusion, acute renal failure, pancytopenia, coagulopathy, hepatocellular injury, cutaneous and GI hemorrhages
- “morulae” seen
- cytoplasmic vacuoles w/ many organisms
- aby positive for *E. canis*
Human Monocytic Ehrlichiosis

Etiology:

\textit{E. chaffeensis}

Vector: (tick)

\textit{Amblyomma americanum}

Pathology:

Diminished peripheral counts likely a result of:

- Sequestration
- Consumption
- Destruction of infected or non-infected cells
Human Monocytic Ehrlichiosis

- **Proinflammatory cytokines** are as high as those generated by *E. coli* LPS

- Infection w/ *E. chaffeensis* almost always symptomatic
  + serologies in asymptomatics likely secondary to related *Ehrlichia* spp.
    e.g. *E. canis*, etc.
Ehrlichia chaffeensis

- natural reservoir
- persistent asymptomatic bacteremia

white-tailed deer

Amblyomma americanum

“Lone Star tick”
Amblyomma americanum

www.cdc.gov/ehrlichiosis/
MMWR Recomm Rep, 2016 vol.65 (2) pp.1-44

*As reported through national surveillance, per 1,000,000 persons per year. Cases are reported by county of residence, which is not always where the infection was acquired.
Ehrlichiosis: Clinical Presentation

Case Distribution

Unpublished data: Univ. of Missouri - Columbia
### Admission signs and symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>30 (100)</td>
<td></td>
</tr>
<tr>
<td>Documented fever</td>
<td>25 (83)</td>
<td></td>
</tr>
<tr>
<td>Chills</td>
<td>22 (73)</td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>19 (63)</td>
<td></td>
</tr>
<tr>
<td>Nausea</td>
<td>15 (50)</td>
<td></td>
</tr>
<tr>
<td>Myalgias</td>
<td>13 (43)</td>
<td></td>
</tr>
<tr>
<td>Arthralgias</td>
<td>10 (33)</td>
<td></td>
</tr>
<tr>
<td>Fatigue or malaise</td>
<td>9 (30)</td>
<td></td>
</tr>
<tr>
<td>Vomiting</td>
<td>8 (27)</td>
<td></td>
</tr>
<tr>
<td>Anorexia</td>
<td>8 (27)</td>
<td></td>
</tr>
<tr>
<td>Back pain</td>
<td>6 (20)</td>
<td></td>
</tr>
<tr>
<td>Mental status changes</td>
<td>6 (20)</td>
<td></td>
</tr>
<tr>
<td>Photophobia</td>
<td>4 (13)</td>
<td></td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>4 (13)</td>
<td></td>
</tr>
<tr>
<td>Diarrhea†</td>
<td>3 (10)</td>
<td></td>
</tr>
<tr>
<td>Rash‡</td>
<td>6 (20)</td>
<td></td>
</tr>
<tr>
<td>Abdominal tenderness</td>
<td>3 (10)</td>
<td></td>
</tr>
<tr>
<td>Cough</td>
<td>2 (&lt;10)</td>
<td></td>
</tr>
<tr>
<td>Dypsnea</td>
<td>1 (&lt;10)</td>
<td></td>
</tr>
<tr>
<td>Testicular pain</td>
<td>1 (&lt;10)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>2 (&lt;10)</td>
<td></td>
</tr>
<tr>
<td>Swollen joints</td>
<td>1 (&lt;10)</td>
<td></td>
</tr>
<tr>
<td>Herpes labialis</td>
<td>1 (&lt;10)</td>
<td></td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>2 (&lt;10)</td>
<td></td>
</tr>
</tbody>
</table>

* Number of patients = 30.
† All had received oral antimicrobial agents before onset of diarrhea.
‡ Two additional patients developed rash during observation.

Ehrlichiosis: Clinical Presentation

Symptom Summary

- Fever
- Chills
- Myalgias
- Malaise
- Nausea
- Vomiting
- Anorexia
- Abdominal pain
- Rash
- Cough
- Arthralgias
- Diarrhea
- MS changes

Unpublished data: Univ. of Missouri - Columbia
# Ehrlichiosis: Clinical Presentation

<table>
<thead>
<tr>
<th>Variables†</th>
<th>Patients</th>
<th>Median Value</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphopenia (&lt;1000×10^6/L)</td>
<td>22/29 (76)</td>
<td>66×10^6</td>
<td>Normal to 192×10^6</td>
</tr>
<tr>
<td>Platelets (&lt;150×10^9/L)</td>
<td>21/30 (70)</td>
<td>119×10^9</td>
<td>48 to 311×10^9</td>
</tr>
<tr>
<td>Leukopenia (&lt;4.3×10^9/L)</td>
<td>17/30 (57)</td>
<td>4.2×10^9</td>
<td>1.6 to 12.2×10^9</td>
</tr>
<tr>
<td>Fibrin degradation products, mg/L</td>
<td>6/8 (75)</td>
<td>. . .</td>
<td>Normal to &gt;40</td>
</tr>
<tr>
<td>Activated partial thromboplastin time, s</td>
<td>8/15 (53)</td>
<td>. . .</td>
<td>Normal to 50</td>
</tr>
<tr>
<td>Prothrombin time</td>
<td>1/14 (7)</td>
<td>. . .</td>
<td>. . .</td>
</tr>
<tr>
<td>Fibrinogen</td>
<td>0/4 (0)</td>
<td>6.2</td>
<td>Normal to 35.4</td>
</tr>
<tr>
<td>Lactic dehydrogenase (&gt;4.2 μkat/L)</td>
<td>17/18 (94)</td>
<td>1.65</td>
<td>Normal to 10.0</td>
</tr>
<tr>
<td>Aspartate aminotransferase (&gt;0.8 μkat/L)</td>
<td>23/27 (85)</td>
<td>1.43</td>
<td>Normal to 22.2</td>
</tr>
<tr>
<td>Alanine aminotransferase (&gt;1.1 μkat/L)</td>
<td>17/23 (74)</td>
<td>1.65</td>
<td>Normal to 16.0</td>
</tr>
<tr>
<td>Alkaline phosphatase (&gt;2.3 μkat/L)</td>
<td>11/25 (44)</td>
<td>2.0</td>
<td>Normal to 18.8</td>
</tr>
<tr>
<td>Total bilirubin (&gt;20.4 mmol/L)</td>
<td>6/25 (24)</td>
<td>15.4</td>
<td>Normal to 92.3</td>
</tr>
<tr>
<td>Hyponatremia (&gt;136 mmol/L)</td>
<td>15/29 (52)</td>
<td>134</td>
<td>Normal to 126</td>
</tr>
<tr>
<td>Blood urea nitrogen, creatinine</td>
<td>1/26 (4)</td>
<td>. . .</td>
<td>. . .</td>
</tr>
</tbody>
</table>

* Laboratory values were obtained within 24 to 48 hours of patient encounter. Three patients who had normal values or were not evaluated initially went on to develop thrombocytopenia, leukopenia, and abnormal liver profiles during hospitalization and before the diagnosis was considered.

† Normal values are in parentheses, which also contain units for the median and range.
# Ehrlichiosis: Clinical Presentation

<table>
<thead>
<tr>
<th>Most Frequent</th>
<th>Frequent</th>
<th>Occasional</th>
</tr>
</thead>
<tbody>
<tr>
<td>leukopenia</td>
<td>anemia</td>
<td>↑ CPK</td>
</tr>
<tr>
<td>lymphocytopenia</td>
<td>morulae</td>
<td>↑ bilirubin</td>
</tr>
<tr>
<td>↑ AST / ALT</td>
<td>CSF pleocytosis</td>
<td></td>
</tr>
<tr>
<td>↓ platelets</td>
<td>FDP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↓ Na</td>
<td></td>
</tr>
<tr>
<td></td>
<td>↑ BUN / Cr</td>
<td></td>
</tr>
</tbody>
</table>
**Ehrlichiosis:** Diagnosis

- **Clinical diagnosis**
- **Ehrlichia PCR** *
  - best prior to treatment
- **Ehrlichia indirect immunofluorescence assay (IFA)**
  - Only 22% positive during first week!
  - Convalescent titers in 4-6 weeks
Ehrlichiosis: Treatment

Doxycycline 100mg p.o. BID 10-14 days

(Rifampin also used with some success.)
Human Granulocytic Ehrlichiosis (HGE) - “Anaplasmosis”

Etiologic agent: *Anaplasma phagocytophilum*

Vector: *Ixodes scapularis* (Northeast)  
*iXodes pacificus* (California)

Pathology:
- infects predominantly **neutrophils** in peripheral blood & tissues
- organisms disseminate to spleen, bone marrow, etc
- intracellular, downregulates phagocyte oxidase activity
Human **Granulocytic** Ehrlichiosis

*Ixodes scapularis*

“blacklegged tick”

Photo/CDC
Fig. 1. Density per 1,000 m² (log scale) of the most abundant species of ticks (nymphs and adults pooled) collected in each of the 95 study sites. The grid used to select the sampling sites is displayed in the background as well as the 100th meridian, western limit of the study area.

* As reported through national surveillance, per 1,000,000 persons per year. Cases are reported by county of residence, which is not always where the infection was acquired.
Human Granulocytic Ehrlichiosis
### Clinical Differences: HME vs HGE

<table>
<thead>
<tr>
<th>Sign, Symptom, or Laboratory Finding</th>
<th>HME Patients with Abnormal Findings (%)</th>
<th>HGA Patients with Abnormal Findings (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>97</td>
<td>94-100</td>
</tr>
<tr>
<td>Headache</td>
<td>81</td>
<td>61-85</td>
</tr>
<tr>
<td>Chills or rigors</td>
<td>67</td>
<td>39-98</td>
</tr>
<tr>
<td>Myalgia</td>
<td>68</td>
<td>78-98</td>
</tr>
<tr>
<td>Malaise</td>
<td>84</td>
<td>98</td>
</tr>
<tr>
<td>Nausea</td>
<td>48</td>
<td>39</td>
</tr>
<tr>
<td>Anorexia</td>
<td>66</td>
<td>37</td>
</tr>
<tr>
<td>Vomiting</td>
<td>37</td>
<td>34</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>25</td>
<td>22</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>36</td>
<td>2-11</td>
</tr>
<tr>
<td>Cough</td>
<td>26</td>
<td>29</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>Confusion</td>
<td>20</td>
<td>17</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>60</td>
<td>50-59</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>68</td>
<td>59-92</td>
</tr>
<tr>
<td>Elevated AST</td>
<td>86</td>
<td>69-91</td>
</tr>
<tr>
<td>Elevated ALT</td>
<td>80</td>
<td>61</td>
</tr>
<tr>
<td>Elevated urea nitrogen</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Elevated creatinine</td>
<td>29</td>
<td>70</td>
</tr>
</tbody>
</table>

ALT, alanine aminotransferase; AST, aspartate aminotransferase; HGA, human granulocytotropic anaplasmosis; HME, human monocytotropic ehrlichiosis.
Human Granulocytic Ehrlichiosis: Treatment

Doxycycline 100mg p.o. BID 10-14 days

(Rifampin also likely to be effective)
<table>
<thead>
<tr>
<th></th>
<th>Human monocytic ehrlichiosis</th>
<th>Human granulocytic ehrlichiosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Agent</strong></td>
<td><em>Ehrlichia chaffeensis</em></td>
<td><em>Anaplasma (E.) phagocytophilum</em></td>
</tr>
<tr>
<td><strong>Vector</strong></td>
<td><em>Amblyomma americanum</em></td>
<td><em>Ixodes scapularis</em></td>
</tr>
<tr>
<td></td>
<td></td>
<td><em>Ixodes pacificus</em></td>
</tr>
<tr>
<td><strong>Geography</strong></td>
<td>midwest, southeast</td>
<td>northeast, northern midwest, California</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td><em>doxycycline</em></td>
<td><em>doxycycline</em></td>
</tr>
</tbody>
</table>
Rocky Mountain Spotted Fever (RMSF)

- first described in the Snake River Valley (Idaho) 1896
- **Ricketts** described illness and demonstrated role of ticks as the vector in western Montana 1906
- Wolbach identified rickettsiae within endothelial cells 1919
Rocky Mountain Spotted Fever

Etiologic agent: *Rickettsia rickettsii*

*Dermacentor variabilis*
(American dog tick)

*Dermacentor andersoni*
(Rocky Mountain wood tick)

*Rhipicephalus sanguineus*
(brown dog tick)

Most common vector

MMWR Recomm Rep, 2016 vol.65 (2) pp.1-44
Rocky Mountain Spotted Fever (RMSF)

_Dermacentor variabilis_
- larval / nymphal stages usually DO NOT bite humans
- active spring -> fall
  – maximum activity late spring / early summer

**Pathology:**
- obligate intracellular bacteria
- reside in the cytosol / occasionally nuclei

- skin
- lymphatics / small blood vessels
- systemic circ
- plt activation / consumption, vasc permeability, sepsis picture
- endothelial injury
- endothelium
- picture
RMSF incidence truly this great?

FIGURE 1. Reported incidence rate* of spotted fever rickettsiosis,† by county — United States, 2000–2013

Per 100,000 persons /yr

RMSF incidence truly this great?
Is case fatality rate really this low in U.S.?

**Figure**: Reported cases of so-called Rocky Mountain spotted fever and case-fatality rates in the USA. From data in reference 7.
Why the low fatality rate?

- **Serological cross-reactivity**
  - *R. parkeri*
  - *R. massiliae*, *R. amblyommi*, *R. felis*

- **↑ December / January cases...**
  - atypical for RMSF
  - perhaps secondary to other relatively **benign** rickettsiosis

- **R. rickettsii** variations in genotypes
  - perhaps some strains less virulent than others

~ 4% carry **any** rickettsiae
< 1 / 1000 **R. rickettsii**
Rocky Mountain Spotted Fever

Clinical presentation:

- incubation 2 – 14 days
- fever, myalgia, headache
- fever > 102º in 90% after 1st 3 days
- RASH
  - 1-3 days (50%)
  - usually 3-5 days...
    - 84 – 91% overall incidence
  - often begins wrists / ankles
  - palms/soles characteristic, but not necessary
- Headache severe... may develop meningitis or meningoencephalitis
- renal / pulmonary involvement
- GI symptoms > 60% patients

Rocky Mountain Spotted Fever (RMSF)

Clinical presentation:

- **if no treatment**, death typically 8 – 15 days
- fulminant disease - death less than 5 days
  - more prominent in African-American individuals
  - G6PD? more severe hemolysis

**Labs:**
- WBC normal typically
- anemia 5 – 30%
- thrombocytopenia 32 – 52%
- hyponatremia 20 – 50%
- elevated AST 36 – 62%
Rocky Mountain Spotted Fever

Diagnosis:

- prior to rash, **clinical and epidemiological**
- do not withhold therapy while awaiting serologies, if clinical suspicion high!

Rash usually develops within 3-5 days of fever onset.

- Antibody: IFA > 1:64 positive
- often turns positive during convalescence
- cross-reactivity w/ other Rickettsia species
- PCR not as reliable except late in course

**Treatment:**

**doxycycline** x 7 days

(+ 2 days after pt becomes afebrile)

?chloramphenicol (not effective in Ehrlichiosis)

Tularemia

“rabbit fever”, “hare fever”, “deerfly fever”

Etiologic agent:  *Francisella tularensis*

Reservoir: squirrels, rabbits, voles, muskrats, water rats, other rodents

Vector: (in U.S.)

- biting flies (Utah, Nevada, California)
- ticks (east of the Rockies)
- blood - skinning animal, infected cut, eye ( "tick squeezing")

1950’s U.S. and USSR looked into use as biologic weapon
Tularemia

Infection:

asymptomatic → acute sepsis and death

virulence of organism, portal of entry, extent of systemic involvement, and immune status of host

Clinical symptoms

- skin lesion appears 3-5 days after exposure
- symptoms can start 1-21 days after exposure
- abrupt onset: fever, chills, headache, malaise, anorexia, fatigue
- pulse – temp deficit (about 40%)
- fever bimodal… can last up to 32 days
- adenopathy (often)
Tularemia: 6 major presentations

Ulcerglandular:
- presentation in 21 – 87% of cases
- tick bites & animal contacts
- enlarged tender, localized adenopathy
Tularemia: 6 major presentations

**Glandular:**
- tender regional adenopathy
- no clear cutaneous lesion
  (may have healed or was small)
- 3 – 20% of cases in U.S.
- when fluctuant, aspirate

**Occuloglandular:**
- 0 – 5% of cases
- conjunctiva (contaminated hands, aerosols)
Pharyngeal tularemia:
- primary invasion through the oropharynx
- contaminated food / water, droplets
- exudative pharyngitis / tonsillitis
- one or more ulcers
- if delayed presentation, may find cervical adenopathy w/out significant fever

Typhoidal:
- febrile illness; no prominent lymphadenopathy
- 5-30% of cases
- difficult to diagnose

Pneumonic:
- primary presentation of pneumonia
- direct inhalation or hematogenous dissemination
FIG. 1. World map showing areas where *F. tularensis* is endemic (shaded).
1 dot placed randomly within county of residence for each reported case

Tularemia has been reported from all states except Hawaii, but is most common in the south central United States, the Pacific Northwest, and parts of Massachusetts, including Martha's Vineyard.

www.cdc.gov/tularemia/statistics
Tularemia:

**Diagnosis:**
- clinical… lab findings non-specific
- inform lab if suspected
- antibody titer
  - typically **negative** during 1st week of illness
  - usually positive after 2, peak at 4-5 weeks

**Treatment:**
- streptomycin 7.5 – 10 mg/kg IM q 12 hrs (cidal)
  - gentamicin (alternative)
  - tetracycline & chloramphenicol (bacteriostatic)
  - quinolones?
Lyme Disease:

Etiologic agent: *Borrelia burgdorferi*

Vector: *Ixodes scapularis, Ixodes pacificus*

History:
- recognized 1976 - Lyme, Connecticut
- group of children thought to have JRA
- similar syndromes in Europe
- syndromes linked with discovery of spirochete
7 – 11 flagella

spirochete
Lyme Disease

*Ixodes scapularis*

“blacklegged tick”

Photo/CDC
Red / Green: $\geq 6$ ticks or $\geq 2$ host-seeking life stages

Blue / Yellow: At least 1 tick of any life stage

Reports by County - 1907-2015

Red / Green: $\geq 6$ ticks or $\geq 2$ host-seeking life stages

Blue / Yellow: At least 1 tick of any life stage

I. pacificus

I. scapularis

Lyme Disease

Pathogenesis:

- organism cross from tick → mammal
- incubation of 3 – 32 days
- organism multiplies locally / local immune response
  Erythema migrans
- after days – weeks, organism disseminates
  - blood, CSF, myocardium, spleen, liver, bone, etc.
- despite active immune response, organism may survive for years
  - downregulation of surface proteins and antigenic variation of a lipoprotein?
Lyme Disease

Clinical Presentation:

Stage I: (localized)

- EM (erythema migrans) 70-80%
- nymph, no memory of tick
- may burn or itch
Lyme Disease

Clinical Presentation:

Stage II: (disseminated infection)

- days – weeks, may develop multiple annular secondary lesions
- smaller, less indurated centers, migrate less
- fade in 3-4 weeks
- associated malaise, fatigue, HA, fever, chills, generalized aches, and regional adenopathy
- occasionally: difficulty w/ mentation, severe HA, hepatitis, generalized LA, sore throat, cough, etc
- weeks – months
  - 15% neurologic abnormalities
  - 5% cardiac involvement
Lyme Disease

Clinical Presentation:

**Stage III: (persistent infection)**

- months after onset, strong humoral and cellular immune responses
- intermittent joint swelling / pain
- inflamed synovial fluid
- 10% may persist w/ joint inflammation after adequate treatment
- 5% of untreated patients - **chronic neurologic manifestations**
  - axonal polyneuropathy
  - encephalomyelitis
  - cognitive impairment
  - bladder dysfunction, etc.
<table>
<thead>
<tr>
<th>System</th>
<th>Localized Stage 1</th>
<th>Disseminated Stage 2</th>
<th>Late Infection</th>
<th>Persistent Stage 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>Erythema migrans (EM)</td>
<td>Secondary annular lesions Malar rash Diffuse erythema or urticaria Evanescent lesions Lymphocytoma</td>
<td>Acrodermatitis chronica atrophicansLocalized scleroderma-like lesions</td>
<td>Prolonged arthritis attacks Chronic arthritis Peripheral enthesopathy Periostitis or joint subluxations below acrodermatitis</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>Migratory pain in joints, tendons, bursae, muscle, bone Brief arthritis attacks Myositis政策 Osteomyelitis政策 Panniculitis政策</td>
<td></td>
<td>Chronic encephalomyelitis Spastic parapareses Ataxic gait Subtle mental disorders Chronic axonal polyradiculopathy</td>
<td></td>
</tr>
<tr>
<td>Neurologic</td>
<td>Meningitis Cranial neuritis, facial palsy Motor or sensory radiculoneuritis Subtle encephalitis Mononeuritis multiplex Pseudotumor cerebi Myelitis政策 Cerebellar ataxia政策</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphatic</td>
<td>Regional lymphadenopathy Regional or generalized lymphadenopathy Spleenomegaly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>Atrioventricular nodal block Myopericarditis Pancarditis</td>
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<tr>
<td>Eyes</td>
<td>Conjunctivitis Iritis政策 Choroiditis政策 Retinal hemorrhage or detachment政策 Panophthalmitis政策</td>
<td></td>
<td>Keratitis</td>
<td></td>
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<tr>
<td>Liver</td>
<td>Mild or recurrent hepatitis Nonexudative sore throat Nonproductive cough</td>
<td></td>
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<tr>
<td>Respiratory</td>
<td></td>
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<tr>
<td>Kidney</td>
<td>Microscopic hematuria or proteinuria</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Genitourinary</td>
<td>Orchitis政策</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constitutional systems</td>
<td>Minor</td>
<td>Severe malaise and fatigue</td>
<td>Fatigue</td>
<td></td>
</tr>
</tbody>
</table>
Reported Clinical Findings for Lyme Disease Cases
United States, 1992-2004
119,965 cases
Two-Tiered Testing for Lyme Disease

First Test

- Enzyme Immunoassay (EIA)
  OR
- Immunofluorescence Assay (IFA)

Positive or Equivocal Result

Negative Result

Consider alternative diagnosis

OR

If patient with signs/symptoms consistent with Lyme disease for \( \leq 30 \) days, consider obtaining a convalescent serum

Second Test

- Signs or symptoms \( \leq 30 \) days
  - IgM and IgG Western Blot
- Signs or symptoms \( > 30 \) days
  - IgG Western Blot ONLY

- IgM western blot: \textbf{2 of 3} bands (23, 39 & 41)
- After acute stage, IgG western blot: \textbf{5 of 10} bands needed
Lyme Disease

Treatment:

- **Early infection**:
  
  Doxy or amoxicillin 2-3 weeks

- **Arthritis** (intermittent or chronic):
  
  Doxy or amoxicillin 30 – 60 days
  PCN G IV or ceftriaxone 14-28 days

- **Neurologic abnormalities**
  
  Ceftriaxone or PCN G 14-28 days
Southern Tick-Associated Rash Illness (STARI)

- Edwin Masters (a.k.a. Master’s disease)
  - Family Medicine - Cape Girardeau, MO
  - 45 cases reported 1991
  - tick bite, EM, fatigue, HA, etc.

- No evidence of Borrellia burgdorferi (multiple studies)

Amblyomma americanum proven not to be adequate host for Borrelia burgdorferi !!!

Blacklegged Tick *Ixodes scapularis*

Lone Star Tick *A. americanum*
Southern Tick-Associated Rash Illness (STARI)

(CID Oct 1st 2005):

Comparison between patients w/ EM from Cape Girardeau and New York

Illness less severe, shorter duration in Missouri

**EM Lesions:** more central clearing; punctum; more circular

Missouri patients w/ fewer lesions

Fewer symptoms of late disease
New Etiology of Lyme Borreliosis

**Lyme borreliosis**
- *Borrelia burgdorferi* sensu lato complex
  - B. garinii
  - B. afzelii
  - B. burgdorferi

Europe

USA
New Etiology of Lyme Borreliosis

Novel agent – B. mayonii

PCR Melting Points

B. afzelii

B. burgdorferi

Mayo Clinic Lab

6 out of 100,545 samples tested

New Etiology of Lyme Borreliosis

*B. mayonii* - Clinical differentiation

- diffuse macular rash not typical of erythema migrans
- 4 of 6 patients = N/V
- 2 of 6 patients = *fever* > 39°C
- 3 of 6 = *neurologic manifestations*

**Babesiosis**

*Ixodes scapularis* ticks

- *B. burgdorferi*  
  Lyme disease
- *A. phagocytophilum*  
  Human Granulocytic Ehrlichiosis
- *Babesia microti*  
  Babesiosis

**Babesiosis**: (usually *B. microti* in U.S.…. few cases of *B. divergens*)

- RBC parasite
- Most cases in Northeast
  - Nantucket Island, Martha’s Vineyard, Cape Cod
  - Block Island (RI), Eastern Long Island (NY)
  - Shelter Island & Fire Island
  - few cases reported in Midwest
- Deer reservoir
Babesiosis

Clinical presentation:
- symptoms 1-4 weeks after tick bite
- fatigue, malaise, anorexia, chills
- intermittent high fever
- hemolytic anemia w/ elevated reticulocyte counts

Diagnosis:
- peripheral smear

Treatment:
- Atovaquone + azithromycin (preferred)
- quinine + clindamycin
Babesiosis

"Tick Malaria"
Symptoms:
- Fever, fatigue, poor appetite, HA, nausea, diarrhea, myalgia or arthralgia
- Leukopenia
- Thrombocytopenia
- Elevated transaminases

Prognosis:
- Very good

Treatment:
- Supportive care

“Ehrlichiosis with a negative test”
2013
• 19 tick collections
• 39,096 ticks

*Amblyomma americanum* = 97.6%
*Dermacentor variabilis* = 2.3%
*Ixodes scapularis* = 1 tick

39,096 -> tested in 3,073 pools

*60 pools* + for Heartland virus via HRTV RT-PCR

All *Amblyomma americanum*

Bourbon Virus

- 50+ yo man - Bourbon County, KS
- Several tick bites spring 2014 - embedded tick just prior to presentation
- Day 1 illness: nausea, weakness, diarrhea
- Day 2: fever, anorexia, chills, HA, myalgia, arthralgia
- Day 3: PCP -> doxy
- Day 4: obtunded
- Hospital: papular rash on trunk
  - WBC: 2,200 (lymphopenia)
  - Plt: 72,000
  - Na 133 / K 3.0 / AST 138 / ALT 86
  - No improvement w/ doxy
  - RMSF / Lyme / Ehrlichia sero-negative
  - Transfer
    - Diffuse maculopapular rash (trunk); petechiae on soft palate and lower ext; bibasilar crackles; left axillary lymphadenopathy
  - Continued fever
  - CT: diffuse abd adenopathy
  - Clinical decline -> transfer to ICU -> progressive lactic acidosis, PEA, death
Whole blood sent to CDC

Plaque reduction assay

Day 6  Day 7  Day 8

Novel Thogotovirus

Bourbon Virus

Tick prevalence?: unknown

Disease incidence?: unknown

Lab testing: CDC via KDHE Lab
Colorado Tick Fever

Etiologic agent:

CTF caused by a coltivirus

Pathogenesis:

- reservoir in mammals (rodents, deer, etc)
- *Dermacentor andersoni*
- March - September
  - Colorado - peak April - June
Colorado Tick Fever
Cases 1990 - 1996
Colorado Tick Fever

Clinical presentation:

- mean incubation 3-4 days
- abrupt fever, chills, intense HA, severe myalgias, hyperesthetic skin
- few abd or resp symptoms
- rash 15%
- acute symptoms resolve in 1 week,
  - recurrent symptoms 2-3 days later
    (diphasic “saddleback” fever curve)
- lassitude, asthenia can persist for weeks / months
  (younger fare better than older)
Colorado Tick Fever

Clinical presentation:
- Infects marrow erythrocytic precursors
  - infected erythroblasts mature
  - viremia lasts for duration of red cell
- leukopenia characteristic

Diagnosis:
- blood culture for virus (BHK-21 cells)
- immunofluorescence on periph blood smear
- IgM - ELISA

Treatment: None
Tick-Borne Relapsing Fever

**Etiology:**
- Borrelia spp.
  - B. hermsii
  - B. parkeri
  - B. turicatae

**Vector:**
- Ornithodoros tick - “soft tick”

**Illness:**
- fever, arthralgias, HA
- later, nausea, cough, photophobia, dizziness, +/- rash
- sx’s few days, absent a week, recurrent for several episodes
Tick-Borne Relapsing Fever

**Diagnosis:**
- peripheral smear
- serology

**Treatment:**
- erythromycin
- PCN’s
- tetracyclines
- chloramphenicol

**Beware:** Jarisch-Herxheimer reaction 54% in one case study (CID 1998;26:122-31)
Questions?