Tick-borne Diseases
2018 Update

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Tick-borne Diseases

- Tick overview
- Common themes
- Cases (well-recognized diseases)
  - RMSF, HME, HGA, Tularemia, Q fever, Powassan
  - Lyme dissertation
- New diseases
  - *R. parkeri*, 364D rickettsiosis
  - *E. ewingii*, *E. muris*-like
  - Heartland, Bourbon
  - *Borrelia mayonii*, *B. miyamotoi*
  - STARI
  - Beef allergy
Tick-borne Diseases

- **What’s the best way to remove a tick?**
  - Burn it with a match
  - Smother it with Vaseline
  - Grab it with your fingers and pull
  - Grab it with tweezers and pull
  - Rotate the body counterclockwise until it releases
  - Pry it off using the tines of a fork
  - Wait for it to drop off naturally
Tick-borne Diseases

- Soft ticks
  - Sheltered environments
  - NO seasonal activity
  - Nidicolous (feeds in the vicinity of the nest)
  - Live up to 10 years; resistant to starvation
  - Feed briefly, but several times per stage

- Argasidae
  - *Ornithodoros* (TBRF, other borrelioses)
Tick-borne Diseases

• Hard ticks
  • Open environments
  • YES seasonal activity
  • Nidifugous (leaves the nest to feed)
  • Live up to 3 years; less resistant to starvation/desiccation
  • Feed slowly (several days), but once and firmly

• Ixodidae
  • *Dermacentor* (RMSF, other SFG rickettsioses)
  • *Amblyomma* (HME, tularemia, Q fever, ATBF, *R. parkeri*, HV)
  • *Ixodes* (Lyme, HGA, MSF, new TBRF)
  • *Rhipicephalus* (RMSF in AZ)
*Ixodes scapularis*
Deer tick, AKA
Black-legged tick

*Amblyomma maculatum*

*Rhipicephalus sanguineus*
Brown dog tick

*Dermacentor variabilis*
Dog Tick

*Amblyomma americanum*
Lone Star Tick

*Ornithodoros hermsi*
Tick-borne Diseases
Tick-borne Diseases

• **Common threads**
  • Incubation period: 2 days - 2 weeks
  • Symptoms: Fever (T ≥ 102 °F), frontal HA
  • Labs: thrombocytopenia, elevated LFTs
  • Rx: doxycycline 100 mg PO bid
  • Sx improve w/treatment in 48-72 hrs
  • Dx confirmed on convalescent Ab tests
Case #1

- 55 y/o farmhand with mild sore throat, severe frontal headache, high-grade fevers (T\(\geq\)102 °F) that began 5 days earlier

- Prescribed amoxicillin over the phone 4 days ago for presumed strep throat

- Pt called PCP 2 days ago after he developed “red spots” on hands; Rx: Z-pak

- Now: family pt to ER-delirious, lethargic
Case #1

- Clinical findings:
  - Responsive only to pain; tachypneic; tachycardic
  - Exam: macular rash on soles of feet

- Labs:
  - WBC = 9.0; Hgb = 11.0; plts = 56,000
  - AST/ALT = 56/48; other LFTs normal
  - Sodium 122
Diagnosis, please
RMSF

- *Rickettsia rickettsii*
  - Vectors: *Dermacentor, Rhipicephalus*
  - Rickettsiae released after 6-10 hrs of tick attachment
  - Target tissue: endothelial cells of every organ
  - Presents clinically as a multisystem vasculitis
  - Macular rash starts ~day 3; petechial rash ~day 6
    - Ankles/wrists first, then trunk/palms/soles
  - Most deaths occur ≤9 days
  - 90% of reported cases between April and September
Figure 3. Number of confirmed Rocky Mountain spotted fever cases by month of onset for each year, 1993–1996, based on case report forms submitted by the states to the Centers for Disease Control.
RMSF

Average annual incidence per 1,000,000 persons, 2000–2007

- Yellow: 0.1–4.9
- Orange: 5.0–14.9
- Red: >= 30.0
FIGURE 4. Average annual incidence of Rocky Mountain spotted fever cases per million population and case-fatality ratio by age group during 1993–1996 in the United States, based on case report data collected by state and territorial health departments. SOURCE: CDC.}

RMSF
RMSF

Figure 8. Historical surveillance for Rocky Mountain spotted fever, incidence and case fatality ratios (CFR) based on national sur-
RMSF

Figure 1. Annual incidence rates of Rocky Mountain spotted fever.
RMSF

• **Typical obstacles to the correct diagnosis**
  • Belief that RMSF is found only in the Rockies
  • Belief that the rash is required for the diagnosis
    • Classic triad of fever, rash, hx of tick exposure: 3-18%
  • Belief that a negative initial Ab test excludes the Dx
  • Reluctance to treat children <8 yrs w/doxycycline
RMSF

Clinical Pearls
- Hx of tick attachment in only 50%
- Initial Ab test almost always negative
- 100% cured if Rx started within 5 days after sx onset
- Mortality increased when:
  - Nonwhite
  - Male
  - Abdominal pain/GI symptoms
  - Age >40 yo
  - Absence of HA
- High-grade fever >5 days in kids: unlikely to be viral (RMSF, Kawasaki, etc)
- Empiric Rx w/doxycycline x 48 hrs?
Case #2

- 45 yo MD presents with 5 day history of:
  - Fevers >102 °F
  - Severe frontal headaches
  - No photophobia or neck stiffness
  - No rash reported
  - Exam findings (next slides)
  - Labs: normal WBC, low platelets, elevated transaminases
Diagnosis, please
Ehrlichiosis

- Etiologic agents:
  - *Ehrlichia chaffeensis*
  - *Ehrlichia ewingii*
  - *Ehrlichia muris*-like agent (Wisconsin, 2009)

- Vectors:
  - *E. chaffeensis*:
    - *Dermacentor variabilis* (dog tick)
    - *Amblyomma americanum* (Lone Star tick)
  - *E. ewingii*
    - *Amblyomma americanum* (Lone Star tick)
Ehrlichiosis

<table>
<thead>
<tr>
<th>Sign, Symptom, or Laboratory Finding</th>
<th>HME Patients with Abnormal Findings (%)</th>
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<tbody>
<tr>
<td>Fever</td>
<td>97</td>
</tr>
<tr>
<td>Headache</td>
<td>81</td>
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<tr>
<td>Chills or rigors</td>
<td>67</td>
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<td>Myalgia</td>
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<td>Malaise</td>
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<td>48</td>
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<tr>
<td>Anorexia</td>
<td>66</td>
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<tr>
<td>Vomiting</td>
<td>37</td>
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<tr>
<td>Diarrhea</td>
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<tr>
<td>Abdominal pain</td>
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<tr>
<td>Rash</td>
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<tr>
<td>Cough</td>
<td>26</td>
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<tr>
<td>Dyspnea</td>
<td>23</td>
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<tr>
<td>Lymphadenopathy</td>
<td>25</td>
</tr>
<tr>
<td>Confusion</td>
<td>20</td>
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</table>
Ehrlichiosis

- **Labs**
  - Leukopenia 60%
  - Thrombocytopenia 68%
  - Elevated AST/ALT 80%
  - Elevated creatinine 30%

- **Diagnosis**
  - CLINICAL SUSPICION
  - Serology (IFA)
  - Peripheral blood smear (insensitive)
  - *In vitro* cultivation (largely unavailable)

- **Treatment**
  - Doxycycline
    - Continue for 3 days after defervescence AND for at least 5-7 days
  - Rifampin (in pregnant patients)
  - Chloramphenicol NOT EFFECTIVE *in vitro*
Case #3

- 36 yo man develops abrupt onset of rigors, fever (103°F) while at desk job
- Returns to work next day in winter coat (this was in mid-July); sent to PCP office
  - Frontal HA, otherwise no localizing signs/sx
  - Physical exam: no rash or lymphadenopathy
  - Labs: WBC 2.3, plt 115, AST 48, ALT 54
Diagnosis, please
Anaplasmosis

- Etiologic agents:
  - Anaplasma phagocytophilum

- Vectors:
  - Ixodes spp. (primarily I. scapularis)
# Anaplasmosis

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<td>17</td>
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Anaplasmosis

- Laboratory abnormalities at presentation
  - Leukopenia 80%
  - Thrombocytopenia 60-90%
  - Elevated AST/ALT 90%

- Diagnosis
  - CLINICAL SUSPICION
  - Serology (IFA)
  - Peripheral blood smear (insensitive)

- Treatment
  - Doxycycline
  - Continue x 3 days once afebrile AND for at least 5-7 days
Case #4

- 69 yo woman develops abrupt onset of rigors, then fever (103°F) 2 days later, develops confusion

- Taken to ER by family
  - Global HA, sore finger
  - Physical exam: (see next slides)
  - Labs:
    - WBC 12.0, mild L shift, plt 112, AST 75, ALT 68
Diagnosis, please
Tularemia

- Etiologic agent: *Francisella tularensis*

- Modes of transmission:
  - Arthropods (ticks, fleas, deer flies, mosquitoes)
  - Animals (cats, dogs)
  - Aerosols (lab workers, farmers, kids)

- Epidemiology
  - Occurs year-round
    - Tick-associated peaks in summer
    - Rabbit-associated peaks in winter
  - Reported in every state of continental USA but more frequent in central states
FIGURE 2. Reported cases of tularemia — United States, 1990–2000

* Based on 1,347 patients reporting county of residence in the lower continental United States. Alaska reported 10 cases in four counties during 1990–2000.

† Circle size is proportional to the number of cases, ranging from 1–39.
Tularemia
Tularemia

- Epidemiology
  - Ticks remain the most common vectors for tularemia in the USA
    - *Amblyomma americanum* (Lone Star tick)
    - *Dermacentor variabilis* (dog tick)
    - *Dermacentor andersoni* (wood tick)

- Clinical Manifestations
  - Incubation period: 1-21 days (mean, 3 days)
  - Fever (>102°F) is the most consistent finding
    - Faget sign (pulse-temperature dissociation) in ~40%
  - Systemic symptoms (chills, headache, fatigue, diarrhea, vomiting) less pronounced than focal sx at site of inoculation
Tularemia

- Clinical Manifestations
  - Ulceroglandular (>40%)
  - Glandular (3-20%)
  - Oculoglandular (<3%)
  - Oropharyngeal (<5% overall; 30% in kids)
  - Pneumonic (7-20%)
  - Typhoidal (5-30%)
  - Other (meningitis, pericarditis, osteomyelitis)
Tularemia

- **Diagnosis**
  - CLINICAL SUSPICION
  - Serology (ELISA)
  - Culture

- **Treatment**
  - Streptomycin
  - Gentamicin
  - Doxycycline
  - Quinolones (other than ciprofloxacin)
Case #5

- 62-year-old farmer/rancher was hospitalized because of frontal headaches, fever and night sweats of two months’ duration

- Laboratory workup showed mildly elevated liver enzymes (ALT=77, AST=50)

- Dismissed after five days with presumed diagnosis of acute sinusitis on levofloxacin without benefit
Case #5

• Ten days later he was readmitted with back pain, fever of 103, abdominal discomfort and elevated LFTs (ALT=80, AST=55)

• Extensive workup including EGD, CT abdomen, HIDA scan and bone scan showed nonspecific findings

• Patient transferred to Wichita for further evaluation by general surgery
Case #5

- Case presentation (continued)
  - Patient was then transferred to our facility for further evaluation
  - Potential occupational exposure to unusual diseases was explored; the patient reported:
    - Spontaneous abortion of calf 2 wks prior to onset of symptoms
    - Helped neighbor (goat rancher) with ill herd
Diagnosis, please
Q Fever

- *Coxiella burnetii*

**Epidemiology:**
- Acquired through inhalation
- Zoonosis (esp. persons exposed to large animals)
- Reservoirs: ticks, birds, mammals (esp. cattle, goats, sheep)
- Endemic worldwide (except New Zealand)

**Clinical manifestations are often mild or self-limited**
- 50% show signs of clinical illness; often subclinical
- Most patients will recover to good health within several months without any treatment
- Rarely fatal; ~1-2% with acute Q fever will die
- Nonspecific signs/symptoms often lead to misdiagnosis
Figure 4. Average annual incidence of Q fever by state, United States, 2000–2004.
Q Fever: Manifestations

Acute (<6 mos)
- Flu-like syndrome (high fever, HA, diffuse myalgias)
- Isolated fever
- Atypical pneumonia
- Hepatitis
- Febrile exanthem
- Pericarditis; myocarditis
- Meningoencephalitis

Chronic (>6 mos)
- Endocarditis or endarteritis
- Osteomyelitis
- Granulomatous hepatitis
- Pseudotumor of the lung
Q Fever: Lab Findings

**Acute (<6 mos)**
- Normal WBC (90%)
- Thrombocytopenia (25%)
- Elevated ALT/AST (70%)
- Smooth muscle autoantibodies (65%)
- Anti-phospholipase antibodies (50%)

**Chronic (>6 mos)**
- Leukocytosis (25%)
- Leukopenia (15%)
- Elevated ALT/AST (40-60%)
- Thrombocytopenia (25-50%)
- Anemia (40%)
- ANA+ (35%)
- RF+ (60%)
Q Fever

- **Diagnosis**
  - CLINICAL SUSPICION
  - Cultures = insensitive, dangerous
  - Serology = best yield
    - Acute infection: Phase II $\geq 1:200$
    - Chronic infection: Phase I $\geq 1:800$
    - 4-fold change in Ab indicates a confirmed case
    - Elevated single Ab or persistent Ab = probable Q fever

- **Treatment**
  - Acute: Doxycycline x 14 days
  - Chronic:
    - Doxycycline + rifampin x $>3$ yrs
    - Doxycycline + hydroxychloroquine (Plaquesnil) x $>1$ yr
Lyme Disease

- Etiologic agents
  - *Borrelia burgdorferi*
  - *Borrelia mayonii*

- Vector: *Ixodes* spp.

- Reservoirs: White-tailed deer, white-footed mouse
Lyme Disease
FIGURE 2. Number of cases of Lyme disease, by county — United States, 2000

* Total number of cases from these counties represented 90% of all 2000 cases.
FIGURE 2. Average rate* of Lyme disease, by county of residence† — United States, 1992–2006§

* Per 100,000 population.
† County of residence was available for 98.1% of cases reported during 1992–2006.
§ During 2003, Pennsylvania reported 4,722 confirmed cases and 1,008 suspected cases.
Lyme Disease

FIGURE 5. Number* of reported Lyme disease cases, by month of illness onset — United States, 1992–2006

* N = 188,340.
Lyme Disease

- Clinical manifestations
  - Stage 1 (cutaneous)
    - Erythema migrans
    - Regional lymphadenopathy
    - Minor constitutional symptoms
Lyme Disease

- Clinical manifestations
  - Stage 2 (disseminated)
    - Meningitis, cranial neuropathies, radiculoneuritis
    - Lymphadenopathy (regional or generalized)
    - Splenomegaly
    - Myocarditis/pancarditis; AV node block
    - Conjunctivitis
    - Microscopic hematuria
    - Severe malaise and fatigue
Lyme Disease

- Clinical manifestations
  - Stage 3 (persistent)
    - Chronic arthritis
    - Chronic encephalomyelitis, spastic paraparesis
    - Acrodermatitis chronica atrophicans
    - Fatigue
Lyme Disease


* N = 150,829.
Lyme Disease

- Diagnosis
  - Stage 1
    - Clinical grounds
    - Culture (100% specific; poor sensitivity)
  - Stages 2 & 3
    - Not indicated without clinical evidence
    - Sequential testing
      - ELISA/IFA first; if positive then Western blot
      - Western blot
        - IgM if symptoms <30 days
        - IgG if symptoms >30 days
“New” Tick-borne Diseases

- Southern Tick-Associated Rash Illness (STARI)
  - Lone star tick (*Amblyomma americanum*)
  - Erythema migrans-like lesion
  - Fever/arthralgias/fatigue
  - Resolved with doxycycline but NOT certain if illness would resolve without Rx
“New” Tick-borne Diseases

- Southern Tick-Associated Rash Illness (STARI)
  - What’s different from Lyme disease?
    - Vector is different (Lone Star tick)
    - STARI patients were more likely to recall a tick bite
    - Incubation period (time from bite to rash) short: 6 days
    - STARI patients w/EM rash = less likely to have other sx
    - Skin lesions of STARI patients were smaller (6-10 cm, vs 6-28 for Lyme), fewer in number, more circular in shape, and had more central clearing
    - STARI patients recovered more rapidly than Lyme pts
“New” Tick-borne Diseases

- Powassan Virus
  - Originally reported in Powassan, Ontario 1958
  - Flavivirus (like WNV): 2 lineages
  - Vectors:
    - *Ixodes scapularis* (Lineage 2)
    - *Ixodes cookei* (Lineage 1)
  - Manifestations—similar to WNV in many respects
    - Asymptomatic
    - Acute febrile illness
    - Encephalitis/meningitis
      - 10-15% mortality
      - 50% of survivors have lifelong sequelae
      - Thalamus usually involved on MRI
Powassan Virus

Powassan virus neuroinvasive disease average annual incidence by county, 2004–2013

Source: ArboNET, Arboviral Diseases Branch, Centers for Disease Control and Prevention
“New” Tick-borne Diseases

- Powassan Virus (continued)
  - Rarely identified: 60 cases 1958-2012 (21 2008-12)
  - Median age 49 yrs (range, 3 mos – 74 yrs)
  - 76% male
  - 29% immunosuppressed
  - 86% illness onset May-August

<table>
<thead>
<tr>
<th>Duration of attachment (minutes)</th>
<th>No. of mice exposed</th>
<th>No. of infected mice</th>
<th>No. of infected ticks</th>
<th>Minimum transmission</th>
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<tr>
<td>15</td>
<td>6</td>
<td>5</td>
<td>8</td>
<td>63%</td>
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<tr>
<td>30</td>
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<tr>
<td>180</td>
<td>5</td>
<td>5</td>
<td>6</td>
<td>83%</td>
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“New” Tick-borne Diseases

- Powassan Virus (continued)
“New” Tick-borne Diseases

- Heartland virus
  - Novel phlebovirus (never before reported in humans)
  - Discovered in 2009 in Saint Joseph, MO
    - 2 adult male farmers in their 50s
      - Fever/anorexia/diarrhea/fatigue
      - Leukopenia/thrombocytopenia
      - Rx w/doxycycline for HGA ineffective, sx worsened
      - Hospitalized 10-12 days
      - Both recovered (1 after 1 month; 1 after 1 year)
  - Case definition has found ~60 cases so far
  - Clinical illness/cytopenias correspond w/viremia
  - Reservoirs: Many; Vector: Lone Star tick
  - Dx: PCR available at CDC
“New” Tick-borne Diseases

- Bourbon virus
  - Novel Thogotovirus
  - Discovered 2014 at KUMC in KCK
  - Pt from Bourbon County, KS w/acute febrile illness
    - High-grade fever
    - Leukopenia/thrombocytopenia
    - Rx w/doxycycline ineffective
    - Developed MOSF then death on day 11 of illness
    - Tissues sent to CDC to look for Heartland virus
  - Dx: PCR testing at CDC (not yet standardized so can only use on patients who meet case definition)
  - Rx: supportive care only
“New” Tick-borne Diseases

- *Borrelia miyamotoi*
  - Another gent of tick-borne relapsing fever (TBRF)
  - *Ixodes scapularis* (unusual for TBRF)
“New” Tick-borne Diseases

- *Borrelia miyamotoi*
  - Clinical manifestations
    - Flu-like illness (F/C/S, HA, myalgias, N/V, cough, sore throat, lymphadenopathy)
    - Relapsing fever (10% of cases in Russia)
    - Erythema migrans-like rash (10% in Russia)
    - Neurologic complications in older/immunocompromised patients
  - Dx: PB smear; serologic testing (CDC)
  - Rx:
    - Doxycycline 100 mg PO q12h x 14 days
    - Ceftriaxone 2 g IV q24h x 14 days
    - Pen G 24 million units IV q24h x 30 days
  - N.B.: watch out for Jarisch-Herxheimer reaction
“New” Tick-borne Diseases

- Meat allergy induced by Lone Star tick bite
  - Beef AND pork
  - Galactose-α-1,3-galactose (“Alpha Gal”) from tick gut
  - Also found in red meat (hamburgers, bacon)
- Symptoms
  - Hives (most common)
  - Vomiting, diarrhea
  - Anaphylaxis 4-6 hours after eating meat
- Exercise-induced anaphylaxis
Tick-borne Diseases

Most commonly recognized/reported

- Rocky Mountain Spotted Fever (RMSF)
- Human monocytotropic ehrlichiosis (HME)
- Human granulocytotropic anaplasmosis (HGA)
- Tularemia
- Q Fever
- Babesiosis
- Lyme Disease
Tick-borne Diseases

- Babesiosis
- Relapsing Fever (TBRF)
- Tick paralysis
- Colorado Tick Fever virus
- Powassan virus encephalitis
- Heartland virus
- Bourbon virus
Tick-borne Diseases

Resources

- [http://www.cdc.gov/ticks/diseases](http://www.cdc.gov/ticks/diseases)
  - Webinar on new agents
  - 2006 summary
  - 2006 original guidelines
  - 2010 re-examination of guidelines
  - Summary of Dx/Rx for Lyme/Anaplasma/Babesia
Thank you