TICK TALK – UPDATE ON TICKBORNE ILLNESSES: EPIDEMIOLOGY AND MANAGEMENT
UPDATE ON LYME AND RICKETTSIAL DISEASES

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Sea Pines CME Course, June 2017
Duke University Medical Center
Disclosures

- None
Acknowledgements

- Paul Lantos, MD
- Ross McKinney, MD
‘Show and Tell’

- What is the name of this tick?
  - Adult tick or Nymph?

- What diseases can it transmit?
Objectives

1. Discuss ticks as vectors
2. Describe the common “tick-borne diseases” seen in the US
3. Describe acute febrile (rickettsial) tick-borne illnesses
4. Review management of more common febrile tick-borne diseases
5. Delineate the presentations & potential sequelae of Lyme Disease
Ticks

• Most important arthropod vector in temperate regions

• Arachnids: ticks and mites
  – Ixodid ticks = hard bodied (most human biters)
  – Argasid ticks = soft bodied, *Ornithodoros spp*

• Three stages: larvae, nymph and adult
To name a few:

**USA**
- RMSF
- Human monocytic ehrlichiosis
- Lyme Disease
- STARI
- R. parkeri spotted fever
- Babesiosis
- Human granulocytic anaplasmosis
- Colorado Tick Fever
- Powassan virus encephalitis
- Q fever
- Tularemia
- Tick paralysis
- **Borrellia mayonii**

**Global**
- African tick bite fever
- Mediterranean spotted fever
- Tick-borne encephalitis
- Tick-borne relapsing fever
- Crimean-Congo hemorrhagic fever
- Kyasanur forest disease
- European Lyme disease
- Omsk Hemorrhagic Fever (OHF)
- Tickborne encephalitis (TBE)
- Anaplasmosis, babesiosis, ehrlichiosis, tularemia, tickborne relapsing fever, RMSF, Powassan disease can acquire internationally also
Common Ticks in United States

- **Blacklegged Tick (Ixodes scapularis)**
  - Adult female
  - Adult male
  - Nymph
  - Larva

- **Lone Star Tick (Amblyomma americanum)**

- **Dog Tick (Dermacentor variabilis)**
The Southeastern Tick Milieu

- *A. americanum* - by far the dominant human-biting tick in the southeastern US
- *D. variabilis* - second most common
- *I. scapularis* rare
- *A. maculatum* emerging

Species Key

○ Amblyomma americanum
◆ Dermacentor variabilis
* Ixodes scapularis
+x Amblyomma maculatum

+ Each symbol represents 1 attached tick.

Fig. 1. Tick attachment sites by species for humans in Georgia and South Carolina, 1995-1998.
Business End of a Tick

extension.unh.edu/News/graphics/tickhead.jpg
Case Presentation

- 15yo M previously well with 4 days of fever (Tmax 39 C) and headaches
- Presents to ED with persistent fever and chills, fatigue, arthralgias, worsening headaches
- Also with abdominal pain and vomiting
- No recent travel, +tick bite ~2 weeks ago
Emergency Department

- Gen: awake, lying in bed, shielding eyes from light
- T 38.4  HR 112  RR 24  BP 142/63  sat 100% on RA
- Wt 118kg (99%)  Ht 189cm (98%)  BMI 33 (98%)
- HEENT: PERRL, oropharynx clear, conjunctival injection
- Neck supple, no LAD
- Lungs: Clear to A
- CV: tachycardic, nl S1, S2, pulses 2+, cap refill <2sec
- Abd: soft, hepatosplenomegaly – both ~2cm below costal margin
- Skin: scattered petechiae throughout. Macular erythematous rash with irregular borders on arms. No rash on palms or soles.
PE cont

- MSK: tender knees, ankles, wrists bilaterally. PIP joints tender

- Neuro: A&O x3, reflexes and strength intact, CN III-XII grossly intact. Sensation intact. No dysmetria, - Romberg
Laboratory Values

<table>
<thead>
<tr>
<th>Value</th>
<th>134</th>
<th>104</th>
<th>6</th>
<th>129</th>
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<tbody>
<tr>
<td>3.9</td>
<td>24</td>
<td>0.7</td>
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</table>

2.0

12

37

66K

Diff: 55% seg0s, 1% bands, 20% lymphs, 10% monos, 5% variant lymphs

ALC=500

Uric acid 4.3
LDH 384

Tot prot 6.3, alb 3.6
AST 75, ALT 98
Alk Phos 216
Differential Diagnosis?

- Sepsis
- Meningitis
- EBV / CMV
- Ehrlichiosis
- RMSF
- Non-infectious etiologies, eg Leukemia
- Others?

- Any guesses as to etiology for his illness?
- Additional clue needed?
Hematology laboratory calls you re: abnormality on blood smear

Photos/J. Stephen Dumler, University of Maryland (left); Bobbi S. Pritt, Mayo Clinic (right)
Acute Febrile Tick-borne Diseases

- Rickettsial illnesses
  - Spotted fever group, including Rocky Mtn Spotted Fever
  - Ehrlichiosis
  - Anaplasmosis

- Babesiosis

- Lyme disease does not cause acute febrile syndrome
Human Monocytic Ehrlichiosis

• *Ehrlichia chaffeensis*
  – Transmitted by lone star tick (*A. americanum*)
  – Rickettsial organism
  – Infects monocytes

• First recognized in 1987

• 40-60% hospitalized, 2-4% mortality
FIGURE 13. Approximate U.S. distribution of *Amblyomma americanum* (lone star tick)
Percent of Ehrlichiosis Cases Reported each Month, 1994-2010

Ehrlichiosis Incidence by Age Group, 2000-2010

Centers for Disease Control. CDC.gov
## Adults with Ehrlichiosis

<table>
<thead>
<tr>
<th>Symptom or sign</th>
<th>Patients, % (no. evaluated)</th>
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<tbody>
<tr>
<td>Fever</td>
<td>97</td>
</tr>
<tr>
<td>Myalgia</td>
<td>57</td>
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<tr>
<td>Headache</td>
<td>80</td>
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<tr>
<td>Malaise</td>
<td>82</td>
</tr>
<tr>
<td>Nausea</td>
<td>64</td>
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<tr>
<td>Vomiting</td>
<td>33</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>23</td>
</tr>
<tr>
<td>Cough</td>
<td>26</td>
</tr>
<tr>
<td>Arthralgias</td>
<td>41</td>
</tr>
<tr>
<td>Rash</td>
<td>31</td>
</tr>
<tr>
<td>Stiff neck</td>
<td>3</td>
</tr>
<tr>
<td>Confusion</td>
<td>19</td>
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<table>
<thead>
<tr>
<th>Laboratory finding</th>
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<tr>
<td>Leukopenia</td>
<td>62</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>71</td>
</tr>
<tr>
<td>Elevated serum AST or ALT level</td>
<td>83</td>
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</table>
### Rocky Mountain Spotted Fever

<table>
<thead>
<tr>
<th>Symptom, sign, or finding</th>
<th>HME</th>
<th>HGA</th>
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</thead>
<tbody>
<tr>
<td>Fever</td>
<td>97 (633)</td>
<td>93 (521)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>57 (250)</td>
<td>77 (516)</td>
</tr>
<tr>
<td>Headache</td>
<td>80 (240)</td>
<td>76 (385)</td>
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<tr>
<td>Malaise</td>
<td>82 (234)</td>
<td>94 (288)</td>
</tr>
<tr>
<td>Nausea</td>
<td>64 (143)</td>
<td>38 (258)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>33 (192)</td>
<td>26 (90)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>23 (197)</td>
<td>16 (95)</td>
</tr>
<tr>
<td>Cough</td>
<td>26 (155)</td>
<td>19 (260)</td>
</tr>
<tr>
<td>Arthralgias</td>
<td>41 (211)</td>
<td>46 (504)</td>
</tr>
<tr>
<td><strong>Rash</strong></td>
<td><strong>31 (286)</strong></td>
<td><strong>6 (357)</strong></td>
</tr>
<tr>
<td>Stiff neck</td>
<td>3 (240)</td>
<td>21 (24)</td>
</tr>
<tr>
<td>Confusion</td>
<td>19 (279)</td>
<td>17 (211)</td>
</tr>
<tr>
<td><strong>Laboratory finding</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Leukopenia</td>
<td>62 (276)</td>
<td>49 (336)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>71 (247)</td>
<td>71 (336)</td>
</tr>
<tr>
<td>Elevated serum AST or ALT level</td>
<td>83 (276)</td>
<td>71 (177)</td>
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</table>

**NOTE.** Data are from [1]. ALT, alanine aminotransferase; AST, aspartate aminotransferase.
<table>
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<th>Characteristic</th>
<th>Percent of Patients</th>
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<td>Confirmed</td>
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<tr>
<td>Fever (&gt;101°F)</td>
<td>100</td>
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<tr>
<td>Headache*</td>
<td>77</td>
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<td>Myalgia*</td>
<td>77</td>
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<tr>
<td>Rash (any)</td>
<td>57</td>
</tr>
<tr>
<td>Abdominal pain*</td>
<td>62</td>
</tr>
<tr>
<td>Nausea/vomiting</td>
<td>57</td>
</tr>
<tr>
<td>Fever/rash/tick bite</td>
<td>43</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>36</td>
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<tr>
<td>Fever/rash/headache*</td>
<td>54</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>50</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>36</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>14</td>
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</table>

*Only obtained from patients >2 years of age. 

P > 0.05 for all comparisons.
## Laboratory Findings in Children with Ehrlichiosis on Admission

<table>
<thead>
<tr>
<th>Findings</th>
<th>Percent of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Confirmed</td>
</tr>
<tr>
<td>Thrombocytopenia &lt;150,000/mm³</td>
<td>93</td>
</tr>
<tr>
<td>Aspartate aminotransferase &gt;55 U/L</td>
<td>92</td>
</tr>
<tr>
<td>Alanine aminotransferase &gt;55 U/L</td>
<td>85</td>
</tr>
<tr>
<td>Albumin &lt;3.0 mg/dL</td>
<td>56</td>
</tr>
<tr>
<td>Lymphopenia &lt;1500/mm³</td>
<td>58</td>
</tr>
<tr>
<td>Leukopenia &lt;4000/mm³</td>
<td>57</td>
</tr>
<tr>
<td>Hyponatremia</td>
<td>54</td>
</tr>
<tr>
<td>&lt;135 mEq/L</td>
<td>54</td>
</tr>
<tr>
<td>&lt;130 mEq/L</td>
<td>8</td>
</tr>
<tr>
<td>Hemoglobin &lt;10 mg/dL*</td>
<td>46</td>
</tr>
<tr>
<td>Bilirubin &gt;1.5 mg/dL</td>
<td>38</td>
</tr>
</tbody>
</table>

*P = 0.025; P > 0.05 for all other comparisons.
Severe Disease due to Ehrlichiosis

Less common:
- “Septic” shock-like picture
- Multiple organ failure
- Respiratory failure
- Severe CNS disease in immunocompromised pts
Diagnostic Techniques for *Ehrlichia*

- Peripheral blood smear
  - Variable sensitivity, 2-38%
- Serology (IFA) – retrospective Dx
  - Paired sera required
  - 4-fold rise in titer to 1:80
- PCR highly sensitive (60-85+%)

*Ehrlichioses in Humans: Epidemiology, Clinical Presentation, Diagnosis, and Treatment. Clin Infect Dis. 2007;45(Supplement 1):S45*
Rocky Mountain Spotted Fever (RMSF)

- Caused by *Rickettsia rickettsii*
  - Mortality 13-25% in pre-antibiotic era
  - Still 20% in untreated
- Transmitted throughout Americas
- ~2000 annual cases in US (MMWR 2010)
- Cases reported throughout most of contiguous US
  - 5 states (NC, OK, AK, TN, MO) account for >60% cases
  - Increasing reports in Arizona
- *Dermacentor variabilis* primary vector
  - < 1 per 1000 ticks carry *R. rickettsii*
RMSF

- Conveyed to human through tick’s saliva
- Requires several hours of attachment (at least 4-6, perhaps 24 hrs) Rickettsiae activated by warm blood meal
- Incubation period 2 - 14 dys (range 1-21)
- Most severe Rickettsial disease in US
Pathogenesis

- *R. rickettsiae* infect endothelium of blood vessels

- Immune reaction causes vasculitis with leaky vessels
  - petechiae, edema, inflammation
FIGURE 20. Immunohistochemical stain demonstrating *Rickettsia rickettsii* (red) in blood vessel endothelial cells

Photo/CDC
Reported RMSF Incidence by County, 2000-2013

MMWR 2016: Diagnosis and Management of Tickborne Rickettsial Diseases — United States. Recommendations and Reports / May 13, 2016 / 65;1–44
RMSF Case Fatality over Time

CDC Surveillance, 1920 - 2010
**RMSF Clinical Manifestations**

<table>
<thead>
<tr>
<th>Symptom</th>
<th>J Pediatrics</th>
<th>J Inf Dzs</th>
</tr>
</thead>
<tbody>
<tr>
<td># subjects (n)</td>
<td>92</td>
<td>262</td>
</tr>
<tr>
<td>Median age (years)</td>
<td>5.8</td>
<td>15</td>
</tr>
<tr>
<td>Fever</td>
<td>98</td>
<td>99</td>
</tr>
<tr>
<td>Rash</td>
<td>97</td>
<td>88</td>
</tr>
<tr>
<td>Palms / Soles</td>
<td>65</td>
<td>74</td>
</tr>
<tr>
<td>Headache</td>
<td>61</td>
<td>91</td>
</tr>
<tr>
<td>Nausea / Vomiting</td>
<td>73</td>
<td>60</td>
</tr>
<tr>
<td>Myalgia</td>
<td>45</td>
<td>83</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>36</td>
<td>52</td>
</tr>
<tr>
<td>Conjunctival redness</td>
<td>30</td>
<td>30</td>
</tr>
<tr>
<td>Altered mental status</td>
<td>33</td>
<td>26</td>
</tr>
<tr>
<td>History of a tick bite</td>
<td>49</td>
<td>84</td>
</tr>
</tbody>
</table>

Rash most profuse on face

Rash relatively sparse on trunk

Rash more profuse distally and on extensor surfaces
Severe RMSF

• Hypotension, coma, severe thrombocytopenia, acute renal failure, gangrene, digit / limb loss

• 73% of patients sought medical care within 3 days
  – 90% of patients within 5 days

• Only 28% received effective antibiotics within 5 days

• 39% had rash at first MD visit

• Only 51% had history of tick contact

• Mortality if treated within 5 days = 6.5%; after 5 days = 22.9%
Gangrene

Cerebral edema

Pulmonary edema

Myocarditis

Photos courtesy of Dr. Chris Paddock and Dr. Gerardo Alvarez Hernandez
Risk Factors for Fatal Outcome

- Delayed onset or absence of rash
- Age <10 years or ≥60 years
- Chronic conditions with signs/symptoms that overlap with RMSF (i.e. alcoholism, chronic lung disease)
- Glucose-6-phosphate dehydrogenase deficiency
- Off-season onset (colder months, first and last cases of the year)
- **Delay in administration of effective therapy (doxycycline)**

Laboratory Manifestations

• Laboratory abnormalities *nonspecific* and *occasional*
  
  – Hyponatremia – usually mild, seen in ≤ 50%
  
  – Mild AST, ALT, and BUN elevations
  
  – Thrombocytopenia
  
  – No characteristic change in WBC

Diagnosis

• Serology – *retrospective Dx*
  – IgG IFA gold standard serologic test
    • Titers rise 7-10 days after infection
  – EIA less reliable
  – Paired convalescent sample **required by State Lab**

• Blood PCR - poor sensitivity for RMSF

• Skin Bx & Immunostaining (70% sens)

• PCR or Culture skin lesions
Treatment – Ehrlichiosis and RMSF

• **Doxycycline** drug of choice
  – 4.4 mg/kg/day divided BID for children
  – 100 mg twice daily, max
  – Duration = 3 days beyond defervescence for RMSF
  – Duration = 7-14 days for HME

• Alternatives for MILD cases (esp in pregnancy)
  – Chloramphenicol (for RMSF)
  – Rifampin (for HME)

• If no defervescence in ~48hrs, consider other diagnoses
Doxycycline Tooth Staining Study

- Short term doxycycline use does **not**:
  - Darken shade of teeth
  - Cause visible staining of teeth
  - Increase risk of enamel hypoplasia

- Doxycycline can be safely administered to children without fear of tooth staining at dose and duration recommended for rickettsial diseases

<table>
<thead>
<tr>
<th>Disease</th>
<th>Incubation period</th>
<th>Common initial signs and symptoms</th>
<th>Cutaneous signs</th>
<th>Common laboratory findings</th>
<th>Estimated case-fatality rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rocky Mountain spotted fever</td>
<td>3–12 days</td>
<td>Fever, headache, chills, malaise, myalgia, nausea, vomiting, abdominal pain, photophobia, anorexia</td>
<td>Maculopapular rash approximately 2–4 days after fever onset in most, might become petechial and involve palms and soles</td>
<td>Thrombocytopenia, slightly increased hepatic transaminase levels, normal or slightly increased white blood cell count with increased immature neutrophils, hyponatremia</td>
<td>5%–10%</td>
</tr>
<tr>
<td><em>Rickettsia parkeri</em> rickettsiosis</td>
<td>2–10 days</td>
<td>Fever, myalgia, headache</td>
<td>Eschar, sparse maculopapular or vesiculopapular rash that might involve palms and soles</td>
<td>Mild thrombocytopenia, mild leukopenia, increased hepatic transaminase levels</td>
<td>—*</td>
</tr>
<tr>
<td><em>Rickettsia</em> species 364D rickettsiosis</td>
<td>—†</td>
<td>Fever, headache, myalgia, fatigue</td>
<td>Eschar or ulcerative lesion with regional lymphadenopathy</td>
<td>—†</td>
<td>—*</td>
</tr>
<tr>
<td><em>Ehrlichia chaffeensis</em> ehrlichiosis (human monocytic ehrlichiosis)</td>
<td>5–14 days</td>
<td>Fever, headache, malaise, myalgia, nausea, diarrhea, vomiting</td>
<td>Rash in approximately 30% of adults and 60% of children, variable rash pattern that might involve palms and soles, appears a median of 5 days after illness onset</td>
<td>Leukopenia, thrombocytopenia, increased hepatic transaminase levels, hyponatremia, anemia</td>
<td>3%</td>
</tr>
<tr>
<td><em>Ehrlichia ewingii</em> ehrlichiosis</td>
<td>—†</td>
<td>Fever, headache, malaise, myalgia</td>
<td>Rash rare</td>
<td>Leukopenia, thrombocytopenia, increased hepatic transaminase levels</td>
<td>—*</td>
</tr>
<tr>
<td><em>Ehrlichia muris</em>-like agent ehrlichiosis</td>
<td>—†</td>
<td>Fever, headache, malaise, myalgia</td>
<td>Rash in approximately 12%</td>
<td>Thrombocytopenia, lymphopenia, leukopenia, increased hepatic transaminase levels, anemia</td>
<td>—*</td>
</tr>
<tr>
<td>Human anaplasmosis (human granulocytic anaplasmosis)</td>
<td>5–14 days</td>
<td>Fever, headache, malaise, myalgia, chills</td>
<td>Rash rare, in &lt;10%</td>
<td>Thrombocytopenia, leukopenia, mild anemia, increased hepatic transaminase levels, increased numbers of immature neutrophils</td>
<td>&lt;1%</td>
</tr>
</tbody>
</table>

*CDC. MMWR 2016*
Can you name this disease?

Considerations:
Lyme Dz
STARI
Hypersensitivity reaction to bite
Cellulitis
Bacterial superinfection of bite
Nummular eczema
Tinea
Spider bite
Lyme Disease
Lyme Disease: Background

• Bacterial agent:
  – *Borrelia burgdorferi*
  – Spirochete
• Transmitted by *Ixodes* spp. ticks
  – *I. scapularis* in eastern US
  – *I. pacificus, I. ricinus, I. persculatus* elsewhere
• Wild rodents - natural reservoir
  – White footed mouse
US Vector-Borne Diseases

**Tick-borne**
- **Lyme** – 38,486
- RMSF – ~ 2500
- HME – 951 (underreported)
- HGA – 1161
- Babesiosis – < 100 ?
- Colorado tick fever – < 100 ?
- Powassan virus – 6

**Mosquito-transmitted**
- **West Nile** – 720
- **LaCrosse** – 70
- EEE – 4
- WEE – ~ 10
- SLV – 12
- California serogroup – 55
- Malaria – 1451
- Dengue – ? Prob hundreds
FIGURE 16. Approximate U.S. distribution of *Ixodes scapularis* (blacklegged tick)
Public Health Impact: Lyme Disease

• 5\textsuperscript{th} most common reportable disease in US
  – Chlamydia, gonorrhea, salmonella, syphilis
  – Incidence slightly higher than new dx of HIV
  – Underreported

• Concentrated geographically
  – Very high disease burden in NE and Midwest US
“Acaralogical” Risk of Lyme

A abrupt N-S gradient of clinical Lyme risk – correlates with tick sampling data
N of 39th parallel – 207,600 km of sampling at 36 sites produced 1384 nymphs
S of 39th parallel – 223,400 km of sampling at 60 sites produced 21 nymphs (5 in NC)

http://www.cdc.gov/ncidod/dvbid/LYME/Id_Incidence.htm
Am J Trop Med Hyg 2012 vol. 86 no. 2 320-327
## Lyme disease cases reported by state, 2005-2015

*confirmed cases per 100,000 population

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<td>11</td>
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<td>Alaska</td>
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Is Lyme Moving South?

Virginia: increasing cases in southern counties over last 5 years

North Carolina: Small # confirmed (local) cases annually
   No marked increase – yet?
Human Lyme in Southeast

- Low # local Lyme cases per year (NC DPH)
- Incidence without marked change in South, to date
- Human incidence small fraction of northeast (CDC data)
  - NE States – incidence 10 – 100 per 100,000; gross underreporting
  - NC, SC, GA – incidence 0.1-0.4 per 100,000
- Canine serosurveillance (C6 peptide)
  - ~6% of dogs positive in VA
  - ~1% of dogs positive in NC and SC
Signal to Noise Problem?

• Most cases are of “cutaneous Lyme”
  • No laboratory proof of diagnosis
  • No clinical verification
  • Indistinguishable from STARI

• False positive serologies
  • Testing in low prob. Illnesses

• Travel histories not always available
  • “Local” cases may be imported

• There are “endemic” counties but infected vectors not found
• Case-based surveillance *insufficient* for vector-borne zoonoses
• *Ixodes* tick surveillance best surrogate measure of human risk
Antibiotic prophylaxis for patients with a tick bite

Single dose of doxycycline for prevention of Lyme disease when all of the following conditions are met:

- Highly endemic area
- Attached tick identified as an adult or nymphal *I. scapularis*
- Tick attached for > 36 hours based on engorgement or history
- Prophylaxis can be started within 72 hrs. of tick removal
- Doxycycline treatment is not contraindicated

Dose = 200 mg po x 1 for adults

From: The Clinical Assessment, Treatment and Prevention of Lyme disease, human granulocytic anaplasmosis and babesiosis: Clinical practice guidelines from the Infectious Diseases Society of America; CID; 2006
Clinical review of Lyme

- Lyme has well-described manifestations

- Pretest probability of Lyme is extremely low if one lacks specific objective findings
Clinical review of Lyme

• Early localized disease: erythema migrans rash

• Early disseminated disease:
  – Meningitis and / or neuropathy (usually CN VII)
  – Carditis (AV block)

• Late disseminated disease:
  – Arthritis (large joints with inflammatory effusions)
  – Chronic encephalopathy (very rare, poorly defined)
Lyme Disease: Clinical Manifestations in Children

- Prospective study: 201 Connecticut children with Lyme disease enrolled between April 1992 & November 1993
- Median age 7yo (range 1 to 21 yo)
- Presenting manifestations:
  - Erythema migrans in 89 %
  - Single EM lesion in 66%
  - Multiple lesions 23%
- Arthritis – 7 %
- Facial palsy – 3 %
- Aseptic meningitis – 1 %
- Carditis – 0.5 %

Erythema Migrans

- 70-80% of patients
- Typically 7-14 days after bite
- Expanding, round, erythematous
  - 5 – 30cm (up to 61cm reported)
  - Single lesion in ~80%
- Up to 2/3rds without “bullseye” appearance
- Diagnostic testing NOT USEFUL in erythema migrans
Treatment of Erythema Migrans

- 14 dys (range 10-21 dys) of oral antibiotics (Doxy, Amox, Cefurox, Azithro)
- Doxycycline is preferred drug (4mg/kg/dy)
- Azithromycin results in more treatment failures
  - Cure rates ~80%
- 10 – 21 days
  - No advantage to longer courses

Awaiting new Guidelines, out end of 2017 or early 2018

Shapiro E. Lyme Disease. NEJM 2014;370:1724
DDx includes STARI

- “Southern Tick-Associated Rash Illness”
- Associated with Lone Star ticks
  - Biologically incapable of transmitting *B. burgdorferi*
- Clinically indistinguishable from Lyme EM
- No evidence of *B. burgdorferi* in STARI lesions
- No known long term “Lyme” sequelae (e.g. arthritis)
- Cause remains unknown (not necessarily an infection)
- No controlled evidence that antibiotics are necessary
  - Some Rx with oral Abx because resembles early Lyme Dz
- MOST EM-rashes in NC & Southeast probably STARI
Southern Tick-associated Rash Illness (STARI)

Life stages of lone star tick
(Amblyomma americanum)
Early Disseminated Lyme: Acute Neuroborrellosis

• 15% of untreated patients
• Presentation: weeks - months after infection

• Meningitis
  – Headache, mild meningeal symptoms
  – Lymphocytic pleocytosis

• Cranial and peripheral neuropathies
  – May coexist with meningitis
  – 6\textsuperscript{th} and 7\textsuperscript{th} cranial nerve palsy common
  – Polyradiculopathy, mononeuritis multiplex
Early Disseminated Lyme: Lyme Carditis

- 5% of untreated patients
- Several weeks after infection
- AV block - any degree, including complete
  - Usually self-ltd and responds to therapy
- Myocarditis / pericarditis (less common)
Treatment of Early Disseminated Lyme

• Meningitis
  – IV Ceftriaxone for 14 days - standard of care
  – Oral doxycycline for 14 days may be equivalent

• Isolated CN palsies (without meningitis)
  – Oral therapy (preferably doxycycline 4mg/kg/dy) for 14 days
  – Beta lactams or macrolides may be effective if no meningitis
    • Amox 50/kg/dy or Cefuroxime axetil 30/kg/dy

• Carditis
  – Oral antibiotics for 14 days; initially IV if hospitalized
  – Consult cardiologist if symptomatic or high degree AV block
Later Onset: Lyme Arthritis

- Most common manifestation in US
- 60% of untreated patients
- Months after onset of illness
- Intermittent attacks of *true arthritis*
  - Typically one or two large joints, esp knee
  - Swelling out of proportion to pain
  - Seldom red
  - Generally less than <100,000 WBC, mostly PMNs
- Treatment = **28** days of oral antibiotics
Lyme Arthritis: Antibiotic-refractory

- ~10% of treated patients
- Persistent inflammation for months to years
  - Histopathology of chronic inflammatory arthritis
- Nearly always PCR and culture negative
  - Both synovial tissue and joint fluid
- HLA-DRB1-associated
- Should be regarded as *autoimmune* phenomenon
  - Anti-inflammatory drugs (NSAIDs, methotrexate)
  - Arthroscopic synovectomy
Lyme Disease: Diagnostic Testing

• Two-step serologic test
  — ELISA
   • Whole cell *B. burgdorferi* lysate
  — Confirmatory Western Blot
   • IgG 10 bands – $\geq 5/10 = \text{positive}$
   • IgM 3 bands – $\geq 2/3 = \text{positive}$
     — only useful in first 4-6 weeks
  — Less sensitive when have Erythema migrans (~38% sens)
  — Neuroborreliosis ~87% sensitivity
  — Lyme arthritis 97-100% sensitivity
Best Practices when Testing for Lyme

1. Order tests correctly:
   - First step = ELISA (aka EIA, aka “total Lyme antibody” or Lyme IgG/IgM)
   - Second step = Western blot (aka immunoblot)
   - WB not interpretable unless ELISA was positive or equivocal!
   - Order “Lyme ELISA with reflex to Western blot”

2. A positive test is insufficient to diagnose Lyme
   - Pt must have a compatible clinical illness
   - Only order a test when pretest probability is reasonably high
   - Pt request alone is not enough to justify testing

3. Use established criteria to interpret a Lyme test
   - eg, 4 positive IgG bands is a NEGATIVE Western blot
Two-Tiered Testing for Lyme Disease

**First Test**
- Enzyme Immunoassay (EIA)
- OR
- Immunofluorescence Assay (IFA)

**Second Test**
- Signs or symptoms ≤ 30 days
  - IgM and IgG Western Blot
- Signs or symptoms > 30 days
  - IgG Western Blot ONLY

**Positive or Equivocal Result**
- Consider alternative diagnosis
- OR
- If patient with signs/symptoms consistent with Lyme disease for ≤ 30 days, consider obtaining a convalescent serum
Outcomes of Lyme disease

• At 1-2 year follow-up people treated with ‘standard’ therapy for confirmed Lyme have good outcomes

• Incidence of chronic symptoms not clearly different in patients with a history of treated Lyme disease

• Several trials of prolonged IV antibiotics for “post-Lyme” patients: virtually no evidence of benefit, abundant evidence of harm
Prognosis

- Most patients treated with antibiotics recover completely
- In patients with persistent or recurrent joint swelling, re-treatment with a second 4-week course may be needed
- Some patients – particularly those diagnosed with later stages of disease – may have persistent symptoms of fatigue, muscle aches, reduced concentration
  - Preferred term for this is Post-treatment Lyme Disease Syndrome (PTLDS)
  - Placebo-controlled trials have not shown a sustained benefit of extended antibiotic treatment
Chronic Lyme Disease

• Controversial; diagnosis mainly given to persons with syndromes of chronic pain or chronic fatigue, or alternative medical diagnoses

• **No pathologic, microbiologic, or clinical definition**

• Background rate of these symptoms very high

• In endemic areas >2/3 of patients referred for Lyme disease are without evidence of active or past infection

• Inappropriate testing responsible for some diagnoses
Clinical Features of Patients (n=6)

- Ages ranged from 10 to 67 years; 4 male, 2 female
- 2 patients had a known tick bite, but all reported exposure to ticks or tick habitat in Minnesota or Wisconsin
- 5 presented with an acute febrile illness
- 3 had potential neurologic involvement (confused speech, profound somnolence, visual difficulties)
- 4 had rash – only 1 was suggestive of an EM
- 1 had arthralgia
Patient Outcomes

- 2 of 6 patients were hospitalized
- All were treated with antibiotics recommended for treatment of Lyme disease
- 5 patients recovered completely, while 1 reported residual joint pain
Tick Removal

- Hot match
- Petroleum Jelly
- Nail Polish

- Which one works best?
- None of the Above!!!!!
Tick Removal

- Use fine tipped tweezers
- Fasten to mouth parts
- Gently pull
- Don’t crush or squeeze tick after removal!
Show and Tell

- What is the name of this tick?
- What diseases can it transmit?

*Amblyomma americanum*
- STARI
- Human monocytic ehrlichiosis (*Ehrlichia chaffeensis*)
- Tularemia
Selected Tick Vectors

Transmit pathogens that cause the following diseases:

- Lyme disease
- Anaplasmosis
- Babesiosis
- Powassan virus disease
- *Borrelia miyamotoi* disease
- Ehrlichiosis
- STARI
- Tularemia
- Rocky Mtn. Spotted Fever
- Tularemia
Conclusions

– RMSF and HME:
  • Cause acute febrile illnesses
  • Can be life threatening, common
  • Clinical manifestations protean
  • Standard of care is empiric treatment (Dx delayed)
  • Clinical suspicion is primary guide to care

– Lyme disease
  • Not life threatening, subacute
  • Manifestations are rather specific
  • Always think about geographic risk and clinical probability
Questions?