LYME DISEASE: A SOUTHERN PERSPECTIVE

Kerry L. Clark, Ph.D.
Associate Professor of
Epidemiology & Environmental Health
Department of Public Health
University of North Florida
Jacksonville, FL
Setting the Record Straight

“...for I search after truth, by which man never yet was harmed.”—Marcus Aurelius

*Meditations. vi. 21.*
What is Lyme Disease?

- Lyme borreliosis infection
  - Worldwide distribution
  - Most common vector-borne disease in U.S.
  - ~20,000 cases recognized* per year
  - Spirochete *Borrelia burgdorferi sensu lato*

*Based on CDC Surveillance Case Definition Criteria*
What is Lyme Disease?

- Multisystem infection
  - Skin
  - Brain
  - Nerve tissue
  - Heart
  - Other organs
    - Signs and symptoms are highly variable
    - Early and late (disseminated) stages
Lyme disease *Borrelia* species

- >20 species worldwide (*B. burgdorferi* s.l.)
- So far, 7 species described in U.S.
  - *B. b. sensu stricto*, *americana*, *andersonii*, *bissettii*, *californiensis*, *carolinensis*, *kurtenbachii*

- Several confirmed pathogens worldwide
  - *B. garinii*, *B. afzelii*, *B. lusitaniae*, *B. valaisiana*, *B. burgdorferi* s.s., *B. kurtenbachii*, and others in Europe

- Question: Is Bbss only pathogenic species in U.S.?
• The Truth
  ■ At least 4 Bbsl species assoc. w/ LD in U.S.
    ▪ *B. b. sensu stricto, americana, andersonii, bissettii*
    ▪ Maybe others (*garinii?*, *afzelii?*)
    ▪ Problems with testing (antibody, culture, PCR)

• The Consequences
  ■ Testing aimed at 1 strain (B31) of 1 species (Bb)
  ■ Reliance on lab testing vs clinical diagnosis
  ■ Misdiagnoses
  ■ Underestimation of disease magnitude
Question

• Does Lyme disease occur in the South?
  ❧ What are some messages we hear from CDC, HCP, PHP, scientists?
    • Lyme is rare to nonexistent in the South
    • We don’t have Lyme; we have STARI
    • Only deer ticks can transmit Lyme, and we don’t have those ticks down here, or
    • Those ticks don’t bite people down here, and
    • Lone star ticks can’t transmit Lyme
    • Positive test results are false positives
    • Even dogs in South test negative, etc.
The Truth

- LD occurs practically worldwide
  - Northern and southern Europe; Northern Africa
  - Mexico
  - Brazil and other areas of South America
  - Large areas of Canada
  - Northeast, Upper Midwest, Far West in U.S.
    - So the southern U.S. is the “hole in the donut?”

- The Consequences
  - Lyme is not recognized in South…
Questions

- Do we have “deer ticks” down here?
- Do they bite people down here?
The Truth

- There is no such thing as the “deer tick”
- We do have blacklegged ticks, and
- Yes, they do bite people

Confirmed LD Vectors in USA: Eastern Blacklegged (Deer) Tick, *Ixodes scapularis* and Western Blacklegged Tick, *Ixodes pacificus*
Geographic Distribution of LD Vectors

Established* and reported** distribution of the Lyme disease vectors Ixodes scapularis (I. dammini) and Ixodes pacificus, by county, United States. 1907-1996

*at least 6 ticks or 2 life stages (larvae, nymphs, adults) identified. **at least 1 tick identified.
LD Seasonal Risk?

Lyme Disease: The Danger Months

*Note: These estimates are based primarily on data from the northeastern USA
Question

- Do we have the white-footed mouse down here?

- What are messages we hear?
  - White-footed mice are the most important host
  - We don’t have Lyme here because we don’t have wfm
The Truth about
*B. burgdorferi* Life Cycles

Cycles also involve other mammals, birds, lizards (maybe other animals and other tick spp.)
What does research on Bb/LD in the Southern U.S. show?
Materials and Methods

- Multiple vertebrate and tick spp.
Testing Methods

- Spirochete culture in BSK (variations)
  - Host-seeking adult ticks
  - Host-attached ticks
  - Wild vertebrate blood, organs, and ear tissue
  - Human blood, EM skin biopsies
  - Ticks removed from humans

- Bb specific and *Borrelia* spp. specific AB tests

- Bb specific PCR and DNA sequence analysis
  - Host-seeking and attached ticks
  - Wild vertebrate blood, ear tissue, dried blood spots ("Nobutos"); FTA cards
  - Human blood, skin biopsies, attached ticks
Research on Presence of B.b.s.l. in Nature in Southern USA—Summary

- Culture Isolation—wild vertebrates
  - South Carolina
    - Rodents*—82/196=41.8%
  - Georgia
    - Rodents*—33/274=12%
  - Florida
    - Rodents*—rodents: 13/200=6.5%
  - Missouri
    - Cottontails (several)
(*prevalence for all cotton rats, cotton mice, woodrats from all sites)
- North Carolina
  - White-footed mice, rice rat, marsh rabbit, raccoon
  - Raccoons—23/87=26%
Research on Presence of B. b. s. l. in Nature in Southern USA—Summary

- **Bb-specific AB or PCR pos results—vertebrates**
  - **South Carolina and Florida**
    - Lizards, 9 species—54% (PCR and sequencing)  
  - **Florida**
    - Small mammals, 7 species—85% (PCR and sequencing)  
  - **AL, FL, GA, MS, NC, SC**
    - Rodents (AB)  
  - **North Carolina**
    - Dogs (C6 AB)  
      (Duncan et al. 2005, Vector Borne Zoonotic Dis. 5: 101-109)
Is it true that “dogs in the Southeast don’t test positive for Lyme?”

- IDEXX Labs 4Dx SNAP Test
  (http://www.dogsandticks.com/diseases_in_your_area.php)
- C6 ELISA antibody test (highly specific for Bb)
- Results for dogs in southern USA since 2007

<table>
<thead>
<tr>
<th>State</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>FL</td>
<td>3,099</td>
</tr>
<tr>
<td>GA</td>
<td>800</td>
</tr>
<tr>
<td>SC</td>
<td>1,119</td>
</tr>
<tr>
<td>AL</td>
<td>208</td>
</tr>
<tr>
<td>MS</td>
<td>34</td>
</tr>
<tr>
<td>LA</td>
<td>44</td>
</tr>
<tr>
<td>OK</td>
<td>464</td>
</tr>
<tr>
<td>TX</td>
<td>1,366</td>
</tr>
<tr>
<td>AR</td>
<td>127</td>
</tr>
<tr>
<td>TN</td>
<td>493</td>
</tr>
<tr>
<td>KY</td>
<td>655</td>
</tr>
<tr>
<td>NC</td>
<td>4,448</td>
</tr>
<tr>
<td>WV</td>
<td>1,669</td>
</tr>
<tr>
<td>MO</td>
<td>378</td>
</tr>
<tr>
<td>VA</td>
<td>29,525</td>
</tr>
<tr>
<td>MS</td>
<td>34</td>
</tr>
</tbody>
</table>

Total (minus VA): **14,904**
Total (w/ VA):     **44,429**
• Culture Isolation—ticks

  ▪ South Carolina and Georgia
    • *I. scapularis* adults—12/864=1.3%
    • *I. affinis* adults—19/74=25.7%
    • *I. minor* (from birds and woodrats)
    • *A. americanum* (from bird)
    • *I. dentatus* (from drag)

  ▪ North Carolina
    • *I. scapularis*
      (Ryan et al. 2000, J. Wildl. Dis. 36:48-55)

  ▪ Missouri
    • *I. dentatus* (from cottontails)
    • *A. americanum L* (from cottontail)

  ▪ Texas
    • *I. scapularis* —3/448=0.7%
    • *A. americanum*—3/354=0.8%
    • *A. maculatum*—1/11=9.1%
- **Bb-specific AB or PCR pos results—ticks**
  - Missouri (ospA IFA)
    - *A. americanum* (1.9%)
    - *D. variabilis* (2%)
  - Florida (PCR and sequencing)
    - *I. scapularis* (4.6%)
    - *A. americanum* (2%)
  - AL, NC, TN, VA (PCR)
    - *A. americanum* (12% from eastern U.S. overall)
  - Northeast Mexico (IFA, PCR and sequencing)
    - *I. scapularis* and *I. texanus* (from hosts)
    - *A. cajennense* (hosts and vegetation)
    - *D. andersoni* (vegetation)
• **Bb-specific PCR pos results—ticks** (Clark et al., unpubl data)
  - Iowa
    - Blacklegged ticks (humans)
    - American dog ticks (humans, dogs)
  - Alabama
    - American dog ticks (dogs)
    - Gulf Coast ticks (dogs)
  - Florida
    - Lone star ticks
    - Blacklegged ticks
    - *Ixodes affinis*
    - *A. tuberculatum* (gopher tortoises)
    - Brown dog ticks
  - Georgia
    - Lone star ticks (vegetation)
  - Tennessee
    - American dog ticks (humans)
• Bb-specific AB or PCR pos results—vertebrates
  - South Carolina and Florida
    • Lizards, 9 species—54% (PCR and sequencing)
  - Florida
    • Small mammals, 7 species—85% (PCR and sequencing)
    • Raccoons, 2/17 (PCR and sequencing)
  - North Carolina
    • Dogs (C6 AB)
      (Duncan et al. 2005, Vector Borne Zoonotic Dis. 5: 101-109)
  - AL, FL, GA, MS, NC, SC
    • Rodents (AB)
• The Truth

- At least 6 Bbsl species infect animals in southern U.S. (rodents, birds, lizards)
  - *B.b. sensu stricto, americana, andersonii, bissettii, carolinensis, kurtenbachii*
  - Maybe others

- Several spp. found in ticks that bite people in South
  - *Bbss, americana, andersonii in blacklegged ticks*
  - *Bbss, andersonii in lone star ticks*
  - In American dog ticks? Brown dog ticks?

• The Consequences

- Multiple tick vectors?
- Extreme ecologic diversity in South complicates our understanding
Question: What about Research on LD in Humans in the Southern USA?

- **Texas:**
  - Spirochetes isolated in BSK II—14 patients w/LLI
    - Skin (8), blood (2), liver (1), bone (1), CSF (1), joint (1)
    - 7 positive with Bb specific AB H5332 (ospA)
  - North Carolina
    - 14 cases of EM and LLI illness at summer camp
      - From the Background: “*Borrelia burgdorferi*, the causative agent of Lyme disease, has never been isolated from a patient thought to have acquired Lyme disease in any southeastern state.”
      - Onset May—Aug; confirmed Aa tick bites in 3 patients
      - Tested using standard ELISA & WB
      - 5 skin biopsies cultured in BSK II—no spirochetes
      - 10 had IgM/IgG p41; 4 had 1-2 Bb-specific IgM/IgG WB bands
• Georgia and South Carolina
  - 23 patients w/ EM lesions; culture, AB, PCR testing
    - Onset April—Oct (most May—Aug)
    - 91% reported tick bite (most likely Aa)
    - 1 isolate of B. garinii (travel history to Europe)
    - 21/23 pos for 41-kDa IgM or IgG on CDC WB
    - 9/23 pos for at least 1 Bb-specific IgM or IgG band
    - 5/23 pos on Bb-specific flaB (p41) PCR; 0/23 ospA PCR pos.
    - 1 PCR pos was B. garinii; other 4 not sequenced/reported? (Felz et al. 1999, Arch. Dermatol. 135:1317-1326)

• Tennessee
  - EM from patient in East TN, April 2003
    - FlaB PCR positive
    - Sequence 99% homologous with Bbss B31 (Haynes et al. 2005, J. TN Acad. Sci. 80:57-59)
• Missouri
  - 22 patients with EM lesions; culture and AB tests
    - 11/22 WCS EIA pos on acute or conv. Sample; 0/22 pos on FLA EIA
    - 0/22 culture pos
    - Novel Aa transmitted agent?; tick-bite reactions?
      (Campbell et al. 1995, J. Infect. Dis. 172:470-480)

• Along came STARI/Master’s disease
  - *Borrelia sp. DNA* discovered in Aa from NJ, NY, TX
    - A RFG species named *B. lonestari*
    - *B. lonestari* suggested as cause of southern LLI
    - Numerous studies show *B. lonetari* in Aa ticks
• More Missouri patient studies
  ▪ 17 cases of EM following Aa tick bites
    • All biopsies culture negative
    • 6/11 showed spirochetes on silver staining
    • 8/17 had 1 or more Bb-specific IgM or IgG WB bands
    • 13/17 had IgM or IgG 41-kDa band

• Case of *B. lonestari* infection after Aa tick bite
  ▪ EM case and Aa tick bite
    • Skin biopsy and tick culture negative; blood PCR neg
    • Skin sample supernatant and tick *flaB* PCR pos
    • Other PCRs neg (23S rDNA; 16S-23S rDNA spacer; 16S rDNA)
    • *flaB* sequences for *B. lonestari*
    • Suggested *B. lonestari* causes EM and LLI indistinguishable from early LD
“The great tragedy of science—the slaying of a beautiful hypothesis with an ugly fact.” — Thomas H. Huxley

- More research on MO patients
  - 30 MO EM patients compared to 143 from NY
  - Tested by culture, ELISA, PCR
    - MO samples culture and ELISA neg
    - MO samples PCR neg for ospA, 16S rDNA
    - 5 MO skin samples flaB PCR+ (100% w/ Bbss B31)
    - Same 5 MO skin samples Bb-specific recA PCR+
    - No evidence of *B. lonestari* in patients
  - 21 MO patients w/ EM compared to 97 NY cases
    - MO EMs smaller, more central clearing, earlier in year, shorter incub. period, less symptoms
    - MO LLI may differ slightly and may be milder (Wormser et al. 2005, Clin. Infect. Dis., 41:958-965)
  - 1/70 MO “STARI” patients tested pos w/ C₆ ELISA
    - C₆ test is neg in “STARI” patients (Philip et al. 2006, Clin. Vaccine Immun. 13:1170-1171)
Florida LLI patient, 2003

• Case history
  ▪ Exposure/onset
  ▪ Signs/symptoms
  ▪ Treatment
2003 Lyme-like illness case in Florida

- BSK culture and AB negative
- PCR testing/DNA sequence results
  - *flaB* gene PCR pos (390-bp)
    - DNA sequence 100% with *B. andersonii* strains
  - *ospA* gene PCR pos (320-bp)
    - DNA sequence 100% with *B. americana* strain from FL scrub lizard; 99.7% with reference strains of *B. americana*.
  - *p66* gene PCR pos (233-bp)
    - DNA sequence 100% with *B. kurtenbachii* (strain 25015); 99.6% with SC152 green anole from SC; 98% with *B. carolinensis* strains
- Treatment; Late signs/symptoms; Follow up
Florida Lyme-like illness case, 2007

Case history

- Exposure
- Onset
- Signs/symptoms
- Skin, blood culture

PCR

- Bbsl flaB+
- 426/427 = 99.8% with B. americana SCW-30h

Treatment and outcome
Florida Lyme-like illness case, 2010, No. 1

Case history

- Lone star tick bite
  April, Duval Co., FL

- Rash onset ~1 week later

- Skin, blood attached tick samples

- Skin and tick PCR pos for Bbsl flaB

- >99% Bbss B31

- Treatment and outcome
Florida Lyme-like illness case, 2010, No.2

- Exposure 1: Aa tick, JAX FL; mid-May; attached 24 hr.
- Exposure 2: 2 wks later, multiple Aa ticks, Fayetteville, GA (1>24 hrs)
- Onset: 5 days after 2nd exposure

Signs/symptoms/treatment

- Relapses

PCR results:
- Nov. 2010: ELBS: Bbsl +; ELBS, urine: Ba. microti +
- Dec. 2011: Finger DBS sample Bbsl and Ba. microti +
- More positives: June 2012, Dec 2012

WB results:
- Jan 2011 (IgM p41); Mar 2011 (NB);
- Jan 2012 (IgM p41; IgG p41, p39, p58)
Table 1. Demographic and clinical characteristics of study patients, and *Borrelia burgdorferi* sensu lato detected in attached ticks (Clark et al. 2013, Int. J. Med. Sci. 10: 915-931)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Gender</th>
<th>Residency (state)</th>
<th>Primary symptoms</th>
<th>Duration of illness</th>
<th>Persistent symptoms</th>
<th>EM lesion</th>
<th>Tick bite history</th>
<th>Tick PCR result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>23</td>
<td>F</td>
<td>GA</td>
<td>Fatigue</td>
<td>8 yr</td>
<td>Fatigue, rashes, iritis, arthralgia, colitis</td>
<td>Multiple, disseminated, recurrent</td>
<td>Single (unknown sp.)</td>
<td>—</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
<td>F</td>
<td>FL</td>
<td>Headache, fatigue, fitful sleep, cognitive</td>
<td>27 yr</td>
<td>Fatigue, cognitive, arthralgia, fever, chills, rashes</td>
<td>Multiple</td>
<td>Multiple (unknown spp.)</td>
<td>—</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>F</td>
<td>FL</td>
<td>Fatigue, headache</td>
<td>2 mo</td>
<td>None</td>
<td>Single</td>
<td>Suspected adult I. scapularis</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td>F</td>
<td>GA</td>
<td>Fatigue, headache, leg pain</td>
<td>3 mo</td>
<td>Not known</td>
<td>No</td>
<td>A. americanum, adult female</td>
<td>B. burgdorferi</td>
</tr>
<tr>
<td>5</td>
<td>44</td>
<td>F</td>
<td>GA</td>
<td>Nausea, arthralgia, lymphadenopathy</td>
<td>3 yr</td>
<td>Fatigue, arthralgia, myalgia, cognitive</td>
<td>Single</td>
<td>Multiple A. americanum</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>38</td>
<td>F</td>
<td>FL</td>
<td>Optic neuritis, fatigue, headache, neck/back pain</td>
<td>12 yr</td>
<td>Fatigue, headache, neck/back pain, GI</td>
<td>Single</td>
<td>Multiple (unknown spp.)</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>50</td>
<td>M</td>
<td>FL</td>
<td>None</td>
<td>2 mo</td>
<td>None</td>
<td>Single</td>
<td>A. americanum, adult female</td>
<td>B. burgdorferi</td>
</tr>
<tr>
<td>8</td>
<td>49</td>
<td>M</td>
<td>GA</td>
<td>Tremors, balance, foot drop</td>
<td>7 yr</td>
<td>Motor function, balance</td>
<td>No</td>
<td>Multiple (A. americanum suspected)</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>42</td>
<td>M</td>
<td>FL</td>
<td>Lymphadenopathy, fatigue, headache, stiff neck</td>
<td>2 yr</td>
<td>Fatigue, headache, stiff neck</td>
<td>No</td>
<td>A. americanum, nymphs and adults</td>
<td>—</td>
</tr>
<tr>
<td>10</td>
<td>69</td>
<td>M</td>
<td>FL</td>
<td>Arthralgia, cognitive, prostatitis</td>
<td>1 yr</td>
<td>Cognitive, prostatitis</td>
<td>No</td>
<td>Uncertain</td>
<td>—</td>
</tr>
</tbody>
</table>
Table 2. Results for Lyme enzyme immunoassay (EIA) and Western Blot (WB) antibody tests, BSK spirochete culture, and *Borrelia burgdorferi* sensu lato PCR test results, and clinical diagnoses of study patients (Clark et al. 2013, Int. J. Med. Sci. 10: 915-931)

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sample&lt;sup&gt;a&lt;/sup&gt;</th>
<th>Lyme EIA</th>
<th>Lyme WB</th>
<th>BSK culture</th>
<th>B. burgdorferi PCR&lt;sup&gt;b&lt;/sup&gt;</th>
<th>Diagnoses&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Serum (Apr 2003)</td>
<td>Neg</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Chronic viral</td>
</tr>
<tr>
<td></td>
<td>Blood (Apr 2003)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
</tr>
<tr>
<td>2</td>
<td>Serum (1994)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Fibromyalgia, CFS, Meniere’s</td>
</tr>
<tr>
<td></td>
<td>Urine (1998)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Disease, RA, lupus, MS,</td>
</tr>
<tr>
<td></td>
<td>Blood (Feb 2004)</td>
<td>—</td>
<td>—</td>
<td>Neg</td>
<td>B. <em>burgdorferi</em></td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>Blood (Feb 2009)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
<td>Babesiosis</td>
</tr>
<tr>
<td>3</td>
<td>Serum (Nov 2007)</td>
<td>Neg</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>Blood (Nov 2007)</td>
<td>—</td>
<td>—</td>
<td>Neg</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
</tr>
<tr>
<td></td>
<td>Skin biopsy (Nov 2007)</td>
<td>—</td>
<td>—</td>
<td>Neg</td>
<td>B. <em>burgdorferi</em></td>
<td>Lyme disease</td>
</tr>
<tr>
<td>4</td>
<td>Serum (Apr 2009)</td>
<td>Neg</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Not known</td>
</tr>
<tr>
<td></td>
<td>Blood (Apr 2009)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
</tr>
<tr>
<td>5</td>
<td>Serum (Apr 2009)</td>
<td>Equivocal</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Sinus infection,</td>
</tr>
<tr>
<td></td>
<td>Serum (Jun 2010)</td>
<td>Neg</td>
<td>—</td>
<td>Neg</td>
<td>—</td>
<td>Sleep apnea</td>
</tr>
<tr>
<td></td>
<td>Serum, Blood (Jul 2010)</td>
<td>—</td>
<td>IgM 18, 23-25, 34, 41, 58</td>
<td>—</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Serum (May 2001)</td>
<td>Pos (1.31)</td>
<td>IgG 41</td>
<td>—</td>
<td>—</td>
<td>Optic neuritis,</td>
</tr>
<tr>
<td></td>
<td>Serum (Nov 2001)</td>
<td>Pos (1.52)</td>
<td>IgM 23; IgG 41</td>
<td>—</td>
<td>—</td>
<td>MS, Lyme</td>
</tr>
<tr>
<td></td>
<td>Blood (Jan 2010)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
<td>Disease</td>
</tr>
<tr>
<td></td>
<td>Blood (Feb 2010)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>Plasma (Dec 2012)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
</tr>
<tr>
<td>7</td>
<td>Serum (Apr 2010)</td>
<td>—</td>
<td>IgM 41; IgG 41</td>
<td>Neg</td>
<td>—</td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>Blood (Apr 2010)</td>
<td>—</td>
<td>—</td>
<td>Neg</td>
<td>Neg</td>
<td>B. <em>burgdorferi</em></td>
</tr>
<tr>
<td></td>
<td>Skin biopsy (Apr 2010)</td>
<td>—</td>
<td>—</td>
<td>Neg</td>
<td>B. <em>burgdorferi</em></td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>Serum (Aug 2010)</td>
<td>—</td>
<td>IgM 41; IgG 41</td>
<td>Neg</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Serum (Jul 2010)</td>
<td>—</td>
<td>IgG 41</td>
<td>—</td>
<td>—</td>
<td>ALS, Lyme</td>
</tr>
<tr>
<td></td>
<td>Serum (Jul 2011)</td>
<td>—</td>
<td>No bands</td>
<td>—</td>
<td>—</td>
<td>Disease,</td>
</tr>
<tr>
<td></td>
<td>Blood (Dec 2011)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
<td>Babesiosis</td>
</tr>
<tr>
<td></td>
<td>Blood (Jun 2012)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
<td>Lyme disease</td>
</tr>
<tr>
<td>9</td>
<td>Blood (Jun 2010)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>DBS (Dec 2010)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
</tr>
<tr>
<td></td>
<td>Serum (Jan 2011)</td>
<td>—</td>
<td>IgM 41</td>
<td>—</td>
<td>—</td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>Serum (Mar 2011)</td>
<td>—</td>
<td>No bands</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Blood/DBS (Dec 2011)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
<td>Lyme disease</td>
</tr>
<tr>
<td></td>
<td>Serum (Jan 2012)</td>
<td>—</td>
<td>IgM 41; IgG 41, 39, 58</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td></td>
<td>Serum/Blood (May 2012)</td>
<td>—</td>
<td>No Bands</td>
<td>—</td>
<td>Neg</td>
<td></td>
</tr>
<tr>
<td></td>
<td>DBS (Jun 2012)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
</tr>
<tr>
<td></td>
<td>Blood/plasma (Dec 2012)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
</tr>
<tr>
<td>10</td>
<td>Serum (Dec 2012)</td>
<td>IFA 1:40</td>
<td>IgM 31, 41, 58; IgG 18, 30, 34, 41, 58</td>
<td>—</td>
<td>—</td>
<td>CJD, Lyme disease</td>
</tr>
<tr>
<td></td>
<td>Plasma (Dec 2012)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>B. <em>burgdorferi</em></td>
</tr>
</tbody>
</table>
Geographic and Genospecies Distribution of *B. burgdorferi* sensu lato DNA in human patients in the USA (Clark et al. *J. Med. Microbiol.* 2014)

<table>
<thead>
<tr>
<th>Genospecies</th>
<th>No. Tested</th>
<th>No. Positive</th>
<th>B. burgdorferi (%)</th>
<th>B. americana (%)</th>
<th>B. andersonii (%)</th>
<th>ND (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>277</td>
<td>118 (42.6)</td>
<td>76 (64.4)</td>
<td>30 (25.4)</td>
<td>4 (3.4)</td>
<td>8 (6.8)</td>
</tr>
</tbody>
</table>
The Truth about LD in South

- Multiple Bbssl spp. causing LD in South
  - *Bbss, B. americana, B. andersonii* (maybe others)
- Multiple tick spp. may be involved
- Year round risk
- Coinfections apparent
- Consequences?
  - Failure to diagnose/treat
  - Unknown risk/magnitude
  - Unknown coinfections
Question

• So, are lone star ticks vectors of Lyme disease?
The Truth about Lone Star Ticks and Lyme

- Abundant, aggressive human biting sp.
- Accepted as vectors of STARI
- Accepted as vectors of *B. lonestari* (RFG sp.)
- Documented infection with *Bbss* and *B. andersonii*
- Removed from patients with documented EM, LLI, AB+ for Bbsl, and PCR + for Bbsl
- Must be considered as possible vectors and studied further

Consequences

- More misunderstanding, misdiagnosis, misinformation....
Question

- Does LD always cause a distinct red (bullseye) rash known as erythema migrans?
  - Do 60-80% of cases really have this rash?
- The Truth re LD rashes
- or
- The Consequences...

Others: KClark, UNF
Question

- How long does a tick have to be attached to transmit LD (or other TBD agents)?
  - Minimum time for transmission 48-72 hrs?

- The Truth
  - Depends on organism, dose, strain, host immunity
  - Longer attached, higher the risk

- Consequences?
  - Failure to treat early
  - More severe acute infections
  - More chronic infections

Source: solosoutheast.com
Question

- Do negative antibody, culture, or PCR tests prove that you don’t have LD

The Truth

- “Absence of proof is not proof of absence”
- Problems with AB testing
- Problems with culture
- Problems with PCR testing
- Lyme is often a clinical diagnosis
- Early treatment is critical for Lyme and many other TBDs

The Consequences or overreliance on clinical lab tests

- Misdiagnosis
- Missed opportunities for cure
- Chronic infections
- Tertiary effects
- Higher case fatality rates
Do southern LD patients show antibodies for LD on 2-tier lab tests? (EIA, WB)

Are positive AB or DNA tests for LD in southern patients false positives?

The Truth

- Many patients in South show AB evidence
- AB patterns may be different
- False pos beliefs based on PPV are flawed
- False assumption of low LD prevalence in South
- Lab test performance is poor only with southern patients? (Consequences are obvious)
Question

- Can LD be cured easily with short course of antibiotics?

The Truth

- Sometimes
- Earlier is often better (but how early?)
- Early recognition is key, but difficult
- A few weeks is not always enough
- Best treatment is not known
- Chronic infection and relapses are common
- Coinfections can complicate treatment
Question

- Following antibiotic treatment, are Lyme-like symptoms just a PLDS? Autoimmune disease? Result of permanent tissue damage?

The Truth

- Probably different reasons for different patients, but...
- Antibiotics sometimes fail to clear infection
- Evidence in mice, dogs, monkeys
- Evidence in humans
Conclusions—What is the truth about Lyme in the South?

Observe always that everything is the result of a change, and get used to thinking that there is nothing Nature loves so well as to change existing forms and to make new ones like them—

Marcus Aurelius

Meditations. iv. 36.
Lyme and other TBDs in the South: The Truth

- 1000s get sick after tick bites (incl. from lone stars)
- Signs and symptoms = LD or LLI
- Some test positive for AB to, or DNA of, Bbsl (= LD)
- Many stay sick after short courses of antibiotics
- Many already chronically infected/ill
- Many get better with more treatment
- Naming it something else (CFS, Fibro, STARI) won’t make it go away
- The pool of prevalent cases is rising
- Other TBDs are also present in South (incl. Babesiosis, Bartonellosis, Ehrlichiosis, Rickettsiosis)
The Consequences

- Erroneous disease statistics
- Inaccurate estimates of incidence/prevalence
- False assumption of low risk
- Misdiagnosis, lack of treatment
- Poor response by PH/other govt agencies epidemic
- Lack of protective behaviors
- Lack of funding for research resulting in:
  - Lack of knowledge of TBD presence/risk
  - Lack of information on tick vectors
  - Knowledge of reservoir hosts
  - Poor ecological understanding overall
TICKED
The Battle Over Lyme Disease in the South

An exclusive e-single by Wendy Orent
The Confounding Debate Over Lyme Disease in the South

The debilitating tick-borne disease is well-documented north of the Mason-Dixon line, but does it exist beyond that? By Wendy Orent | Friday, November 01, 2013

Entomologist Kerry Clark places a tick from the north Florida underbrush into a vial. Photo: Sarah Beth Glicksteen
“Clark Model” of Lyme ecology in the Southern U.S.
Purposes of Surveillance

- Assess public health status of disease
- Track diseases of PH importance
- Estimate magnitude of the problem
- Portray natural history of the disease
- Evaluate control/prevention measures
- Monitor changes in infectious agents
- Planning and use of PH resources

How would we be graded on our surveillance of Lyme disease? Other tickborne diseases?
Purpose of Surveillance

“The reason for collecting, analyzing, and disseminating information on a disease is to control that disease...Collection and analysis should not be allowed to consume resources if action does not follow...

--WH Foege, 1976

Are we not trying to improve surveillance because we don’t know what action to take to treat, control or prevent the disease?