What’s New In Tick-borne Disease?
Lyme Disease
Relapsing Fever
and beyond…

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Objectives

1. Understand the epidemiology of tick-borne diseases and the ticks that vector the diseases.

2. Recognize the growing list of tick-borne diseases.

3. Recall the testing available for detection of tick-borne diseases.
Anatomy of the tick...
Hard Shell Tick (Ixodid) vs Soft Shell (Agasid)

https://www.cdc.gov/dpdx/ticks/index.html
Hard Ticks - Life Cycle

https://www.cdc.gov/dpdx/ticks/index.html
Ixodid Ticks – male vs. female

female

male

https://www.cdc.gov/dpdx/ticks/index.html
Hard Shelled Ticks of the Northeast

- *Ixodes scapularis*
  “Deer tick or black-legged tick”

- *Rhipicephalus sanguineus*
  “Brown dog tick”

- *Dermacentor variabilis*
  “American Dog Tick”

- *Amblyomma americanum*
  “Lonestar Tick”

https://www.cdc.gov/dpdx/ticks/index.html
Amblyomma americanum

Lone Star Tick
(Amblyomma americanum)
Amblyomma americanum

- *Ehrlichia ewingii*
- *Ehrlichia chaffeensis*
- *Francisella tularensis*
- STARI (Southern Tick Associated Rash Illness)
- Heartland virus

Human monocytic ehrlichiosis
Rhipicephalus sanguineus

Brown Dog Tick
(Rhipicephalus sanguineus)
Rhipicephalus sanguineus

- *Rickettsia rickettsii* (Rocky mountain spotted fever)
  **In the southern USA only**
Dermacentor variabilis
**Dermacentor variabilis.**

- *Ehrlichia* spp. (Human monocytic ehrlichiosis)
- *Rickettsia rickettsii* (Rocky mountain spotted fever)
- *Francisella tularensis* (Tularemia)
Ixodes scapularis
Ixodes scapularis

- *Borrelia burgdorferi* (Lyme disease)
- *Borrelia mayonii*
- *Borrelia miyamotoi* (Tick-borne relapsing fever-like)
- Deer tick virus (Powassan virus, lineage II)
- *Babesia* spp.
- *Anaplasma phagocytophilum*
  (Human granulocytic Anaplasmosis)
Easiest way to identify

Inverted anal groove
Smaller than you may expect

Smaller than you may expect

Blacklegged Tick (*Ixodes scapularis*)

- Adult female
- Adult male
- Nymph
- Larva

sesame

poppy

https://www.cdc.gov/lyme/transmission/index.html
Harder to identify when “full”

https://www.cdc.gov/dpdx/ticks/index.html
Why are the ticks so bad this year?

A song of humans, hosts, forests, and food!
Evolution of Food – 1800s
Evolution of Food – Late 1900s-2000s
Mast Year
White-footed mouse
http://www.npr.org/sections/goatsandsoda/2017/03/06/518219485/forbidding-forecast-for-lyme-disease-in-the-northeast
http://www.npr.org/sections/goatsandsoda/2017/03/06/518219485/forbidding-forecast-for-lyme-disease-in-the-northeast
- *Borrelia burgdorferi* (Lyme disease)
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- *Babesia* spp.
- *Anaplasma phagocytophilum* (Human granulocytic Anaplasmosis)
Lyme Disease
Lyme disease (LD)

- *Borrelia burgdorferi* and *B. mayoni* (in N. America)
  - Gram-negative spirochete, motile by polar flagella
- Fastidious, not cultured in the clinical laboratory
- Vector
  - *Ixodes scapularis* (eastern/central)
  - *Ixodes pacificus* (west coast regions)
  - Infected *Ixodes* (nymph & mature adult) MUST feed >24 hours for transmission
    - @24 hours 5% of infected ticks will transmit
    - @48 hours 50% of infected ticks will transmit
    - @96 hours 100% of infected ticks will transmit
Symptoms

• Early LD or Stage 1 (3-30 days post bite)
  – Red, expanding rash called erythema migrans (EM) or “bull’s eye rash” (7-14 days)
    • Present in up to 80% of cases
  – Fatigue, chills, fever, headache, muscle and joint aches, and swollen lymph nodes
    • All cases present w/combinations of these symptoms
Symptoms

• Early disseminated LD or Stage 2 (days to weeks)
  – Additional EM lesions in other areas of the body
  – Facial or Bell's palsy
  – Severe headaches and neck stiffness due to meningitis
  – Pain and swelling in the large joints
  – Shooting pains that may interfere with sleep
  – Heart palpitations and dizziness due to changes in heartbeat

• Symptoms will resolve over weeks without treatment but can lead to serious complications
Symptoms

• Late disseminated LD or Stage 3 (months to years)
  – Can occur even after treatment for Lyme
    • Muscle & joint pain
    • Cognitive defects ("slow")
    • Sleep disturbance
    • Fatigue
Diagnostic tests

• Shortly after bite –
  – Silver stain (not diagnostic)
  – PCR from lesion biopsy

• Second stage of disease (dissemination)
  – *Serology (may be negative due to therapy)*
  – PCR from joint fluid, lesion
    • Blood and CSF are poor samples

• Late stage of illness
  – *Serology testing only*
Case Presentation

• 21 year old male from central Nova Scotia
• Experienced outdoorsman, hiker, hunter, and fisherman
• 3 day fishing and camping weekend in Andover, Maine
  – Memorial Day, 2002
• Noted tick attached to calf (unknown duration), removed with fishing pliers, cauterized pliers and wound with whiskey
• Continued fishing and camping
Case cont.

Lovejoy Bridge, Ellis River

http://maine.gov/mdot/historicbridges/coveredbridges/lovejoybridge/

https://lightscapesphotography.wordpress.com/page/5/
Case cont.

- 3 days post-camping trip developed rash on right calf

(not the actual rash)

- No other symptoms

- No physician seen (remember it is 2002)
Fast Forward

• 2012 – Now 31 year old microbiologist (and laboratory director)

• Participates in lab blood draw for QC purposes as “negative serum sample” for Lyme disease ELISA and Western blots

• + total antibody ELISA (screen)
  – Not a great negative QC point…

• Just for fun…
  – IgM blot – negative
  – IgG blot positive 7 of 10 bands

• Does this patient have Lyme disease?
No…but it is not always that easy

• 2003-2009 – Patient lived in Edmonton, Alberta Canada
  – Not a lyme endemic region
  – One vacation to lyme endemic region in 2006 & 2009
    • No observed tick bites, no rashes, no other symptoms

• 2009-2017 – Patient lived in Salt Lake City, UT
  – Not a lyme endemic region

• Patient grew up in central Maine
Case 2.

- 37 year old male from Andover, Massachusetts
- Never hikes, hates camping, generally disgusted by insects and nature
- Enjoys sitting in his back yard drinking, BBQing, and entertaining friends and family
- Enjoys golfing (2-3 rounds/week) – but he’s not very good at it
- Does not recall a tick bite
- No rash
- Develops flu-like illness; body aches, headache, low grade fever
Case 2. Continued

- Patient tested for LD
- Screen: ELISA +
- Immunoblot:
  - IgM + (3 of 3 bands)
  - IgG + (6 of 10 bands)

- Is this LD?
- YES. Clear cut LD
Quiz: What activity is the highest risk for LD in New England?

1. Camping
2. Hiking
3. Golfing
4. Yard work
5. Sleeping in cabins
Current State of LD Testing

Two-Tiered Testing for Lyme Disease

**First Test**

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

**Second Test**

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

**Outcome**

- Positive or Equivocal Result
- Negative Result

- Consider alternative diagnosis
- OR
- If patient with signs/symptoms consistent with Lyme disease for ≤ 30 days, consider obtaining a convalescent serum
Screening Assays

• Classic:
  - Whole Cell Lysate antigen source ELISA

• Evolved:
  - C6 peptide ELISA (26-amino acid recombinant region of VslE)
    • Immunetics/Oxford/Quest
  - VslE Chemiluminescent Immunoassay (CIA)
    • Diasorin (FDA clearance 2007)
  - rVslE1/pepC10 (OspC) ELISA
    • Zeus (FDA clearance 2013)
### Screening Assay Performance

**“Standard”**

<table>
<thead>
<tr>
<th>Assay</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Patients with non-LD infections or conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>WCS ELISA</td>
<td>74.9</td>
<td>97.7, 98.4</td>
<td>96.4</td>
</tr>
<tr>
<td>WCS ELISA + WB</td>
<td>35.2</td>
<td>77.3, 95.9</td>
<td>99.5</td>
</tr>
<tr>
<td>C6 ELISA</td>
<td>66.5</td>
<td>88.6, 98.4</td>
<td>98.8</td>
</tr>
<tr>
<td>C6 ELISA + WB</td>
<td>34.5</td>
<td>75, 95.1</td>
<td>99.5</td>
</tr>
<tr>
<td>VlsE CIA</td>
<td>69.8</td>
<td>100</td>
<td>99.5</td>
</tr>
<tr>
<td>VlsE/pepC10 kELISA</td>
<td>67.2</td>
<td>88.5, 94.1</td>
<td>99.2</td>
</tr>
</tbody>
</table>

**“Newer”**

<table>
<thead>
<tr>
<th>Assay</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Patients with non-LD infections or conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>VlsE/pepC10 kELISA</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

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*WCS, whole-cell sonicate; VlsE, variable major protein (Vmp)-like sequence, expressed; WB, Western blot; ELISA, enzyme linked immunosorbent assay; CIA, chemiluminescent immunoassay; kELISA, kinetic ELISA.*

*Data from healthy donors from regions in which Lyme disease is endemic and from those in which it is not endemic were combined.*

*Lyme disease stages 2 and 3 were not separated out in this study.*

---

Back to the Algorithm

Two-Tiered Testing for Lyme Disease

First Test

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

OR

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

National Center for Emerging and Zoonotic Infectious Diseases
Division of Vector Borne Diseases | Bacterial Diseases Branch
Details on the Blots

• IgM blot: 2 of 3 conserved bands*
  – Only run on patients with suspected symptom onset <30 days
  – If positive and IgG blot is negative after 30 days = false positive
  – Blot criteria do not apply after 30 days of symptoms

• IgG blot: 5 of 10 conserved bands*
  – Difficult to interpret in patients from endemic regions with unclear history
    • Think case 1 😊

*Unchanged since 1995*

CDC. Morb Mortal Weekly Rep. 1995. 44(31);590-591
Blots

- Western Blot
- Line Immunoassay
Automated Immunoblotting & Densitometry

<table>
<thead>
<tr>
<th>Test:</th>
<th>Borrelia B31 ViraStrip® IgG</th>
<th>Strip:</th>
<th>LGG0627178715-16</th>
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<table>
<thead>
<tr>
<th>Bands:</th>
<th>93</th>
<th>66</th>
<th>58</th>
<th>45</th>
<th>41</th>
<th>39</th>
<th>30</th>
<th>26</th>
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<td>104</td>
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<td>122</td>
<td>090</td>
<td>081</td>
<td>136</td>
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<table>
<thead>
<tr>
<th>kDa</th>
<th>Intensity to Cut-off</th>
</tr>
</thead>
</table>

Patient Strip: 16

Cut-Off Strip:

Band-Locator: VM LG BL
Do we really need blots?
Alternative Two-Tier algorithm

TABLE 2 Comparison of the traditional TTTA to a 2-EIA TTTA and the C6 ELISA alone in sera from patients with well-characterized Lyme disease

<table>
<thead>
<tr>
<th>Testing algorithm</th>
<th>Stage 1 (n = 114)</th>
<th>Stage 2 (n = 26)</th>
<th>Stage 3 (n = 29)</th>
<th>Healthy donors (n = 1,246)</th>
<th>Patients with non-LD infection or condition (n = 54)</th>
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</thead>
<tbody>
<tr>
<td>Traditional</td>
<td>42.1</td>
<td>73.1</td>
<td>100</td>
<td>99.4</td>
<td>100</td>
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<tr>
<td>C6 ELISA alone</td>
<td>56.1</td>
<td>100</td>
<td>100</td>
<td>98.4</td>
<td>98.1</td>
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<tr>
<td>2-ELISA</td>
<td>52.6</td>
<td>100</td>
<td>100</td>
<td>99.4</td>
<td>100</td>
</tr>
</tbody>
</table>

$\downarrow$ (27-44%)
$\uparrow$ Accuracy (27%)

**Alternative Two-Tier algorithm**

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-Tier Tests</strong></td>
<td><strong>First-Tier Tests</strong></td>
</tr>
<tr>
<td>VlsE CLIA</td>
<td>VlsE CLIA</td>
</tr>
<tr>
<td>WCS EIA</td>
<td>WCS EIA</td>
</tr>
<tr>
<td>WCS EIA</td>
<td>C6 EIA</td>
</tr>
<tr>
<td><strong>Second-Tier Tests</strong></td>
<td><strong>Second-Tier Tests</strong></td>
</tr>
<tr>
<td>C6 EIA</td>
<td>C6 EIA</td>
</tr>
<tr>
<td>C6 EIA</td>
<td>C6 EIA</td>
</tr>
<tr>
<td>VlsE CLIA</td>
<td>VlsE CLIA</td>
</tr>
</tbody>
</table>

![Diagram](image)

- CDC’s Lyme Serum Repository specimens used
  - Carefully curated – clinically well defined positives
  - Common interfering conditions for “negatives” and non-endemic volunteer negatives

Revisiting the Lyme Disease Serodiagnostic Algorithm: the Momentum Gathers

Adriana R. Marques
Karen C. Carroll, Editor

Standard 2-tiered algorithm (STT)

First-tier immunoassay

Positive or Equivocal

IgG and IgM Western blot

Interpretation uses standardized criteria: at least 2 of 3 bands for a positive IgM Western blot, and 5 of 10 bands for a positive IgG Western blot

Illness duration less or equal to 30 days

Use both IgM and IgG Western blot results

Illness duration more than 30 days

Use only IgG Western blot results

No further testing*

Modified 2-tiered algorithm (MTT)

First-tier immunoassay

Positive or Equivocal

Different first-tier immunoassay

Positive overall result

Negative overall result*

Negative
<table>
<thead>
<tr>
<th>Reference(s) (no.)</th>
<th>MTT algorithm</th>
<th>STT algorithm</th>
<th>Test program</th>
<th>Acute-phase EM sensitivity (%)</th>
<th>Test program</th>
<th>Acute-phase EM sensitivity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Branda et al. (16)</td>
<td>WC Vidas f/b C6 EIA</td>
<td>WC Vidas f/b WB</td>
<td>52.6</td>
<td>WC Vidas f/b WB</td>
<td>42.1</td>
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<td>Branda et al. (27)</td>
<td>WC W EIA f/b C6 EIA</td>
<td>C6 EIA f/b WB</td>
<td>38.2</td>
<td>C6 EIA f/b WB</td>
<td>36.4</td>
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<tr>
<td></td>
<td>WC W EIA f/b VlsE CLIA</td>
<td>WC W EIA f/b WB</td>
<td>36.4</td>
<td>VlsE CLIA f/b WB</td>
<td>34.5</td>
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<td></td>
<td>VlsE CLIA f/b C6 EIA</td>
<td>WC W f/b WB</td>
<td>54.5</td>
<td>WC Vidas f/b WB</td>
<td>25.4</td>
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<td>Molins et al. (28)</td>
<td>WC Vidas f/b C6 EIA</td>
<td>WC Vidas f/b WB</td>
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<td>Molins et al. (29)</td>
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<td>LYM/G Vidas f/b WB</td>
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<td>LYM/LYG f/b C6 EIA</td>
<td>42.5</td>
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<tr>
<td>Pegalajar-Jurado et al. (4)</td>
<td>WC Captia f/b C6 EIA</td>
<td>WC Captia f/b WB</td>
<td>55</td>
<td>WC Captia f/b WB</td>
<td>50</td>
<td></td>
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<tr>
<td></td>
<td>WC Captia f/b VlsE CLIA</td>
<td>WC Captia f/b WB</td>
<td>57.5</td>
<td>WC Captia f/b WB</td>
<td>42.5</td>
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<tr>
<td></td>
<td>VlsE CLIA f/b C6 EIA</td>
<td>C6 EIA f/b WB</td>
<td>50</td>
<td>VlsE CLIA f/b WB</td>
<td>42.5</td>
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<tr>
<td>Wormser et al. (11, 25)</td>
<td>WC EIA f/b C6 EIA</td>
<td>C6 EIA f/b WB</td>
<td>58.4</td>
<td>C6 EIA f/b WB</td>
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<tr>
<td></td>
<td>WC f/b WB</td>
<td>WC f/b WB</td>
<td>38.3</td>
<td>WC f/b WB</td>
<td>38.3</td>
<td></td>
</tr>
</tbody>
</table>
Examples of Future Areas of Investigation

• Novel/expanded antigen investigations for multiplex antibody detection
  – Bead-based detection

• Immuno-PCR (iPCR)
  – Optimize high specificity of C6 peptide with amplification of PCR
  – Reporter antibody contains DNA tag which is amplified after binding C6 specific antibodies

• Metabolomic profiling

https://www.cdc.gov/lyme/diagnostictesting/labtest/otherlab/index.html
Metabolomic profiling

- CDC study to detect early LD with better sensitivity
- Characterize low-molecular-weight (<15kDa) molecules in patients with early LD vs absence or baseline in healthy controls
- Liquid chromatography mass spectrometry
- 44 markers for early LD mainly lipids and lipophilic molecules
- More sensitive (88%) than traditional two-tier algorithm (43%) and 2-ELISA methods (48%)
- Not ready for clinical labs & will require FDA clearance

Examples of Unapproved Testing for Diagnosis

- Urine antigen detection
- Culture, immunofluorescence staining, or cell sorting of cell wall-deficient or cystic forms of *B. burgdorferi*
- Lymphocyte transformation tests
- Quantitative CD57 lymphocyte assays
- “Reverse Western blots”
- In-house criteria for interpretation of immunoblots
- IgM or IgG tests without a previous screening test

https://www.cdc.gov/lyme/diagnosistesting/labtest/otherlab/index.html
LD in Summary

- LD is a complicated infection to diagnose
  - Symptoms and exposure history can be difficult to accurately ascertain
- Emotionally and politically charged
- Technological advancements have been slow to materialize
  - New avenues of testing show promise but require more clinical validation
Case of the Chills

- 56 yo male returned from fishing vacation in southeastern California mountains 7 days prior to symptom onset
  - Stayed in upscale resort rental cabins
  - Did not recall any insect bites, no documented ticks seen
  - Spring 2012
- Fevers >104°F, 3x over ~2 d
  - Drenching sweats followed by intense chills
  - Symptoms resolved for a week then returned
- No other recent travel history
Tick Born Relapsing Fever (TBRF) and beyond
Tick Borne Relapsing Fever (TBRF)

- Causative organism in the USA...
  - *Borrelia hermsii*
  - *Borrelia parkeri*
  - *Borrelia turicatae*
  - ***Borrelia miyamotoi***
  
  Vector →

- Vector →
  - *Ornithodorus hermsi*
  - *Ornithodorus parkeri*
  - *Ornithodorus turicata*
  - *Ixodes scapularis*

**TBRF genetic group, but clinically not TBRF**
Approximate Geographic Distribution

- B. hermsii
- B. parkeri
- B. turicatae
- B. miyamotoi
Case Distribution

https://www.cdc.gov/relapsing-fever/distribution/index.html
Hard Shell Tick (Ixodid) vs Soft Shell (Agasid)

https://www.cdc.gov/dpdx/ticks/index.html
Ornithodorus spp.

Argasidae life cycle

https://www.cdc.gov/dpdx/ticks/index.html
TBRF

• Recurring febrile episodes ~3 days, separated by afebrile period ~7 days

>75%: headache, myalgia, chills, nausea
>50%: arthralgia, vomiting
>25%: abdominal pain, dry cough, eye pain, diarrhea, photophobia, neck pain

https://www.cdc.gov/relapsing-fever/clinicians/index.html
The Illness

• Fever up to 106.7°F “chill phase” (10-30 mins)
  – May become delirious, agitated, tachycardic and tachypneic

• Followed by the “flush phase”
  – Drenching sweats and a rapid decrease in body temperature.
  – Transiently hypotensive.

• Patients who are not treated will experience several episodes of fever before illness resolves.

https://www.cdc.gov/relapsing-fever/clinicians/index.html
Recovery

- **Treatment:**
  - Doxycycline – 2x daily, 7 days
- **Immune control**

https://www.cdc.gov/relapsing-fever/clinicians/index.html
Antigenic shift

- Genomic organization unique
- Allows shift of antigen on cell surface
  - “Hide and seek”
- Eventually WBCs win

https://www.cdc.gov/relapsing-fever/clinicians/index.html
Testing

- Peripheral blood smear
- IgG serology
- Real-time PCR
Blood smear

- Peripheral blood smear, performed like blood parasite screen or CBC
  - Giemsa, Wright, or Wright-Giemsa
- Good for initial diagnosis, low sensitivity
- Turn-around-time = hours
- Requires skilled readers, patience, and experience
Blood Smear in the Literature

In Reality
In Reality
In Reality (with Photoshop assistance)
In Reality (with Photoshop assistance)
Serology

- Retrospective diagnosis or support of recent diagnosis
- Four-fold rise in IgG titer
- Cross-reactivity with Lyme
  - Lyme false-positives
- Not widely available
  - Imugen (Oxford)
  - Quest Diagnostics
PCR

• High sensitivity
• High specificity (if well designed)
• No FDA cleared assays
• Challenges
  – Detect all relevant species to N. America vs Eurasia/Africa or both
  – Do NOT detect Lyme *Borrelia* species
  – Find samples or organism to validate with
Remember this patient?

Patient sample tested by in-house design, sequenced positive for *B. hermsii*.

- Patient stayed at cabin in southeastern California mountains
PCR Development at ARUP

- Designed to detect *B. hermsii*, *B. parkeri*, *B. turicatae*, and *B. miyamotoi* (identical sequence) from blood
  - Can also detect: *B. crocidurae*, *B. duttoni*, *B. hispanica*, *B. recurrentis*, and *B. microti*
    - TBRF *Borrelia* spp. from Europe, Asia, Africa
    - Differ by one base pair, slightly less sensitive – can differentiate this group by melt curve analysis
    - Will not detect *B. persica* (Middle Eastern endemic)
- No cross-reactivity with Lyme *Borrelia* spp or 68 other pathogens
  - Including *Anaplasma*, *Babesia*, and multiple *Plasmodium* species
PCR Testing in Prime Time

• Available commercially at major reference labs:
  – ARUP Laboratories
  – Mayo Medical Laboratories
  – Quest Diagnostics
TBRF In Summary

• TBRF causes a textbook illness reminiscent of malaria or *Babesia* but with distinct patterning of fevers

• Caused by many species of *Borrelia*
  – Vectored by several different ticks in different regions

• Detected by multiple mechanisms, commercially available

• Likely underreported due to insensitivity of blood smear
  – PCR is significantly more sensitive
A Fatal Headache

• 5 yo boy admitted w/ right-sided headache, drowsy, fever 101ºF
  – Abnormal brain EEG, normal CSF count
• 2 days later fever 103ºF, lymphocytic predominance in CSF
  – Became unconscious and unresponsive to stimuli
• 4 days after admission, completely comatose and encephalitic
  – Patient ceased breathing in the afternoon
• 6 days later passed away

...the year was 1958...

...the town was Powassan, Ontario

...no tick bite was ever reported

Deer Tick Virus
or Powassan virus, lineage II
Deer Tick Virus (DTV)

• DTV is one genotype of Powassan virus
  – Powassan virus lineage I = POWV = *Ixodes cookei*
  – Powassan virus lineage II = DTV = *Ixodes scapularis*

• Flavivirus closely related to tick-borne encephalitis group of viruses in Europe & Asia

• Discovered in 1958 in brain tissue
  – Fatal pediatric encephalitis in Powassan, Ontario

Case Distribution

• Likely underreported, but possibly increasing
  – 1958 – 1998 = 27 cases reported
  – 2003 – 2016 = 85 cases reported
• Cases found everywhere *Ixodes* exist
  – Colorado as rare exception
  – Incidentally found in *Dermacentor andersoni*

Case Distribution – ArboNET 2018

https://diseasemaps.usgs.gov/mapviewer/
Case Distribution – ArboNET 2019

https://diseasemaps.usgs.gov/mapviewer/
Symptoms

Clinical Diagnosis

Symptomatic/retrospective
  - Serology – IgM of serum or CSF

Post mortem
  - Culture of virus
  - PCR detection of viral RNA
  - Histopathology with immunohistochemistry

*None available through commercial labs – CDC or state PHL only*
IgM Serology

**DTV In Summary**

- Emerging, life threatening tick-borne viral illness
  - Vectored by *Ixodes* tick
- Likely underreported infection
  - Very limited testing capacities
  - Should only be investigated after more common causes ruled out
- Cases with encephalitis are likely to be identified (or maybe not)
Questions?