The Diagnosis & Treatment of Tickborne Diseases in Vermont

Introduction by:
Bradley J. Tompkins, MS, MPH
Tickborne Disease Program Chief & Epidemiologist
Vermont Department of Health
Tickborne Diseases Indigenous to Vermont

1. Lyme Disease
2. Anaplasmosis
3. Babesiosis
4. *Borrelia miyamotoi*
5. Powassan Virus Disease
   - Rare disease – last reported case in Vermont was in 1999
   - Underdiagnosed (?) – testing is only available through public health lab (CDC)
   - [www.healthvermont.gov/disease-control/tickborne-diseases/powassan-virus](http://www.healthvermont.gov/disease-control/tickborne-diseases/powassan-virus)
Tickborne Diseases Indigenous to Vermont (continued)

![Graph showing the number of reported cases of Lyme Disease, Anaplasmosis, and Babesiosis from 2008 to 2017.](image)

- **Lyme Disease**
- **Anaplasmosis**
- **Babesiosis**
Blacklegged Tick (*Ixodes scapularis*)

- Responsible for transmitting all reported tickborne diseases indigenous to Vermont
- Infection rate of ticks collected in Vermont:
  - *Anaplasma phagocytophilum*: 8%
  - *Babesia microti*: 2%
  - *Borrelia burgdorferi*: 51%
  - *Borrelia miyamotoi* (*small sample size*: <1%)

*Vermont Department of Health*
Demographics of Lyme Disease in Vermont

- Vermonters of all age groups are at risk for Lyme
- Higher risk groups:
  - Children between 5-14 years
  - Middle-aged & older adults
  - Males
Seasonality of Lyme Disease in Vermont

- Cases of Lyme disease occur throughout the year
- Over half all cases become sick in June & July
Diagnosis and Treatment Tickborne Diseases in Vermont
Part I:
Lyme Disease

Jean Dejace, MD
Infectious Disease Physician
The University of Vermont Medical Center
Objectives

- Common clinical presentations
- Diagnosis and testing pitfalls
- Typical treatment regimens
- Outcomes
- Review some of the evidence behind current treatment guidelines
- Controversy
Primer: Laboratory Testing In Lyme Disease

- Testing is imperfect
  - Lyme is difficult to culture
    - insensitive
    - takes several weeks to grow
  - Diagnosis is based on clinical presentation and serologic testing
- Sensitivity of serology (CDC 2-tiered testing)
  - Erythema migrans: <50%
  - Early disseminated disease: ~80%
  - Late disease: >95%

References:
Medscape 2016 CME pitfalls review
Aguero 2005
Two-Tier Testing

- **First: Enzyme Immunoassay**
  - tests for IgG and IgM
  - rapid, easily automated
  - easy to interpret: positive/negative/equivocal
  - not as specific
    - cross-reacting Ab in e.g. syphilis, leptospirosis, mono, autoimmune disease, periodontal disease

- **If positive or equivocal EIA, then Western Blot**
  - Highly specific
Two-Tier Testing

- Problems with the Western Blot
  - Costly
  - Subjective interpretation on the laboratory end
  - 10 IgG bands and 3 IgM bands are tested

- Results
  - 2 or more IgM bands = positive
  - 5 or more IgG bands = positive

- Typically sent to reference labs
High frequency of false positive IgM immunoblots for *Borrelia burgdorferi* in Clinical Practice

V. Serbini, N. Ndubwe, Z. Chang, M. E. Cox and G. P. Wormser
Division of Infectious Diseases, New York Medical College, Valhalla, NY, USA

**Abstract**

Although it is known that two-tier serologic testing for Lyme disease may be associated with false positive results on the IgM immunoblot, this problem has never been systematically studied in the clinical practice setting. In a retrospective investigation of patients referred to the private adult practice of an Infectious Diseases physician for possible for Lyme disease, 50 of 182 patients (27.5%, 95% CI: 21.1–34.6) were found to have a false positive IgM immunoblot. 78.0% of these patients had received unnecessary antibiotic therapy. Failed positive results were not restricted to any single commercial laboratory. Research on alternative testing strategies that eliminate the IgM immunoblot entirely is warranted.


Vermont Department of Health
Lyme Specialty Labs and Alternative Criteria

- As part of this investigation, blood from 40 healthy controls were sent to reference and specialty labs.
  - No history of prior diagnosis or treatment for Lyme
  - No history of Lyme-like symptoms
  - No history of another major medical disorder
  - Lack of residence or recent exposure to highly Lyme-endemic area

- 57.5% of healthy controls had a positive Lyme blot at one well-known specialty lab. None were positive by two-tier testing using CDC criteria.

Vermont Department of Health
A Comparison of Lyme Disease Serologic Test Results From 4 Laboratories in Patients With Persistent Symptoms After Antibiotic Treatment

Brian A. Fallon,1 Martine Pasciuta,2 Samantha W. Coffman,3 and Carl Bremer4
Departments of 1Psychiatry, 2Biostatistics, Mailman School of Public Health, 3Neurology, Columbia University, and 4Lourdes-Delhi Earth Observatory of Columbia University, Palisades, New York

[See the Editorial Commentary by Dattwyler and Amabili on pages 1711-3.]

Background. As the incidence of Lyme disease (LD) has increased, a number of “Lyme specialty laboratories” have emerged, claiming singular expertise in LD testing. We investigated the degree of interlaboratory variability of several LD serologic tests—whole cell sonicate (WCS) enzyme-linked immunosorbent assay (ELISA), immunoglobulin M (IgM) and immunoglobulin G (IgG) Western blots (WBs), and an ELISA based on the conserved sixth region of variable major protein-like sequence expressed (V6)—that were performed at 1 university laboratory, 1 commercial laboratory, and 2 laboratories that specialize in LD testing.

Methods. Serum samples from 37 patients with posttreatment Lyme syndrome, as well as 40 medically healthy controls without prior LD, were tested independently at the 4 laboratories.


Vermont Department of Health
A good review on testing is available here:

**Current Guidelines, Common Clinical Pitfalls, and Future Directions for Laboratory Diagnosis of Lyme Disease, United States**

Diagnosis of Early Localized Lyme Disease

- Predominantly clinical based on erythema migrans
  - Present in ~75% of cases
  - Typically 1-2 weeks after tick exposure (3-30 day range)

72% of reported cases MMWR 2008-2015

Vermont Department of Health
Erythema Migrans

“Classic” Lyme Disease Rash

Round or oval expanding erythematous skin lesion that develops at the site of tick bite
Should be >5cm
Sometimes no bullseye, central clearing or homogeneously erythematous. Can be more purpuric. Can have central vesicles or crust. Can be pruritic.
Common in axillae, groin/belt line, behind the knee

Recommended: [https://www.cdc.gov/lyme/signs_symptoms/rashes.html](https://www.cdc.gov/lyme/signs_symptoms/rashes.html)
Vermont Department of Health
Diagnosis of Early Localized Lyme

- Systemic symptoms can occur in patients with single EM as well as in disseminated disease, resembling a viral syndrome without respiratory symptoms.

- 79 patients with EM (14 with multiple)
  - 68% had systemic symptoms
    - Fatigue – 54%
    - Arthralgia/Myalgia – 44%
    - Headache – 42%
    - Subjective fever/chills – 39% (documented in 16%)

The Clinical Spectrum of Early Lyme Borreliosis in Patients with Culture-confirmed Erythema Migrans

Robert B. Nadelman, MD, John Nowakowski, MD, Gilda Forszter, RN, Neil S. Goldberg, MD, Susan Bittker, MS, Denise Cooper, BS, Maria Aguero-Rosenfeld, MD, Gary P. Winstead, MD, Vahaha, New York

Am J Med. 1996 May;100(5):502-8
Diagnosis of Early Localized Lyme Disease

- In the presence of a typical EM rash, laboratory testing is not necessary and can confound the diagnosis
  - Serologic testing is insensitive in early localized disease
  - If serology sent in the presence of a typical EM rash, therapy should not be stopped if testing returns negative
Diagnosis of Early Localized Lyme Disease

- **If there is diagnostic uncertainty…**
  - Obtain baseline and follow-up serology 4 weeks later
  - Can treat patient empirically based on your clinical suspicion and their preference, or await repeat testing
- **Caveats**
  - If the patient has known history of Lyme disease or previously positive serology, repeat testing is unlikely to be helpful. You have to decide on treatment without testing.
  - If you make a decision in your office to pursue the testing strategy without treatment, and the initial test returns positive, then don’t wait 6 weeks to treat.
Clinical Features of Early Disseminated Lyme

- Weeks to months after infection
- Typical presentations
  - Skin
  - Cardiac
  - Neurologic
Early Disseminated Lyme: Skin

Multiple rashes, disseminated infection

Photo Credit: Bernard Cohen

Description:
Early disseminated Lyme disease

[https://www.cdc.gov/lyme/signs_symptoms/rashes.html] Vermont Department of Health
Early Disseminated Lyme: Cardiac

- Uncommon (<2% of cases reported to CDC)
- Typically manifests as AV block within 2 months of infection
  - can be life-threatening if severe
- Can occur in isolation, or with EM/neurologic disease
- Diagnosis
  - History (endemic area, tick exposure)
  - Clinical features (i.e., recent or current EM rash)
  - EKG
  - Most have positive serology

Vermont Department of Health

In Steere’s original carditis case series published in 1980, 15 of 20 had EM
1.5% carditis: MMWR 2008-2015 data from 275k cases
https://www.cdc.gov/mmwr/volumes/66/ss/pdfs/ss6622-H.pdf
Early Disseminated Lyme: Cardiac (continued)

Morbidity and Mortality Weekly Report (MMWR)

Three Sudden Cardiac Deaths Associated with Lyme Carditis — United States, November 2012–July 2013

Weekly
December 13, 2013 / 62(49):993–996

Vermont Department of Health
Early Disseminated Lyme: Neurologic

- About 1 in 8 reported cases
- Most common presentation is cranial neuropathy
  - Typically CN VII, can be bilateral
  - ~8% of reported Lyme cases have facial palsy
- Aseptic meningitis (often concurrently with above)
  - Less common, ~1% of reported Lyme cases
  - Less severe presentation than bacterial meningitis
    - Subacute headache, neck stiffness are typical
- Radiculopathy

Incidence data: MMWR 2008-2015 data
Early Disseminated Lyme: Neurologic

- LP to evaluate meningitis symptoms
  - CSF will show moderate lymphocytic pleocytosis
- Most have positive serology (~80%)
- In some cases of diagnostic uncertainty (e.g. previously positive serology) can consider:
  - CSF antibody index (must draw concurrent serum)

80%: Wormser 2013 Single Tier Testing w/ C6 Peptide compared w/ two-tier testing
Clinical Features of Late Lyme Disease

- **Arthritis**
  - Most commonly occurs months after infection
    - Can be weeks or years
    - Can present in colder months, when other forms less common
  - Eventually develops in ~60% of untreated patients
  - Currently in ~25% of reported cases
    - More patients diagnosed and treated in early stages
    - Remains most common manifestation of disseminated disease
Clinical Features of Late Lyme Disease

- Arthritis
  - Objective evidence of joint inflammation
    - Warmth, swelling, redness
    - Contrast: diffuse arthralgias can occur in early disease
  - Mono or oligoarticular
    - In either case, typically involves the knee
    - Other large joints or TMJ can be involved
  - Pain relatively minimal and fever rare
    - Contrast with septic arthritis
  - Intermittent
    - Episodes of arthritis last weeks to months if untreated
Clinical Features of Late Lyme Disease

- **Arthritis**
  - **Diagnosis**
    - Objective evidence of joint inflammation + serology
    - Synovial fluid analysis: cell count, crystals, culture
      - Establish presence of inflammatory arthritis (i.e. elevated WBC)
      - Rule out other etiologies (septic arthritis, crystal arthropathy)
      - Lyme: typically mild/moderate elevation in WBC <25,000
Treatment

- **Overview**
  - PO doxycycline is the treatment of choice in most cases
  - IV ceftriaxone should be used for a limited number of indications
  - Short courses of therapy are the standard of care
Treatment of Tick Bites

- 482 subjects who had removed an *Ixodes* tick acquired in Westchester County, NY in the past 72 hours
- They were randomized into 2 groups
  - 235 received a single 200mg dose of doxycycline
  - 247 received placebo
- Primary outcome
  - Development of EM rash

Largest study on this topic by far. Other smaller ones are in the Discussion section. The others found no benefit.
Results

- Placebo group: 8 of 247 developed EM (3.2%)
- Doxycycline group: 1 of 235 developed EM (0.4%)

89% follow up at 6 weeks

Best evidence we’ve got, but imperfect. Large confidence interval due to small # of EM. Hard to justify giving longer courses based on this (ie >240 unnecessary 3 week courses since relatively few people seem to develop EM/Lyme after a bite)
A single dose of 200mg doxycycline is offered if
- *Ixodes* tick attached for >36h
- Prophylaxis can be started within 72h of removal
Treatment of Early Localized Lyme

- **Treatment is PO**
- 1 of 3 antibiotic regimens is recommended
  - Doxycycline 100mg BID
    - Note: doxycycline also treats anaplasma (others do not)
  - Amoxicillin 500mg TID
  - Cefuroxime 500mg BID
- **Duration**
  - 14-21 days (10 days is effective with doxycycline)
 Treatment of Early Localized Lyme

- Evidence for good clinical outcomes
- Notable studies
- Luger et al., 1995: 232 subjects, doxy vs. cefuroxime
  - Success or improvement in
    - 95% of doxycycline treated patients
    - 90% of cefuroxime treated patients

Comparison of Cefuroxime Axetil and Doxycycline in Treatment of Patients with Early Lyme Disease Associated with Erythema Migrans

STEVEN W. LUGER, PHILIP PAPARONE, GARY F. WORMSER, ROBERT B. NADELMAN, Edgar Grunwald; Gema Gomez; Michael Wniewelski; and Jeffrey J. Collins

Old Lyme Family Practice, Old Lyme, Connecticut; Lyme Disease Center for South Jersey, Absecon, New Jersey; Division of Infectious Disease, Department of Medicine, New York Medical College, Westchester County Medical Center, Valhalla, New York; Skidmore Island, New York; and Glaxo Inc., Research Triangle Park, North Carolina
Treatment of Early Localized Lyme

- Evidence for good clinical outcomes
- Notable studies
  - Wormser et al., 2003: 180 subjects
    - 60 received IV CTX x1 + 10 days PO doxycycline
    - 61 received 10 days PO doxycycline
    - 59 received 20 days PO doxycycline
  - No significant difference in outcomes at 20 days, 3 months, 12 months or 30 months

Similar efficacy, notably even 10 days doxy
Treatment of Early Localized Lyme

- Evidence for good clinical outcomes

- Notable studies
  - Kowalski et al., 2001
  - Retrospective study of 607 patients with early Lyme
  - 93% treated with doxycycline
  - Outcomes: “treatment failure-free” at 2 years
    - ≤ 10 days of antibiotic: 99%
    - 11-15 days of antibiotic: 98.9%
    - ≥ 16 days of antibiotic 99.2 %
Treatment of Early Localized Lyme

- 100 patients with erythema migrans recruited 1991-2000
  - Treated on presentation
  - Assessed 2011-2013
  - Outcome: Health Related Quality of Life by SF-36v2
- Results:
  - Mean follow-up 15.4 years
  - Scores similar to general U.S. population

Paper on improvement/same as general population
## Treatment of Early Disseminated Lyme

- **Disseminated erythema migrans**
  - Treatment is same as localized EM

- **Cardiac disease**
  - Hospitalize with cardiac monitoring if
    - Symptomatic (e.g. syncope)
    - Advanced heart block
  - May need to consider temporary pacemaker
  - Treat hospitalized patients with IV ceftriaxone initially
  - Duration: 14-21 days (can complete with PO therapy)

Vermont Department of Health

Hospitalize: symptomatic (dyspnea, syncope, chest pain), 2\textsuperscript{nd}/3\textsuperscript{rd} AV block or PR >300ms
IV CTX is expert opinion
Treatment of Early Disseminated Lyme

- **Neurologic disease**
  - Isolated cranial nerve palsy without signs of meningitis (e.g. headache, nuchal rigidity) is often treated with the typical PO antibiotic regimens.
    - Palsy can take several weeks to resolve
  - Meningitis and radiculopathy are preferably treated with IV ceftriaxone 2g daily for up to 28 days
Treatment of Late Lyme Disease

- Arthritis
  - PO therapy is preferred (decreased cost and side-effects)
    - Doxycycline 100mg BID for 28 days
    - Amoxicillin 500mg TID for 28 days
    - Cefuroxime 500mg BID for 28 days
  - Symptoms often slow to resolve
  - If persistent symptoms weeks to months after initial Rx
    - Either:
      - Repeat PO therapy x28 days (typically if incomplete response)
      - IV ceftriaxone x28 days (typically if little to no response to PO)

Vermont Department of Health
## Treatment of Late Lyme Disease

- **Arthritis**
  - If symptoms persist after two courses of antibiotics
    - Trial NSAIDs or hydroxychloroquine
    - Consider methotrexate if severe
  - If symptoms still persist for several months
    - Consider arthroscopic synovectomy

--

Review for reference
Diagnosis and Treatment of Lyme Arthritis

Sheila L. Anikar, MD, Allen C. Steere, MD

KEYWORDS
- Lyme disease
- Borrelia burgdorferi
- Lyme arthritis
- Antibiotic-refractory arthritis
- Inflammatory arthritis

KEY POINTS
- Lyme arthritis is a late disease manifestation, usually beginning months after the tick bite. Patients may not report an antecedent tick bite or erythema migrans.
- Patients have intermittent or persistent attacks of joint swelling and pain, primarily in 1 or a few large joints, especially the knee, without prominent systemic manifestations.
- The diagnosis is supported by 2-tier serologic testing for Borrelia burgdorferi by enzyme-linked immunosorbent assay and immunoglobulin G Western blotting.
- Initial treatment is a 30-day course of oral doxycycline or amoxicillin. For patients with an insufficient response to oral treatment, intravenous therapy with ceftriaxone is recommended.
- A minority of patients may have persistent synovitis for months or several years after oral and intravenous antibiotic therapy, which is treated with antiinflammatory agents, disease-modifying antirheumatic drugs, or synovec ruins.

Review: Possible Indications for IV Therapy

- There are three:
  - Neurologic disease
  - Advanced atrioventricular block
  - Refractory arthritis
- PO therapy is otherwise the standard of care.
Long-term Follow-up of Patients with Culture-Confirmed Lyme Disease

John Nowakowski, MD, Robert B. Nadelman, MD, Rebecca Sell, Donna McKenna, L. Frank Cavaliere, MD, Diane Holmgren, Adriana Gaidici, MD, Gary P. Wormser, MD

PURPOSE: To determine the long-term outcome of patients with culture-confirmed Lyme disease.

METHODS: We analyzed data collected prospectively on adult patients from a highly endemic area in New York State who were diagnosed with early Lyme disease between 1991 and 1994. Patients with culture-confirmed erythema migrans were evaluated at baseline, 7 to 10 days, 21 to 28 days, 3 months, 6 months, 1 year, and annually thereafter. All patients were treated with antibiotics at the time of diagnosis.

RESULTS: We evaluated 96 cases on 709 separate occasions (median, eight evaluations per case). The erythema migrans rash resolved within 3 weeks in all of the 94 evaluable cases, none of whom developed an objective extracutaneous manifestation of Lyme disease. Of the 81 cases who were followed for ≥1 year, all but 8 (10%) were asymptomatic at their last visit, a mean (± SD) of 5.6 ± 2.6 years into follow-up, and only 8 (4%) were symptomatic at every follow-up visit. Intercurrent tick bites were reported by 45 cases (47%), and 14 (15%) developed a second episode of erythema migrans. Four other cases who were asymptomatic seroconverted between years 2 and 5.

CONCLUSION: The long-term outcome of patients with erythema migrans after antibiotic therapy was excellent, but patients from a highly endemic area in New York State remained at high risk of re-exposure to ticks and reinfection. Subjective symptoms during follow-up evaluations tended to be mild to moderate, intermittent, and associated with more symptomatic illness at the time of initial diagnosis. Am J Med. 2003;115:91–96. ©2003 by Excerpta Medica Inc.
Outcomes

- 96 patients with erythema migrans
  - All treated with short course antibiotics on presentation
  - All evaluable patients (94/96) resolved EM at 3 weeks
  - No objective findings of late Lyme disease in any patient
  - Asymptomatic
    - >50% at 10 days
    - 80% at 28 days
    - 90% at 6 months
Chronic, Non-Specific Symptoms

- **Fatigue**
  - Present in up to 30% of the general population
- **Muscle and joint aches without objective clinical or laboratory evidence of inflammation**
- **Difficulty concentrating, mental “slowness”**
- **Post-Treatment Lyme Disease Syndrome**
  - Often referred to as “chronic Lyme”

Chronic fatigue 25%
Chronic, Non-Specific Symptoms

- Is there a basis for Lyme as a chronic infection?
  - DNA (PCR) has been found in tissue after antibiotic treatment in animals.
  - Overwhelmingly, no borrelia has grown from culture after treatment in these animal experiments (i.e. active division suggesting a viable pathogen).
  - There is no true animal model for PTLDS or “chronic Lyme” because the symptoms are subjective and the animals can’t tell you if they have e.g. fatigue or joint pain.
  - More here: https://www.cdc.gov/lyme/pdfs/PersistenceTranscript.pdf
    https://www.cdc.gov/lyme/pdfs/PersistenceWebinarSlides.pdf

Vermont Department of Health
Experts from a dozen countries agree, also Sweden, Finland, Norway, Netherlands, Poland, Slovenia, Switzerland
Persistent Non-Specific Symptoms

- 4 notable randomized human trials regarding prolonged antibiotic therapy for Lyme have been published. They reached similar conclusions.
- Neurology 2003
- Neurology 2008

TWO CONTROLLED TRIALS OF ANTIBIOTIC TREATMENT IN PATIENTS WITH PERSISTENT SYMPTOMS AND A HISTORY OF LYME DISEASE

MARK S. KLEMPNER, M.D., LINDEN T. HILL, M.D., JANINE EVANS, M.D., CHRISTOPHER H. SCHMO, PH.D., GARY M. JOHNSON, RICHARD P. TREYNO, B.S., DELORA NORTON, M.P.H., LOIS LEVY, M.S.W., DAME WALL, R.N., JOHN McCALL, MARK KOSENKO, M.A., AND ARTHUR WERNSEN, M.D.

Vermont Department of Health
Persistent Non-Specific Symptoms (continued)

CME

Study and treatment of post Lyme disease (STOP-LD)

A randomized double masked clinical trial

L.B. Krupp, MD; L.G. Hyman, PhD; R. Grinsen, PhD; P.K. Coyle, MD; P. Melville, RN; S. Ahn, PhD; R. Dattwyler, MD; and B. Chandler, MPA

A randomized, placebo-controlled trial of repeated IV antibiotic therapy for Lyme encephalopathy

Background: Optimal treatment remains uncertain for patients with cognitive impairment that persists or recurs after standard IV antibiotic therapy for Lyme disease. Methods: Patients had well-documented Lyme disease, with at least 3 weeks of post-IV antibiotic, chronic meningitis, MRI finding, and objective memory impairment. Healthy individuals were used as controls for practice effects. Participants were randomly assigned to 12 weeks of double-masked treatment with IV ceftriaxone or IV placebo at baseline to antibiotic therapy. The primary outcome was improvement in the repetition error score of the Rey Auditory Verbal Learning Test (RAVLT) after 24 weeks. Results: A total of 56 participants were randomized. Group differences were statistically significant according to longitudinal mixed effects models.

The NEW ENGLAND JOURNAL OF MEDICINE

Randomized Trial of Longer-Term Therapy for Symptoms Attributed to Lyme Disease

Vermont Department of Health
115 patients
- 57 with positive IgG Western Blot
- 58 with history of EM but negative serology
- 1 or more: diffuse MSK pain, cognitive impairment, radicular pain, paresthesias or dysesthesias
- All had been previously treated

Randomized into 2 groups
- Treatment: 30 days IV ceftriaxone then 60 days PO doxycycline
- Placebo: 30 days IV dextrose then 60 days PO placebo

Seronegative patients required to have documentation of EM rash by physician
Results

Primary outcome: improvement in Quality of Life

[https://www.rand.org/content/dam/rand/www/external/health/surveys_tools/mos/mos_core_36item_survey.pdf]

Measured at 30, 60, 180 days

Trial stopped when interim analysis of 115 patients at 180 days showed no significant difference

Quality of life measured by Medical Outcomes Study Short-Form General Health Survey (SF-36)
Neurology 2003

- 55 patients
  - History of physician documented EM or late Lyme disease with positive serology
  - Severe fatigue (score >4) on Fatigue Severity Scale
  - All treated with standard therapy within past 6 months

- Randomized into two groups:
  - 28 days IV ceftriaxone
  - Placebo

Modified version of fatigue severity scale is one of the figures in the article
Results at 6 months

Primary outcomes
- 1. change in score on fatigue scale
- 2. cognitive speed/impairment as measured by A-A Test
- 3. clearance of OspA Ag in CSF

Fatigue
- 9.1% improvement in the placebo group: mean score 5.5
- 22.1% improvement in ceftriaxone group: mean score 4.4

No significant difference in cognitive or biologic outcomes

Alpha arithmic test (reaction time)
Should we prescribe ceftriaxone?

- Is the improvement in fatigue clinically significant?
  - Antibiotic group still >4 (severe fatigue)
- 4 of 55 patients (7%) experienced life-threatening adverse events
- The authors conclude “STOP-LD…suggests that repeated courses of antibiotic treatment are not indicated for persistent symptoms following Lyme disease including those related to fatigue and cognitive dysfunction, particularly in light of the frequency of serious adverse events.”

Those are the final words in the paper.
37 patients
- history of Lyme symptoms
- positive IgG Western Blot
- memory impairment
- already received 3 weeks ceftriaxone

Randomized
- 23 received 10 weeks ceftriaxone
- 14 received IV placebo

Vermont Department of Health
Results

Primary outcome

- Neurocognitive performance as measured by index score incorporating motor, psychomotor, attention, memory, verbal fluency

At 12 weeks

- Some improvement in drug-treated group compared to placebo

At 24 weeks

- Improvement was not sustained in the drug-treated group
Neurology 2008

- 26% of ceftriaxone group experienced adverse effects.

- Authors’ conclusion:
  - “considering both the limited duration of cognitive improvement and the risks, 10 weeks of IV ceftriaxone...is not an effective strategy for sustained cognitive improvement”
280 patients
- History of clinical Lyme disease or positive serology
- Persistent symptoms attributed to Lyme
  - MSK pain, arthralgia, neuralgia, sensory disturbance, cognitive disturbance, fatigue etc.
- All received 14 days of IV ceftriaxone initially

Randomized
- 12 weeks PO doxycycline
- 12 weeks PO clarithromycin-hydroxychloroquine
- 12 weeks PO placebo

~10% had not been treated so all got CTX initially
Results

- Primary outcome: quality of life measured by SF-36
- All 3 groups showed improvement from baseline at 14 weeks
- No significant difference was found between the study groups
Prolonged Antibiotics

- Theories regarding possible benefits remain untested hypotheses.
- No human trial data shows overall benefit.
- The best current clinical data does not support prolonged courses of antibiotics for post-treatment Lyme disease syndrome.

Vermont Department of Health
Cancers in brain, stomach and lung
Review

- Even the best available Lyme testing is imperfect and should be interpreted in the context of the patient’s clinical presentation. Alternative testing should be carefully scrutinized.
- Lab testing is unnecessary in early localized Lyme presenting with EM rash. Just treat.
- Short courses of therapy (in most cases given PO) remain the standard of care in treating Lyme disease.
- Lyme causes longer-term subjective symptoms in a minority of patients, and although there is some animal evidence of undetermined relevance regarding persistence, current human trial evidence does not support prolonged antibiotic treatment.

Vermont Department of Health
Anaplasmosis
The Emergence of Anaplasmosis in Vermont
Seasonality of Anaplasmosis in Vermont

- Most cases occur in the spring and summer.
- A second smaller, spike in cases occur in the autumn when adult blacklegged ticks are active.
Skewed Disease Burden for Anaplasmosis

- Males are at greater risk
- Most cases are in older adults
Diagnosis and Treatment of Tickborne Diseases in Vermont

Part 2:
Anaplasmosis, Babesiosis and *Borrelia miyamotoi*

Dr. Marie J. George
Medical Director, Infectious Disease
Southwestern Vermont Healthcare
Human Anaplasmosis

- Other name: Human Granulocytic Anaplasmosis (HGA)
- Organism is an obligate intracellular bacteria similar to *Rickettsia*
- First described in 1990s with inclusions seen in granulocytes rather than monocytes (as in ehrlichiosis)
## HGA – Clinical presentation

- Acutely ill patient, usually 3-15 days after tick bite (range)
- Fever – often >102 degrees, headache, myalgia-sudden onset
- Rash uncommon <10%
- Meningoencephalitis ~1% – but often severe, associated with ARDS
HGA Clinical

- Range of presentation: asymptomatic – fatal encephalitis or shock/sepsis/acute renal failure/ARDS
- 36% require hospitalization
- PE usually entirely non-localizing but patients acutely ill due to high fever, rigors, headache and malaise
<table>
<thead>
<tr>
<th>Frequency of complaint</th>
<th>Symptom, Sign, or Laboratory Abnormality (number patients evaluated)</th>
<th>Median % (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Common</td>
<td>Fever (794)</td>
<td>100 (90-100)</td>
</tr>
<tr>
<td></td>
<td>Malaise (391)</td>
<td>97 (90-98)</td>
</tr>
<tr>
<td></td>
<td>Headache (648)</td>
<td>82 (64-93)</td>
</tr>
<tr>
<td></td>
<td>Myalgia (789)</td>
<td>76 (67-87)</td>
</tr>
<tr>
<td></td>
<td>Arthralgia (661)</td>
<td>56 (27-69)</td>
</tr>
<tr>
<td></td>
<td>Elevated serum ALT or AST (397)</td>
<td>83 (63-98)</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenia (566)</td>
<td>75 (61-91)</td>
</tr>
<tr>
<td></td>
<td>Leukopenia (566)</td>
<td>55 (47-71)</td>
</tr>
<tr>
<td>Less common</td>
<td>Stiff neck (64)</td>
<td>45 (34-48)</td>
</tr>
<tr>
<td></td>
<td>Nausea (521)</td>
<td>39 (35-49)</td>
</tr>
<tr>
<td></td>
<td>Cough (523)</td>
<td>29 (20-30)</td>
</tr>
<tr>
<td></td>
<td>Elevated serum creatinine (199)</td>
<td>49 (25-71)</td>
</tr>
<tr>
<td></td>
<td>Anemia (198)</td>
<td>28 (6-44)</td>
</tr>
<tr>
<td>Uncommon</td>
<td>Diarrhea (317)</td>
<td>21 (13-28)</td>
</tr>
<tr>
<td></td>
<td>Vomiting (312)</td>
<td>20 (19-29)</td>
</tr>
<tr>
<td></td>
<td>Confusion (470)</td>
<td>17 (17-18)</td>
</tr>
<tr>
<td></td>
<td>Rash (469)</td>
<td>6 (3-10)</td>
</tr>
</tbody>
</table>

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; IQR, interquartile range
*Erythema migrans where described.

- Leukopenia (may not be present on presentation and occur after hospitalization)
- Thrombocytopenia
- Leukocytosis with left shift – **high WBC does not rule out anaplasmosis!**
- Hepatitis (primarily transaminitis, alk phos can be moderately elevated)
- Renal insufficiency/pre-renal azotemia
Wright stain or Giemsa stained peripheral blood smears demonstrate intracytoplasmic morulae in neutrophils – not the usual way to diagnose but may be high yield in 1st week of illness

**PCR in blood or CSF from acutely ill patient highly sensitive and specific**

- Acute and convalescent serology (IFA) indicates four-fold rise
  - IgG most sensitive
  - IgM less sensitive for diagnosis of acute infection (use PCR)
Secondary opportunistic infections can occur simultaneously or following HGA – fungal infections (candida), other bacterial infections (strep, staph)
- Secondary infections are associated with high fatality

Patients at greatest risk of secondary infection – elderly, immunosuppression, chronic inflammatory or neoplastic illness
Tetracycline antibiotics are drugs of choice and every effort must be made to use them. Be wary of reports of “allergy.” This is rare; treat nausea preemptively with antiemetics.

Although some patients can resolve infection without antibiotics, recommended to treat all patients

Start prescription before testing is finalized

<table>
<thead>
<tr>
<th>Antibiotic drug</th>
<th>Patient age (years)</th>
<th>Antibiotic dose</th>
<th>Duration (days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline hydrochloride</td>
<td>≤ 8</td>
<td>2.2 mg/kg 2 times daily IV(^{\text{a}}) or PO(^{\text{b}})</td>
<td>4 - 5(^{\text{c}})</td>
</tr>
<tr>
<td></td>
<td>&gt; 8</td>
<td>100 mg 2 times daily IV or PO</td>
<td>10 - 14(^{\text{d}})</td>
</tr>
<tr>
<td>Tetracycline HCl</td>
<td>&gt; 8</td>
<td>500 mg 4 times daily PO</td>
<td>10 - 14</td>
</tr>
<tr>
<td>Rifampin</td>
<td>Pediatric(^{\text{e}})</td>
<td>20 mg/kg/d (max. 600 mg) in 2 divided doses PO</td>
<td>5 - 7(^{\text{f}})</td>
</tr>
<tr>
<td></td>
<td>Adult(^{\text{g}})</td>
<td>300 mg 2 times daily PO</td>
<td>5 - 7</td>
</tr>
</tbody>
</table>

\(^{\text{a}}\) Intravenous administration; \(^{\text{b}}\) Oral administration; \(^{\text{c}}\) Until fever has resolved and three additional days; \(^{\text{d}}\) 14 days recommended if suspected co-incubating B. burgdorferi infection; \(^{\text{e}}\) Individuals aged 16 years or less; \(^{\text{f}}\) Short duration since therapy not directed towards co-incubating B. burgdorferi infection; \(^{\text{g}}\) Individuals aged 18 years or older.

HGA Treatment

- Prescribe doxycycline to children or pregnant women with HGA regardless of age; Continue doxy for 48 hours after resolution of fever (usually 5-7 days) – especially if serious infection.

- Rifampin – second line therapy. Consider use with pregnancy, young children who are not seriously ill. Must follow for full resolution and no relapse.
HGA Outcomes

- Most resolve fever and feel greatly improved after 1-2 doses of doxycycline. Short hospital stays, hepatitis resolves within days-weeks. Leukopenia and thrombocytopenia should improve after 24 - 48 hours of treatment
- Death 0.1 - 1.2%
- Complicating ARDS, ARF, encephalitis, neuropathy
- Unclear if protective antibodies develop for second infection
  (personal note: I had a patient in 2017 who had infection and full prescription of doxy; second infection 3 weeks later)
HGA Coinfection With Other Tickborne Infections

- Any of the infections caused by *Ixodes* can be acquired at the same time as *Anaplasma*
- Coinfection cases in the USA:
  - *Anaplasma* and Lyme
    (present in 2-11.7% of patients)
  - *Anaplasma* and babesiosis
  - *Anaplasma* and *Borrelia miyamotoi*
Peripheral nerve problems can occur after original infection – usually occur after symptoms of *Anaplasma* have resolved:

- Cranial nerve palsies
- Brachial plexopathy
- Demyelinating polyneuropathy, myelitis
Babesiosis
Babesiosis in Vermont

- Only 63 cases reported in Vermont (2008-2017)
- Cases more common in older adults
  - Range: 9 – 83 years
  - Median age: 63 years
- ~70% of cases get sick June-August
- ~30% of cases are hospitalized
- Cases have predominately been reported from southern Vermont

Median age:
- Lyme Disease cases: 49 years
- Anaplasmosis cases: 62 years

Vermont Department of Health
Babesiosis

- A protozoan parasite that infects erythrocytes. It is an obligate intracellular pathogen

- Human illness in Vermont is caused by *Babesia microti*
**Babesia Life Cycle**

- Ticks inject sporozoites into humans and target RBCs (do not need liver phase)
- Infected RBCs (trophozoites) circulate through organs, including spleen
- Parasite matures and grows inside RBC, replication by budding.
- One ring ➔ two “figure 8”
- Two rings ➔ tetrad “Maltese Cross”
- After division, merozoites destroy RBCs; seek new RBC cells to invade cycle of intracellular infection
Babesiosis - Other Modes of Transmission

- Blood supply now screened, in several states, including Massachusetts
- Blood transfusion – Most common transfusion-related infection in U.S.
- Transplacental – 1/5 - fatal outcome, rare, case report

DOI: 10.1128/CMR.00067-12
Babesiosis - Clinical

- **Range:**
  - Asymptomatic
  - Mild, moderate disease
  - Severe infection (hemolysis/death)
### Babesiosis - Clinical: Asymptomatic

- Healthy hosts
- Low parasitemia (seroprevalence in New England is highest rate in U.S. Range 0.5-16% Block Island, Nantucket)
- Self-limited, but until resolved host can transmit by blood donation
Babesiosis - Clinical: Mild-Moderate Disease

- 1-4 weeks after bite or 1-9 weeks (or up to 6 months) after transfusion
- Malaise, fatigue, fever, anorexia, nausea, nonproductive cough, arthralgia
- Less common symptoms: hyperesthesia, sore throat, abdominal pain, conjunctival infection, weight loss, photophobia
- PE: hepatomegaly, splenomegaly, red throat, jaundice, retinopathy in infants. Rash is RARE (If present, look for coinfection with another tickborne illness)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Outpatient (n=41)</th>
<th>Inpatient (n=173)</th>
<th>Total (n=214)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>68</td>
<td>89</td>
<td>85</td>
</tr>
<tr>
<td>Fatigue</td>
<td>78</td>
<td>79</td>
<td>79</td>
</tr>
<tr>
<td>Chills</td>
<td>39</td>
<td>68</td>
<td>63</td>
</tr>
<tr>
<td>Sweats</td>
<td>41</td>
<td>56</td>
<td>53</td>
</tr>
<tr>
<td>Headache</td>
<td>75</td>
<td>32</td>
<td>39</td>
</tr>
<tr>
<td>Myalgia</td>
<td>37</td>
<td>32</td>
<td>33</td>
</tr>
<tr>
<td>Anorexia</td>
<td>25</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Cough</td>
<td>17</td>
<td>23</td>
<td>22</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>31</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Nausea</td>
<td>22</td>
<td>9</td>
<td>16</td>
</tr>
</tbody>
</table>

Outpatient cases are from Ruebush et al. and Krause et al. Inpatient cases are from White et al. and Hatcher et al.
Babesiosis - Clinical: Severe Disease

- Usually >50 years old, immunocompromised, pregnant or splenectomized
- *B. divergens* associated with more severe infection
- ARDS, hemolytic anemia, CHF, DIC, renal failure, prolonged relapsing infection
- Death - 10% of hospitalized patients – higher if acquired with pregnancy, transfusion or if previously splenectomized
Babesiosis - Laboratory

- Signs of hemolysis-decreased Hgb and Hct, increased LDH
- Low leukocyte count
- Low platelets (2nd most common lab abnormality)
- Renal failure
- Blood peripheral smear may show organisms incidently in RBCs

Types of Leukocytes

- Basophil
- Neutrophil
- Eosinophil
- Monocyte
- Lymphocyte (T cell and B cell)
Babesiosis - Diagnosis

- Epidemiology of travel to endemic area or transfusion within last 6 months
  - Tick exposure may not be reported
- Thin blood smear (Wright or Giemsa stained)
  - Ring forms (early infection)
  - No hemozoin in rings
  - No gametocytes
  - Tetrads present
- PCR - BOTH sensitive and specific
- Serology – fourfold rise in IgG after four weeks - confirms recent infection; single IgG does not distinguish old from new infection
Babesiosis - Relapsing Infection

- Occurs in patients with immunosuppressive disease, elderly, splenectomy, HIV infection. Can occur in healthy patients
- May have positive PCR which is persistently positive or became negative then positive again
- May require 6 plus weeks of antimicrobial therapy – alternative regimens noted in treatment section
- Close clinical follow-up: repeat smears, repeat PCRs to confirm resolved infection
### Babesiosis - Treatment

<table>
<thead>
<tr>
<th>Category</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Asymptomatic</strong></td>
<td>- If PCR positive or blood smears positive</td>
</tr>
<tr>
<td></td>
<td>- Do not prescribe for single positive serology only</td>
</tr>
<tr>
<td></td>
<td>- 7 days atovaquone and azithromycin</td>
</tr>
<tr>
<td><strong>Mild-Moderate</strong></td>
<td>- Atovaquone and azithromycin: 7-10 days (preferred) or clindamycin and quinine</td>
</tr>
<tr>
<td></td>
<td>- Adverse reactions: 15% atovaquone and azithromycin; 72% clindamycin and quinine</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td>- Clindamycin and quinine (can give oral or IV)</td>
</tr>
<tr>
<td></td>
<td>- +/- exchange transfusion (parasitemia &gt;10%; severe anemia Hgb&lt;10g/dl or/+ liver/renal failure)</td>
</tr>
<tr>
<td><strong>Relapsing</strong></td>
<td>- Treat up to 6 weeks with clindamycin and quinine, atovaquone /proguanil, clindamycin and doxycycline, azithromycin and doxycycline, artemisinin, atovaquone and doxycycline, atovaquone/azithromycin and clindamycin</td>
</tr>
</tbody>
</table>
## Babesiosis - Treatment

<table>
<thead>
<tr>
<th>Antimicrobials</th>
<th>Dose</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Atovaquone plus azithromycin</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Atovaquone</td>
<td>Adult: 750 mg</td>
<td>Every 12 hours</td>
</tr>
<tr>
<td></td>
<td>Child: 20 mg/kg (maximum 750 mg/dose)</td>
<td>Every 12 hours</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>Adult: 500 to 1000 mg</td>
<td>On day 1</td>
</tr>
<tr>
<td></td>
<td>250 to 1000 mg</td>
<td>On subsequent days</td>
</tr>
<tr>
<td></td>
<td>Child: 10 mg/kg (maximum 500 mg/dose)</td>
<td>On day 1</td>
</tr>
<tr>
<td></td>
<td>5 mg/kg (maximum 250 mg/dose)</td>
<td>On subsequent days</td>
</tr>
<tr>
<td><strong>Clindamycin plus quinine</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clindamycin</td>
<td>Adult: 600 mg</td>
<td>Every 8 hours</td>
</tr>
<tr>
<td></td>
<td>Child: 7-10 mg/kg hours (maximum 600 mg/dose)</td>
<td>Every 6-8</td>
</tr>
<tr>
<td>Intravenous administration</td>
<td>Adult: 300-600 mg</td>
<td>Every 6 hours</td>
</tr>
<tr>
<td></td>
<td>Child: 7-10 mg/kg hours (maximum 600 mg/dose)</td>
<td>Every 6-8 hours</td>
</tr>
<tr>
<td>Quinine</td>
<td>Adult: 650 mg</td>
<td>Every 6-8 hours</td>
</tr>
<tr>
<td></td>
<td>Child: 8 mg/kg (maximum 650 mg/dose)</td>
<td>Every 8 hours</td>
</tr>
</tbody>
</table>

All antibiotics are administered by mouth unless otherwise specified. All doses administered for 7 to 10 days except for persistent relapsing infection.

Borrelia miyamotoi

Vermont Department of Health
Newly Recognized Tickborne Disease in Vermont

- First cases in Vermont were reported in 2016
  - 2016: 7 cases
  - 2017: 13 cases

- Case Characteristics (n = 20)
  - Age:
    - Range: 4 – 80 years
    - Median: 64 years
  - Gender: 50% female
  - Illness onsets range from May – October
  - 20% of cases have been hospitalized

Vermont Department of Health
Borrelia miyamotoi General

- It is not a true relapsing fever pathogen

- IS NOT: fever – resolution - sudden hypotension fever/severe symptoms

- IS: fever, HA, malaise – resolution - recurrences of same symptoms. “Relapsing fever-like illness”
Borrelia miyamotoi Identification/Diagnosis Difficulties

- Genetically related to B. burgdorferi species, and shares 4 of 10 antigens with Lyme Borrelia
  - Distinctive illness
  - Difficulty with cross reactivity on antigen and antibody assays

- No animal model
- Serology has false negatives
- Low numbers of clinical cases
B. miyamotoi Clinical case series: Russia 2011

- 64 cases
- Fever, fatigue, headache – greater than 90%
- “Relapsing” fever 11% – 2-3 episodes, each lasted 2-5 days, mean 9 days between.
- Rash – rare, EM-like – 4%
- Patients had positive PCR for B. miyamotoi, also had increased serology for Lyme
- Elevated LFTs common – 68%
- Most did not have cytopenias


Vermont Department of Health
B. miyamotoi Clinical Features/Epidemiology

Other case series:
<table>
<thead>
<tr>
<th>Symptom</th>
<th>US (n = 51)</th>
<th>Russia (n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever, chills</td>
<td>96%</td>
<td>98%, 35%*</td>
</tr>
<tr>
<td>Headache</td>
<td>96%</td>
<td>89%</td>
</tr>
<tr>
<td>Myalgia</td>
<td>84%</td>
<td>59%</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>76%</td>
<td>28%</td>
</tr>
<tr>
<td>Malaise/fatigue</td>
<td>82%</td>
<td>98%</td>
</tr>
<tr>
<td>Rash/EM&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8%</td>
<td>9%</td>
</tr>
<tr>
<td>Gastrointestinal symptoms&lt;sup&gt;d&lt;/sup&gt;</td>
<td>6%</td>
<td>30% (nausea)</td>
</tr>
<tr>
<td>Respiratory symptoms&lt;sup&gt;e&lt;/sup&gt;</td>
<td>6%</td>
<td>na</td>
</tr>
<tr>
<td>Neurological symptoms&lt;sup&gt;f&lt;/sup&gt; (dizziness, confusion, vertigo)</td>
<td>8%</td>
<td>na</td>
</tr>
<tr>
<td>Stiff neck</td>
<td>na</td>
<td>2%</td>
</tr>
</tbody>
</table>

*Fever and chills were reported in separate categories.
<br>*Authors noted in most patients the headaches were severe.
<br>*US patients were described as having a rash. Russian patients were noted for having a single erythema migrans.
<br>*For US patients, GI symptoms included nausea, abdominal pain, diarrhea, anorexia. For Russian patients, GI symptoms included nausea and vomiting.
<br>*Laborored breathing or short of breath. Not reported.

B. miyamotoi Clinical - Important Observations

- At least one person has resolved infection without meds
- Transmission in blood transfusion has been demonstrated in mice. No human cases described yet
- Meningoencephalitis described in U.S. patients: progressive decline of cognition, gait unsteadiness over weeks to months, no fever
Clinical experience in Bennington – patients may be sick enough to be admitted, acutely ill over several days - 2 weeks, younger persons sicker but report lower fever, confusion prevalent, similar to anaplasmosis, LFTs always elevated, cytopenia +/-. Cases of meningoencephalitis were prominent and severe in patients with immunocompromised conditions (lymphoma, use of Rituximab, neutropenia)
Borrelia miyamotoi - Diagnosis

- Serologic testing of antibody to glpQ specific antibodies by 2 tier tests (IgG) 4 weeks apart – NOT preferred for acute illness, OK for look back
- 10% of Borrelia miyamotoi cross-reacted with Borrelia burgdorferi in study by Krause et al., Emerging Infectious Disease 2014. 20: 1183-90
- Therefore PCR is the preferred method to differentiate the two infections acutely and serology can look back more specifically for Borrelia miyamotoi
Borrelia miyamotoi Diagnosis

- Look for specific comment notation when ordering “Borrelia PCR”

- Testing lab may indicate “Positive for Borrelia,” then indicates species detected
  - *Borrelia miyamotoi* will be present anytime there is an active, untreated infection
Borrelia miyamotoi Treatment

- Treatment is based on clinical series and case reports. Devised due to comparison with other Borrelia infections
- No trials for duration, dose, type of antibiotics
  - Doxycycline 100g every 12 hours for 7-14 days in normal adults with acute infection
  - Ceftriaxone 2-4 weeks or PCN G. 24mu per day for 4 weeks - meningoencephalitis
  - Amoxicillin, cefuroxime – similar to Lyme treatment (use for intolerance of doxycycline, children under age 8, pregnant women)
  - Jarisch-Herxheimer reported in Russian series in 15% of patients, sometimes severe with hypotension

Vermont Department of Health
Thank You

- Thank you for viewing the course material

- Please return to the Health Department website (www.healthvermont.gov/TickborneDiseaseCME) to apply for continuing education credits through the Vermont Area Health Educations Centers (AHEC)

- Comments or questions? Please contact Bradley.Tompkins@vermont.gov