UPSTATE
MEDICAL UNIVERSITY
State University of New York

Lyme Disease:
An Overview and the Struggle with Chronic Symptoms

Kristopher M. Paolino, MD, MTM&H

28 Jan 2019

Conflicts

I currently have no conflicts of interest to include any financial ties to any products discussed.

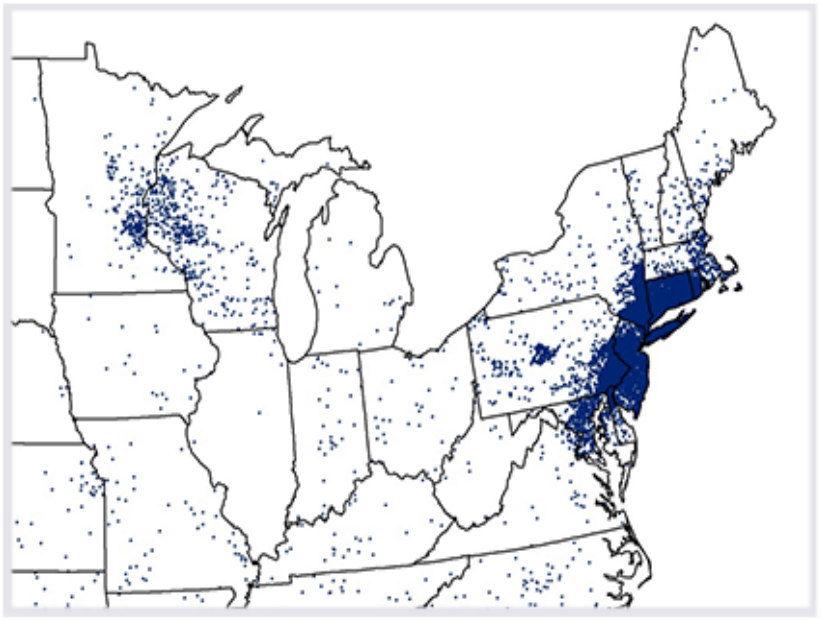
Outline

- Brief Overview
- Diagnostics
- Chronic Symptoms
- Treatment
- Prevention
- Dangers

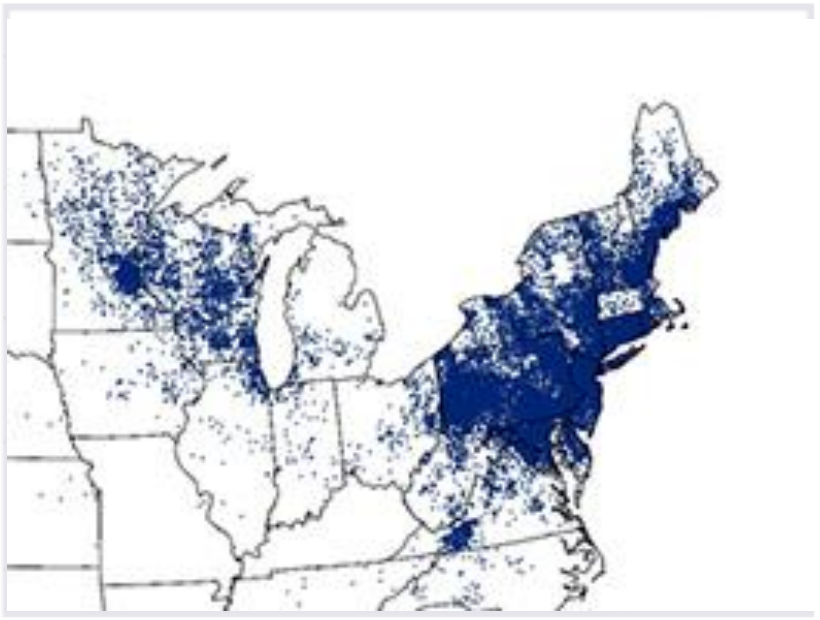
Lyme Disease

- Disease
  - *Borrelia burgdoferi* sensu stricto
  - Tick borne infection
  - Primary sites of transmission include the Northeast, Upper Midwest, and Northern California
  - Clinical presentation varies in patients later in disease

Reported Lyme Disease Cases in 1996 and 2014



1996

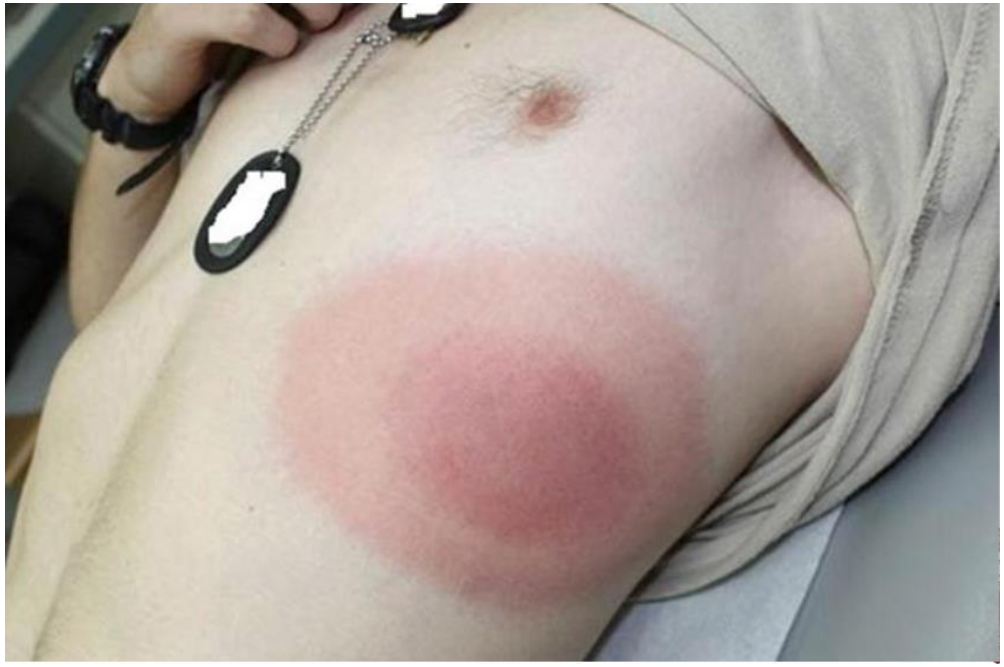


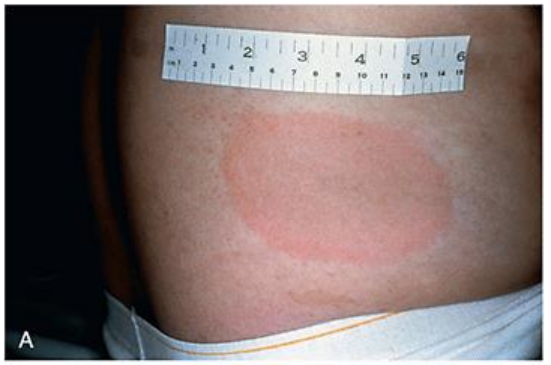
2017

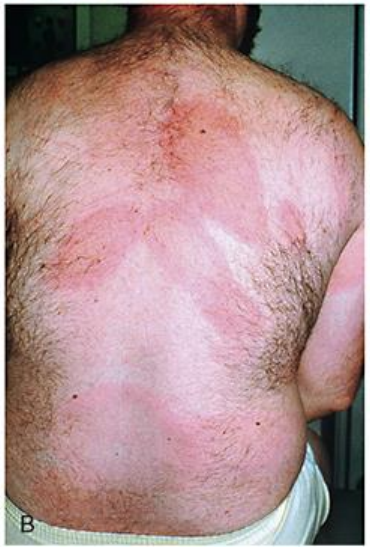
Data source: CDC (Centers for Disease Control and Prevention). 2015. Lyme disease data and statistics. www.cdc.gov/lyme/stats/index.html. Accessed December 2015.

For more information, visit U.S. EPA's "Climate Change Indicators in the United States" at www.epa.gov/climate-indicators.

Lyme Disease







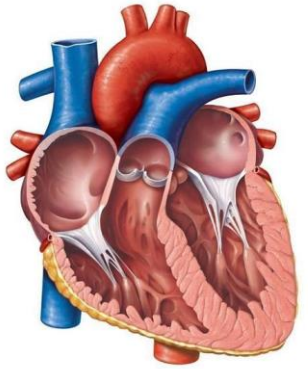
PPID

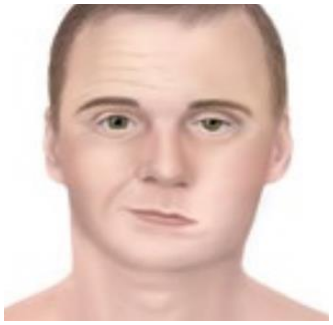
Lyme Disease

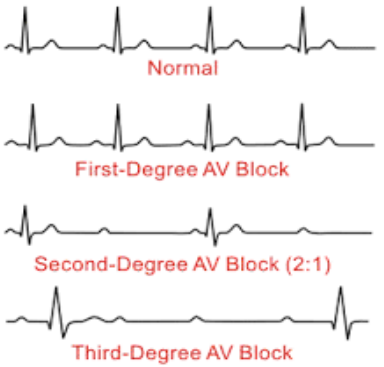
- Syndromes
  - Early localized (Erythema migrans)
  - Early disseminated
  - Late disseminated
  - Chronic post-treatment symptoms

N Engl J Med. 2001 Jul 12;345(2):115-25.
PPID

Lyme Disease







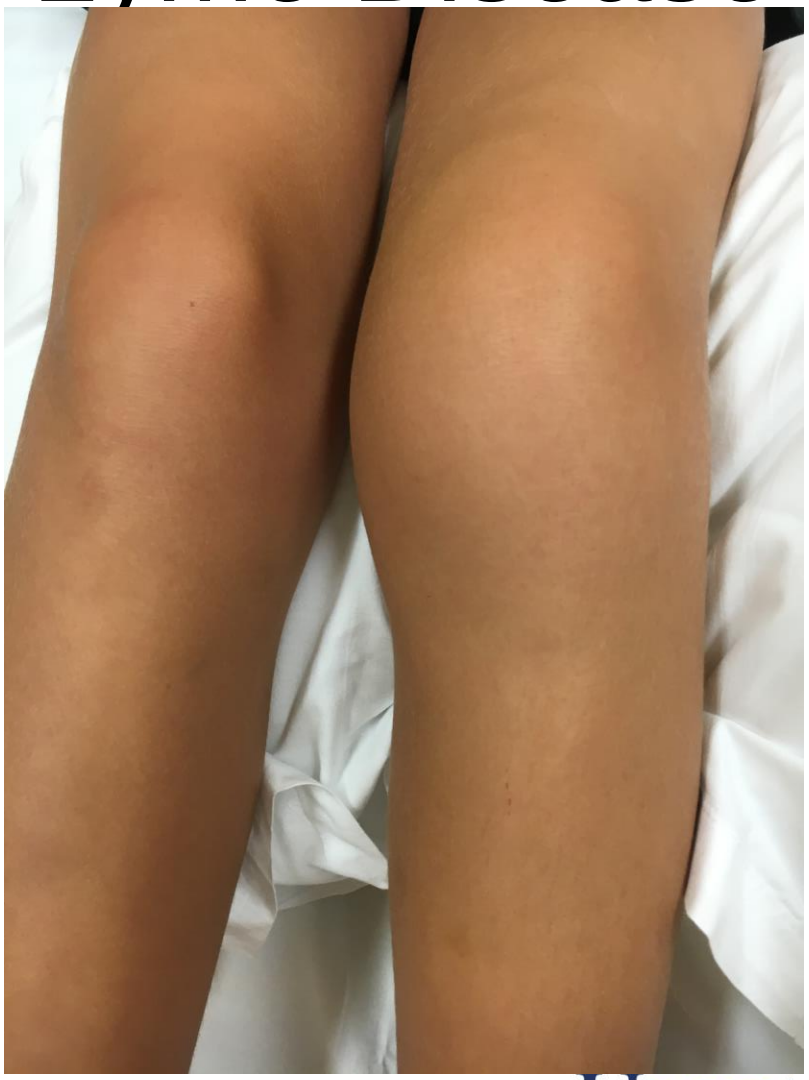
Lyme meningitis

Lyme arthritis

Lyme carditis

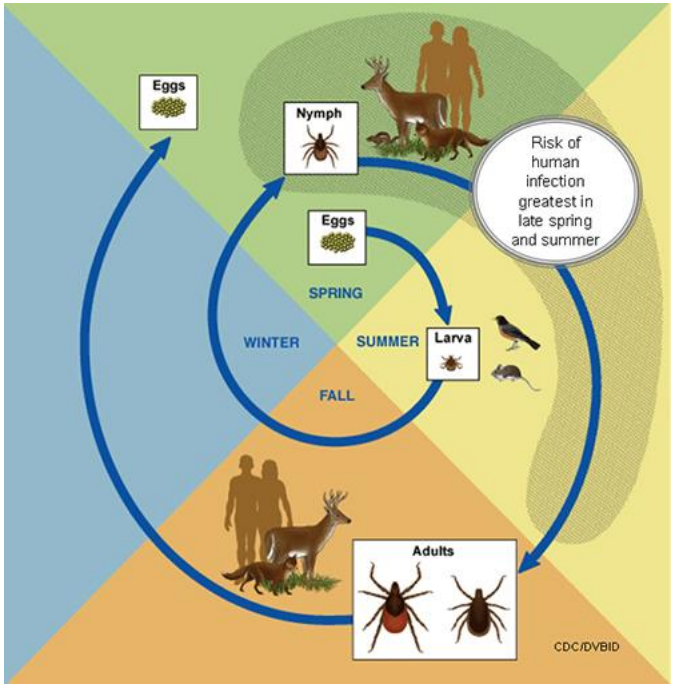
https://www.cdc.gov/lyme/resources/TickborneDiseases.pdf

Lyme Disease



Lyme Disease

- Vector



CDC

NIH

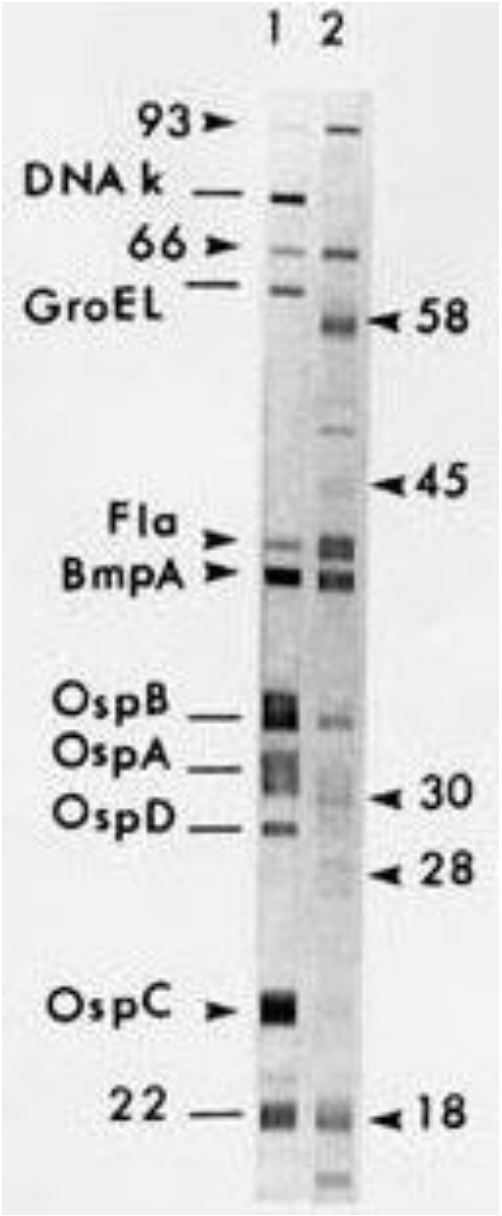
Lyme Disease

Lyme Disease

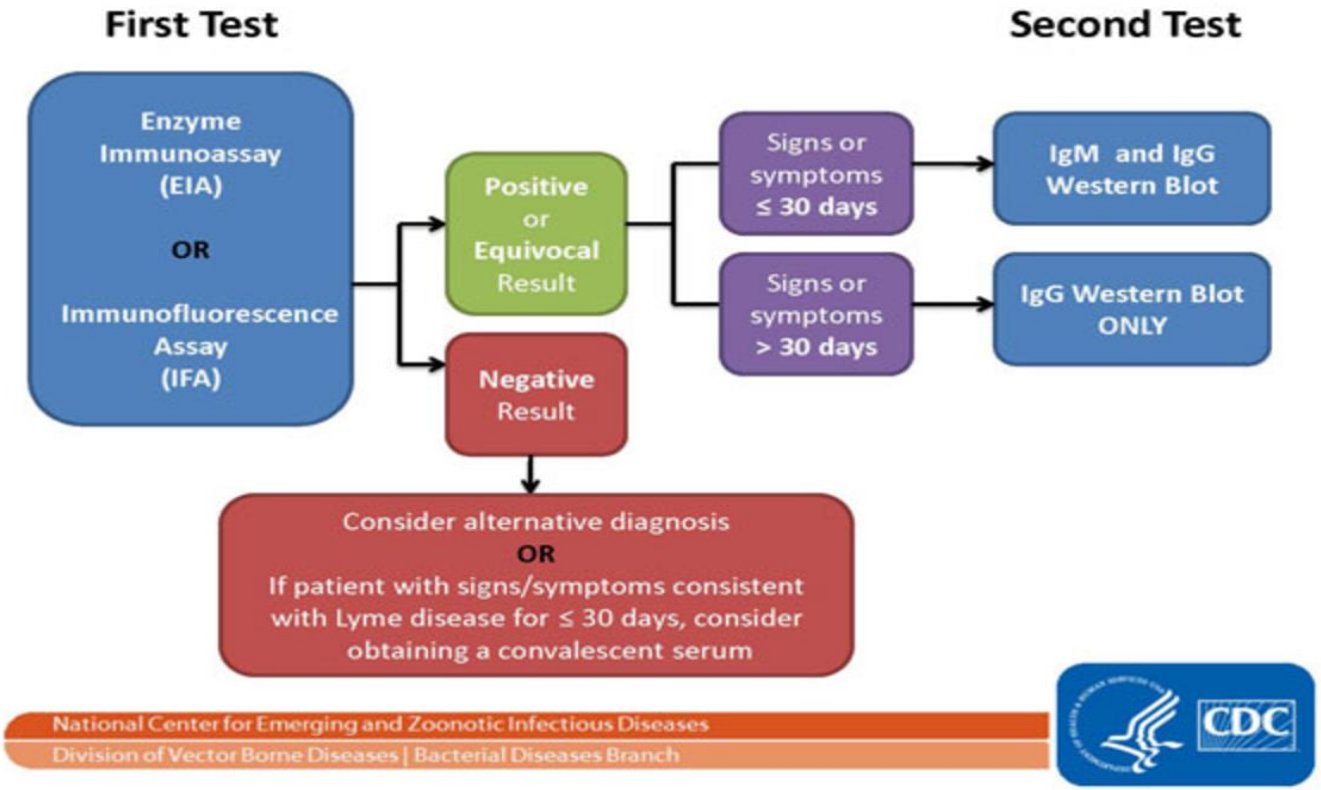
- Treatment
  - Doxycycline
  - Amoxicillin
  - Cefuroxime
  - Ceftriaxone
  - Cefotaxime
  - Penicillin G

Diagnostics

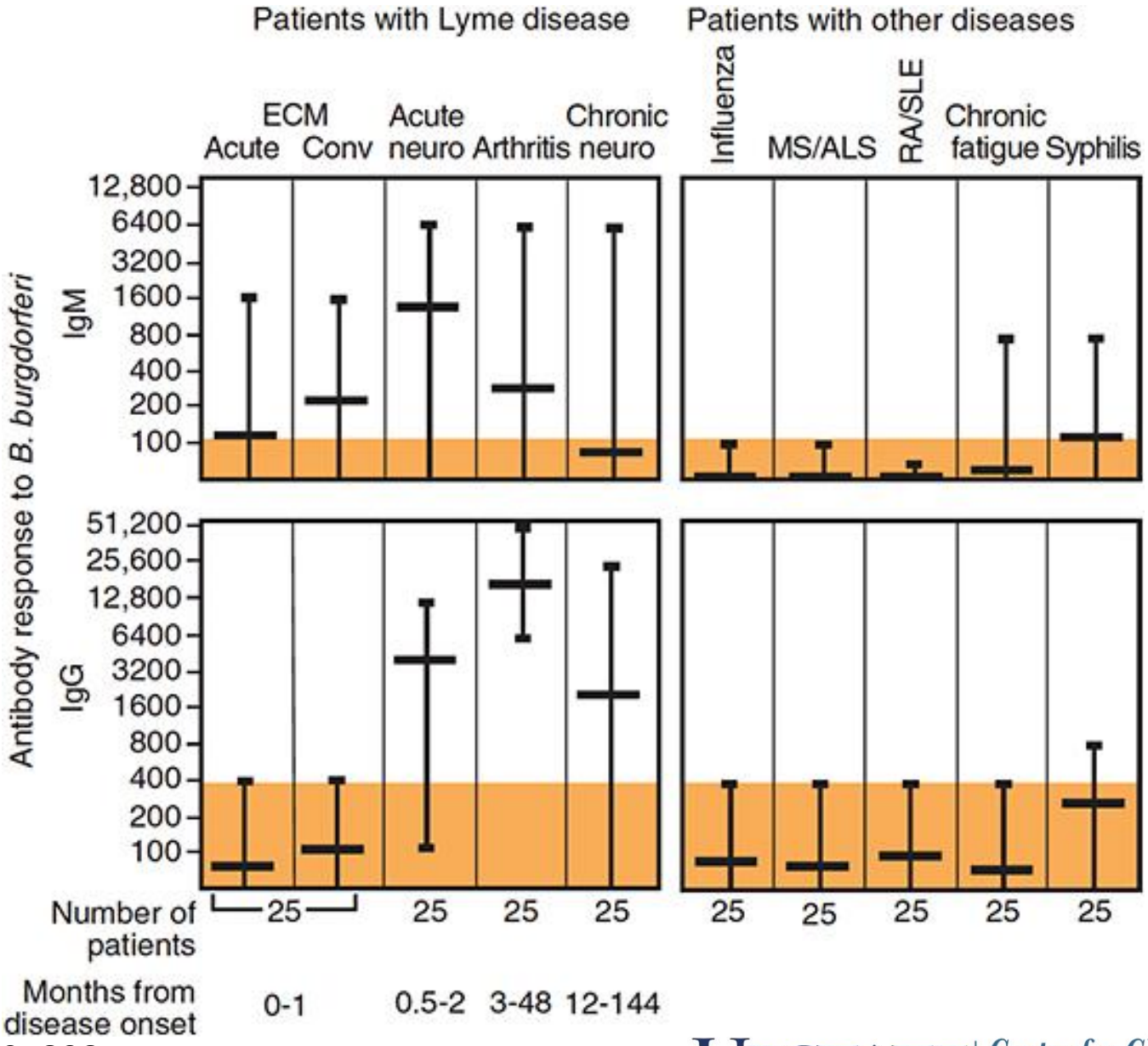
- Standard
  - Clinical (EM rash)
  - Two Step testing
    - ELISA
    - Immunoblot
      - Combination of 23 and 41kDa bands may be false positive for IgM testing
      - Half the population has 41kDa IgG reactivity



Two Step Testing Approach



Onset of Symptoms	Antibody/EIA	Bands to Consider
First few weeks	IgM	2 of the following: 24, 39, 41
After first few weeks	IgG	5 of the following: 18, 23, 28, 30, 39, 41, 45, 58, 66, 93



JID 1993; 16: 392.

UPSTATE MEDICAL UNIVERSITY | Center for Global Health and Translational Science

Diagnostics

- PCR
  - Only recommended for use in synovial fluid
  - Burden of organism not found to be in sufficient quantities for blood or CSF

Arthritis Rheum. 2011; 63: 2238-47

Diagnostics

- C6 peptide ELISA
  - Comparable to two tiered testing
  - IgG antibodies develop early
  - May have higher sensitivity in patients infected with other genotypes
  - Titers may indicate response to treatment

CID. 2008; 47(2): 188
Eur J Clin Microbiol Infect Dis 23: 615-8
Clin Vaccine Immunol. 15: 115-19.
j Clin Microbiol. 41; 4955-4960
Clin Diagn Lab Immunol. 12: 1069-74

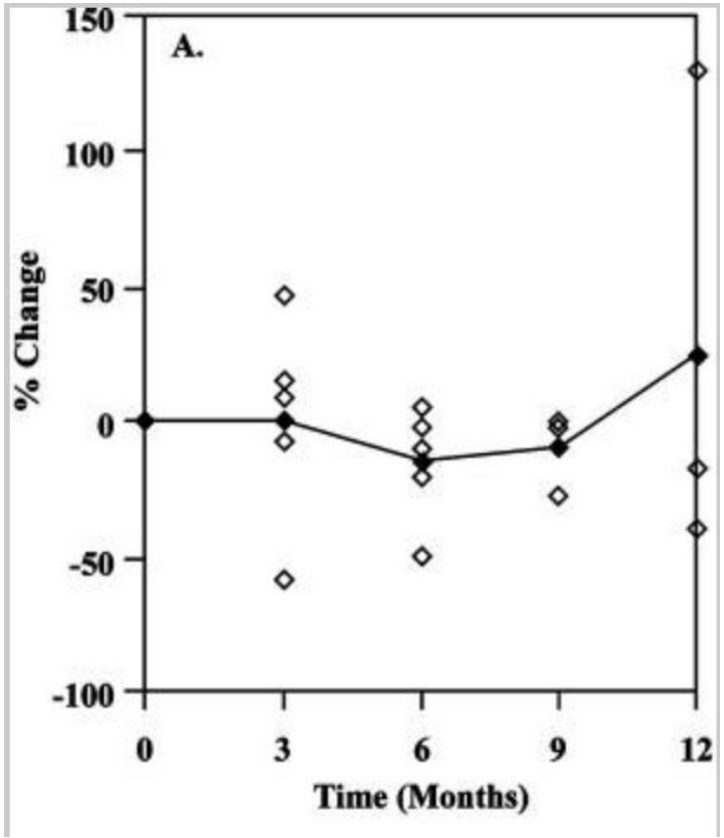
Diagnostics

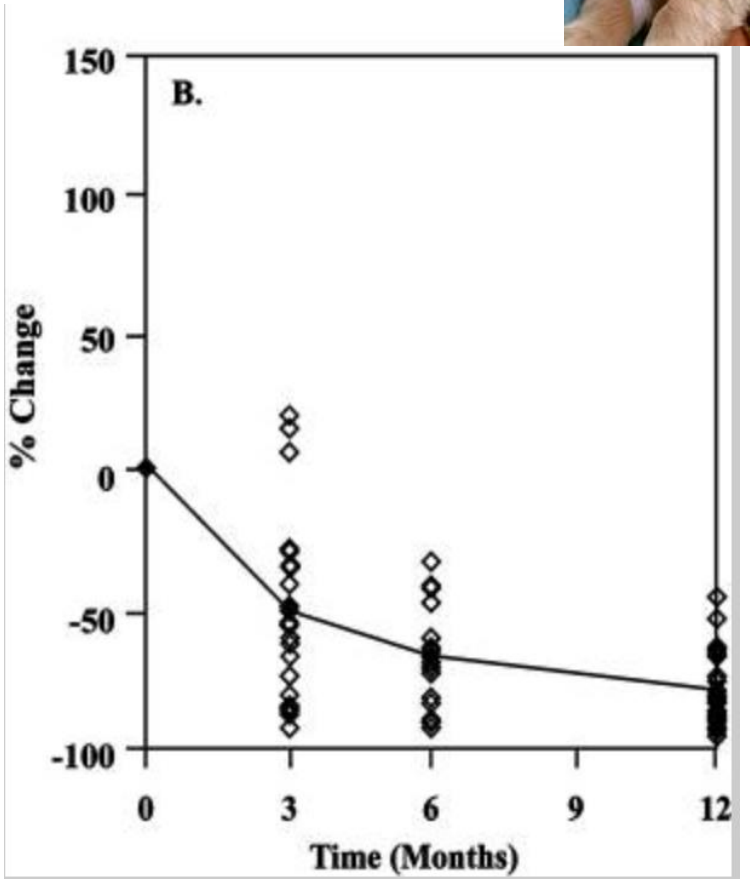
	Two-tier testing with sonicate ELISA and Western blot							
	IgM		IgG		IgM or IgG		IgG VlsE C6 peptide ELISA	
Variable	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**	**Sensitivity**	**Specificity**
Erythema migrans								
Acute phase	25	99	11	99	29	99	29	96
Convalescent phase	55	99	18	99	64	99	56	96
Acute neurologic or cardiac abnormalities	85	99	85	99	100	99	100	96
Arthritis or chronic neurologic abnormalities	NA	…	100	99	100	99	100	96

NOTE. Sensitivity was determined on the basis of serum samples from 76 patients with erythema migrans, 13 patients with acute neurologic or cardiac abnormalities, and 31 patients with arthritis or chronic neurologic abnormalities. Specificity was determined on the basis of serum samples from 86 healthy subjects from an area in which Lyme disease was endemic and serum samples from 50 subjects from an area in which Lyme disease was not endemic. NA, not applicable.

CID. 2008; 47(2): 188

Diagnostics

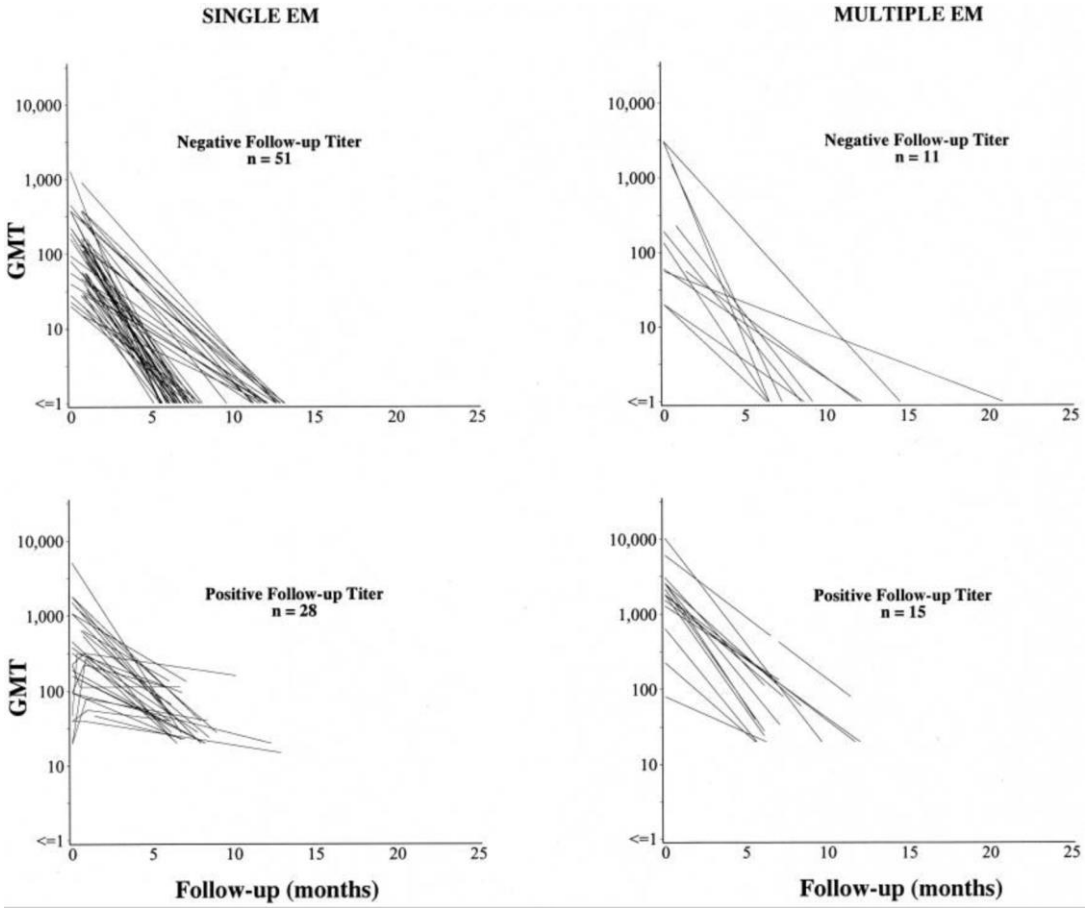




Clin Vaccine Immunol. 15: 115-19.

UPSTATE MEDICAL UNIVERSITY | Center for Global Health and Translational Science

Diagnostics



Clin Diagn Lab Immunol. 12: 1069-74

Diagnostics

- Shortcomings of Current Diagnostics
  - Insensitive early in the course of illness
  - Sensitivity may be lower if infected with a different genotype
  - Indirect tests
  - False positives
  - ”Bad” reference laboratories

JID. 2003; 187: 1187-1199

Diagnostics

Many tests to diagnose Lyme, but no proof they work

Unregulated procedures can be costly, sow confusion

The Boston Globe

Diagnostics

IGeneX Inc.

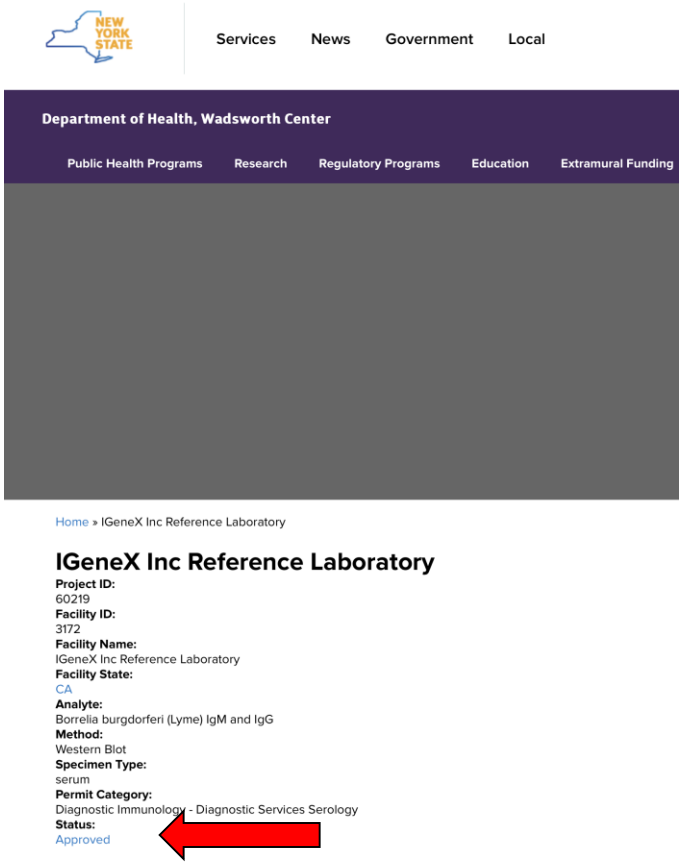
Table 2. Number and Percentage of False-Positive Serologic Test Results and Discordant Pairs for 40 Medically Healthy Controls (University Reference Laboratory Versus Commercial and Lyme Specialty Laboratories)

	University Reference Laboratory	Commercial Laboratory			Specialty Laboratory A			Specialty Laboratory B		
Test	No. Positive[a] (%)	No. Positive[a] (%)	*P* Value	Disc Pairs	No. Positive[a] (%)	*P* Value	Disc Pairs	No. Positive[a] (%)	*P* Value	Disc Pairs
?/+ ELISA	5 (12.5)	3 (7.5)	.683	6	1 (2.5)	.125	4	3 (7.5)	.683	6
C6 ELISA	. . .	. . .	. . .	. . .	0	. . .	. . .	0	. . .	. . .
WB IgM (CDC)	5 (12.5)	0	.074	5	1 (2.5)	.125	4	8 (20.0)	.505	9
WB IgM (laboratory)	. . .	. . .	. . .	. . .	1 (2.5)	.125[b]	4	15 (37.5)	.024	16[b]
WB IgG (CDC)	1 (2.5)	0	1.00	1	0	1.00	1	3 (7.5)	.480	2
WB IgG (laboratory)	. . .	. . .	. . .	. . .	0	1.00[b]	1	11 (27.5)	.004	10[b]
2-tier: ?/+ ELISA & WB IgG	0	0	. . .	0	0	. . .	0	1 (2.5)	1.000	1
2-tier: C6 ELISA & WB IgG	. . .	. . .	. . .	. . .	0	. . .	. . .	0	. . .	. . .
2-tier: ?/+ ELISA & C6 ELISA	. . .	. . .	. . .	. . .	0	. . .	. . .	0	. . .	. . .
+ WB IgM or IgG (CDC)	5 (12.5)	0	.074	5	1 (2.5)	.133	4	10 (25.0)	.182	9
+WB IgM or IgG (laboratory)					1 (2.5)	.133	4	23 (57.5)	<.001	22

CID 2014. 59(12): 1705-10.

UPSTATE MEDICAL UNIVERSITY | Center for Global Health and Translational Science

Diagnostics



PRESS RELEASE

New York State Grants Approval of IGeneX's Newly Developed Lyme ImmunoBlot Tests

Published: Aug 7, 2018 12:00 p.m. ET

Lyme ImmunoBlots (IgM and IgG) represents quantum leap in test performance over the traditional B. burgdorferi Western blots.

MarketWatch

UPSTATE MEDICAL UNIVERSITY | *Center for Global Health and Translational Science*

Diagnostics

What about the patients with chronic symptoms and repeatedly negative tests?

Chronic Symptoms

- Symptoms
  - General malaise (i.e. feeling unwell)
  - Arthritis, arthralgias, or myalgias
  - Headaches
  - Brain fog
  - Fatigue
  - Pain and paresthesias

Chronic Symptoms

- Antibiotic-refractory Lyme arthritis
  - Synovial cell hyperplasia
  - Vascular proliferation
  - Infiltration of mononuclear cells (T cells)
  - Upregulation of adhesion molecules
  - May be more likely with RST1 strains
  - Vast majority of these patients are negative on culture and PCR

Arthritis Rheum. 2006; 54: 3079-86
Nat Rev Immunol. 2004; 4: 143-52.

Chronic Symptoms

- Antibiotic-refractory Lyme arthritis
  - Some mouse models with high pathogen load have shown that spirochetal antigens are retained near cartilage surfaces after antibiotic therapy
  - Patients often homozygous for TLR1 polymorphism (1805GG)
  - HLA-DR specific alleles (DRB1 0101 and 0401)
    - Endothelial cell growth factor autoantibodies

J Clin Invest. 2012:122: 2622-2660
Arthritis Rheum. 2012: 64: 1497-1507
Arthritis Rheum. 2008.; 58:3892-3901
Arthritis Rheum. 2013; 65: 186-196.

Table 3 Summary of studies reporting genetic biomarkers in antibiotic-refractory LA in humans

Study	Biomarker class	Biomarker(s)	Assay	Summary of results
Lochhead et al. 2017 [12]	miRNA	miR-146a, miR142, miR17, miR-155, miR-223, miR20a, let-7a, let-7c	PCR	miR-146a, miR142, miR17, miR-155, miR-223 and miR20a were higher in post- vs. pre-antibiotic treated A-RLA
				miR-146a, miR142, miR17, miR-155, miR-223, miR20a, let-7a and let-7c were higher in A-RLA compared with osteoarthritis
Lochhead et al. 2015 [29]	miRNA (extracellular)	miR-146a, miR-155 (inflammatory signature), miR-30fam (vascularization signature), miR223, miR142	qPCR	miR-146a, miR-155, miR-223 and miR-142 were higher in A-RLA compared with antibiotic-responsive LA
				miR-146a, miR-155, miR-30fam, miR223 and miR-142 were upregulated in A-RLA compared with osteoarthritis patients

Infect Dis Ther. 2018 Nov 30 (Epub ahead of print)

Chronic Symptoms

- Chronic Neurologic Manifestations
  - Chronic axonal polyneuropathy with radicular pain or distal paresthesias
  - Lyme encephalopathy
    - Subtle cognitive disturbances

Neurology. 1992; 42: 303-11
NEJM. 1990.; 323: 1438-1444. .

Chronic Symptoms

- Persistent Infection?
  - Some animal studies indicating persistence
  - Several RCTs have not provided evidence that retreatment with prolonged courses of antibiotics significantly help
    - One study indicated improvement in fatigue
    - One small study indicated a temporary cognitive improvement

Am J Path. 2018; 188(3): 672-82.
NEJM. 2001; 345(2): 85.
Neurology. 2003.; 60(12): 1916.
Neurology. 2003; 60(12): 1923
Neurology. 2008; 70(13):992
NEJM. 2016;374(13):1209-20.

Chronic Symptoms

- Wrong diagnosis
  - Other infections
  - Co-infections
  - Autoimmune disorders

Chronic Symptoms

Table 3. Factors associated with incomplete response according to age (middle-aged versus young and elderly versus young).

	OR (95% CI) [a]	*p* Value [b]
Age		0.038
Middle-aged vs. young	1.57 (1.04–2.37)	0.031
Elderly vs. young	1.94 (1.12–3.37)	0.018
Time from enrolment		<0.001
2 months vs. 14 days	0.48 (0.37–0.63)	<0.001
6 vs. 2 months	0.50 (0.36–0.68)	<0.001
12 vs. 6 months	0.47 (0.32–0.70)	<0.001
Sex (female vs. male)	1.43 (1.01–2.02)	0.041
Presence of comorbidities	0.85 (0.59–1.24)	0.399
Multiple EM vs. solitary EM	1.67 (1.08–2.58)	0.022
Presence of LB-associated constitutional symptoms at enrolment (yes vs. no)	8.47 (5.79–12.38)	<0.001

1220 European adults

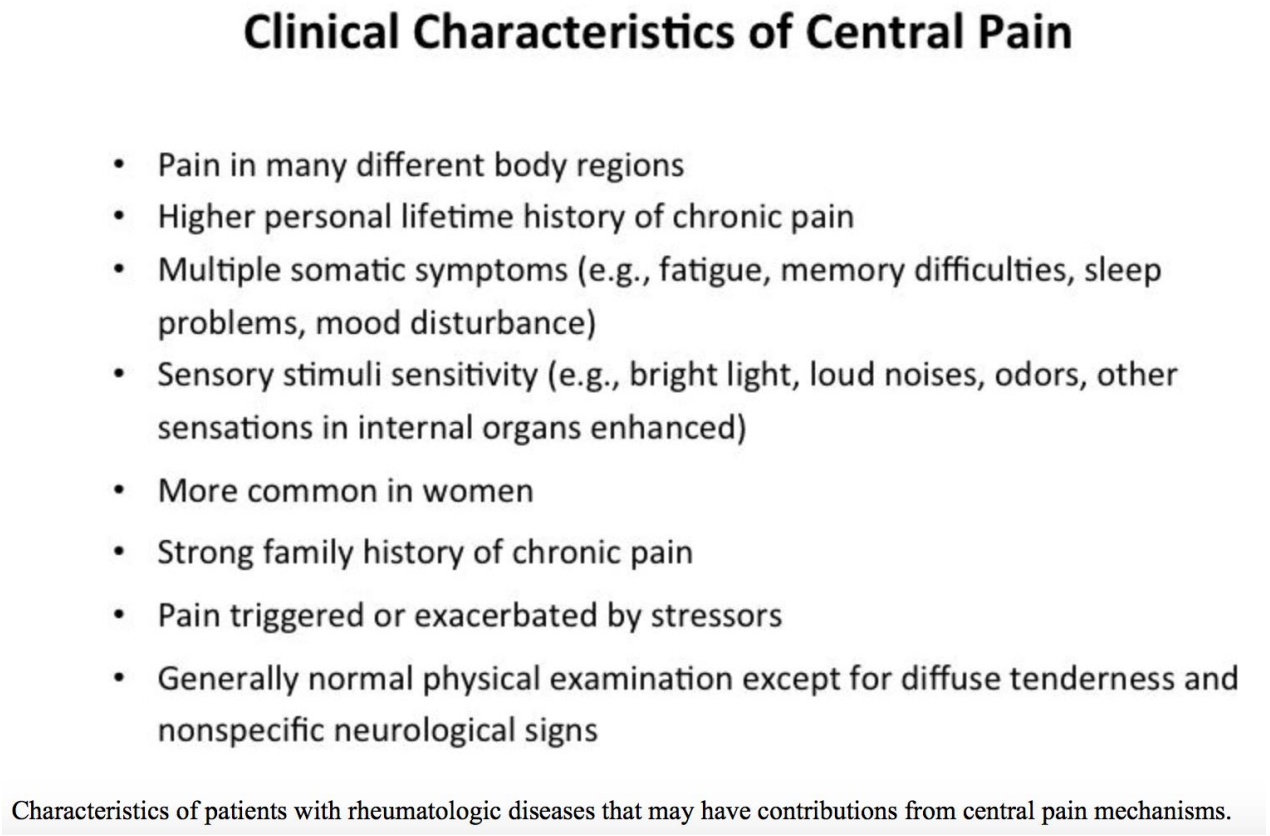
J. Clin. Med. 2018, *7*(12), 506

Treatment

What is there to do?

Treatment

Figure 3



Characteristics of patients with rheumatologic diseases that may have contributions from central pain mechanisms.

Arthritis Rheum. 2013; 65: 291-302

Treatment

- Gabapentin
  - Pilot study performed
  - Pain improved in 9/10 patients

- DMARDS such as methotrexate or infliximab have been used for antibiotic refractory arthritis

Dermatology. 2005;211(2):123-7
Arth & Rheum 2006;54(1):3079-86.

Treatment

Dangers

- Misdiagnosis

Case 2. A man in his late 30s presented with a 4-year history of fatigue, abdominal pain, and loose stools. Previous evaluations demonstrated stable mesenteric lymphadenopathy. Although he lived in an area where Lyme disease is rare, reported no history of erythema migrans, and had negative Lyme serologic test results, he was diagnosed with chronic Lyme disease by a physician and treated with antibiotics (Table). Subsequently, the patient discontinued treatment and was reevaluated by a gastroenterologist and an oncologist. Findings from a gastric biopsy demonstrated stage IV mucosa-associated lymphoid tissue lymphoma; successive Lyme serologic test results were negative. Findings from a mesenteric lymph node biopsy and positron emission tomographic scan demonstrated stage IV classic Hodgkin lymphoma, for which the patient underwent chemotherapy. He died 2 years later of complications of advanced lymphoma.

JAMA Intern Med. 2015; 175(1):132-33.

Dangers

- Line infections

Death from Inappropriate Therapy for Lyme Disease

A 30-year-old woman died as a result of a large *Candida parapsilosis* septic thrombus located on the tip of a Groshong catheter. The catheter had been in place for 28 months for administration of a 27 month course of intravenous cefotaxime for an unsubstantiated diagnosis of chronic Lyme disease.

Morbidity and Mortality Weekly Report

Serious Bacterial Infections Acquired During Treatment of Patients Given a Diagnosis of Chronic Lyme Disease — United States

Natalie S. Marzec, MD[1]; Christina Nelson, MD[2]; Paul Ravi Waldron, MD[3]; Brian G. Blackburn, MD[4]; Syed Hosain, MD[5]; Tara Greenhow, MD[6]; Gary M. Green, MD[6]; Catherine Lomen-Hoerth, MD, PhD[7]; Marjorie Golden, MD[8]; Paul S. Mead, MD[2]

CID. 2000;31(4):1107-9
MMWR. 2017;66(23).607-9.

Dangers

Death Due to Community-Associated *Clostridium difficile* in a Woman Receiving Prolonged Antibiotic Therapy for Suspected Lyme Disease

To the Editor—*Clostridium difficile* infections can occur outside the hospital in association with antibiotic use and can result in fulminant colitis and death. In December 2009, the Minnesota Department of Health investigated a death due to *C. difficile* of a 52-year-old woman with no recent hospitalizations.

Clin Infect Dis. 2010;51:369–370.

UPSTATE MEDICAL UNIVERSITY | *Center for Global Health and Translational Science*

Dangers

Antibiotic adverse effects

December 2016

Antibiotic Treatment for Chronic Lyme Disease—Say No to the DRESS

Clifford M. Marks, AB[1]; John E. Nawn, MD[2]; Julie A. Caplow, MD[2]

» Author Affiliations | Article Information

JAMA Intern Med. 2016;176(12):1745-1746. doi:10.1001/jamainternmed.2016.6229

Acta Clinica Belgica ›

International Journal of Clinical and Laboratory Medicine

Volume 72, 2017 - Issue 2

Case Report

Ceftriaxone-induced immune hemolytic anemia as a life-threatening complication of antibiotic treatment of 'chronic Lyme disease'

Maarten De Wilde, Marijn Speeckaert, Rutger Callens & Wim Van Biesen

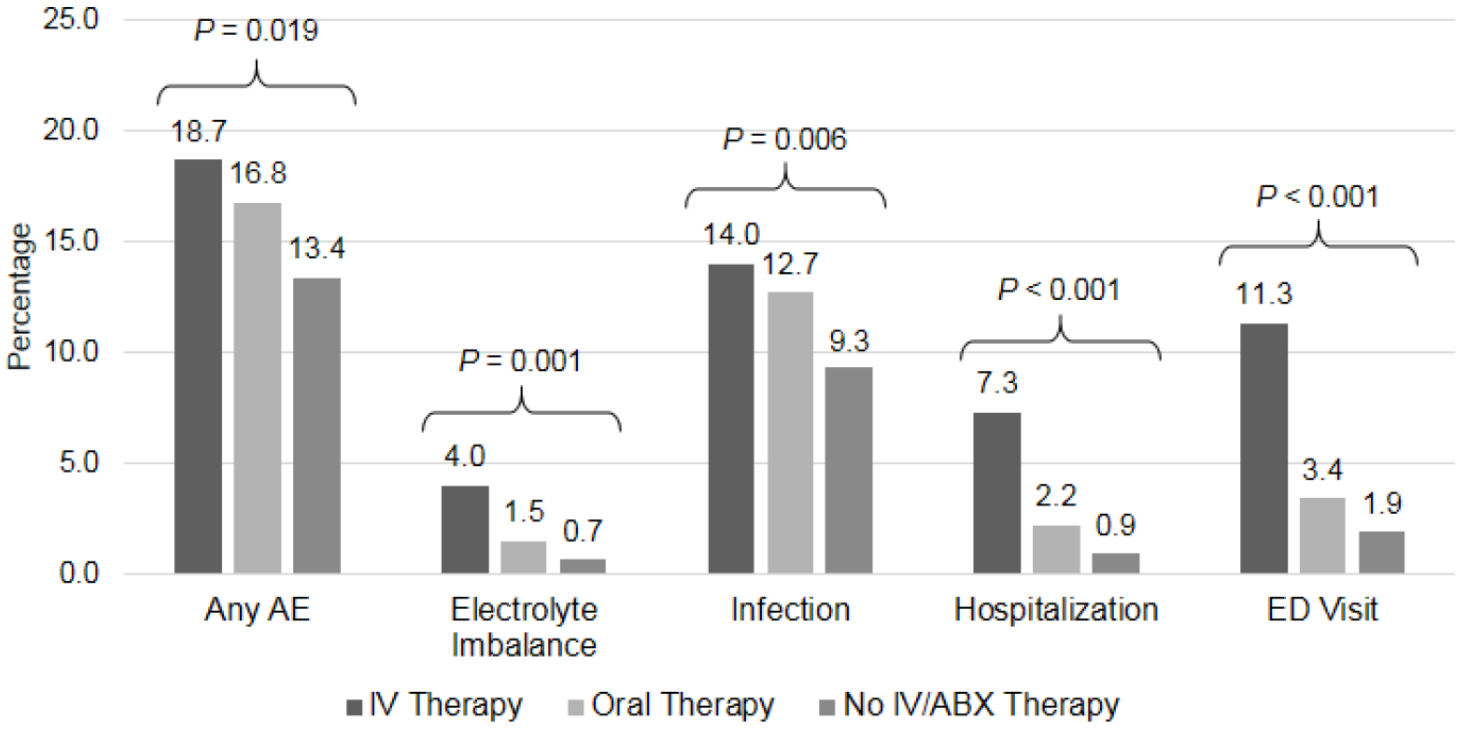
Pages 133-137 | Published online: 12 May 2016

Dangers

- Retrospective cohort analysis of medical and pharmacy claims of patients with PLDS
  - Infections increased by 22% and 17% in the IV and Oral treatment groups respectively
  - Emergency room visits were 11.3% vs 0.9% in IV treated compared to untreated patients respectively

CID 2018. In press

Dangers



CID 2018. In press

UPSTATE MEDICAL UNIVERSITY | Center for Global Health and Translational Science

Dangers

Clinical Infectious Diseases

IDSA Infectious Diseases Society of America

hivma hiv medicine association

Article Navigation

ACCEPTED MANUSCRIPT

Holistic approach in patients with presumed Lyme borreliosis leads to less than 10% of confirmation and more than 80% of antibiotics failure

Elie Haddad ✉, Kahina Chabane, Stéphane Jaureguiberry, Gentiane Monsel, Valérie Pourcher, Eric Caumes

Clinical Infectious Diseases, ciy799, https://doi.org/10.1093/cid/ciy799

Published: 18 September 2018 **Article history** ▾

In about 300 patients consulting for a presumed Lyme Borreliosis, this diagnosis was confirmed in less than 10% of patients whereas 80% were found with another disease. Overall the presumptive treatment administered before or after referral failed in about 80%.

CID 2018 Nov 21 (Epub ahead of print)

UPSTATE MEDICAL UNIVERSITY | *Center for Global Health and Translational Science*

Controversy

- Need for additional research
- Subpar diagnostics
- Suffering patients

Who is right?

Prevention

- PPE
  - DEET (~25%)
  - Picaridin
  - Permethrin (not for skin)

- Doxycycline 200 mg PO x 1 if given within 72 hours of engorged tick

NEJM. 2001; 345(2): 79

UPSTATE MEDICAL UNIVERSITY | Center for Global Health and Translational Science

Prevention

- Lymerix
  - OspA vaccine approved in late 90s
  - Immunogenic and efficacious
  - Controversy over lyme arthritis type symptoms in vaccine recipients
    - Specific epitopes of concern (hLFA-1)

Epidemiol Infect 2007; 135:1-8

Prevention

Table 1. Immunogenicity and Safety Results of the SmithKline Beecham Phase III Clinical Trial [3]

Variable	Vaccine group	Placebo group	Efficacy	*P*
Definite Lyme disease, no. of cases				
Year 1	22	41	49%	<.001
Year 2	16	66	76%	<.001
Asymptomatic Lyme disease, no of cases				
Year 1	2	13	83%	.001
Year 2	0	15	100%	.001
Adverse events after vaccine, % of subjects				
Arthralgia	3.9	3.5		.34
Myalgias	3.2	1.8		<.001
Achiness	2.0	1.4		.01
Late arthralgia (>30 days after receipt of dose)	1.3	1.2		.54

Adapted from NEJM. 1998; 339: 209-15.

Prevention

valneva

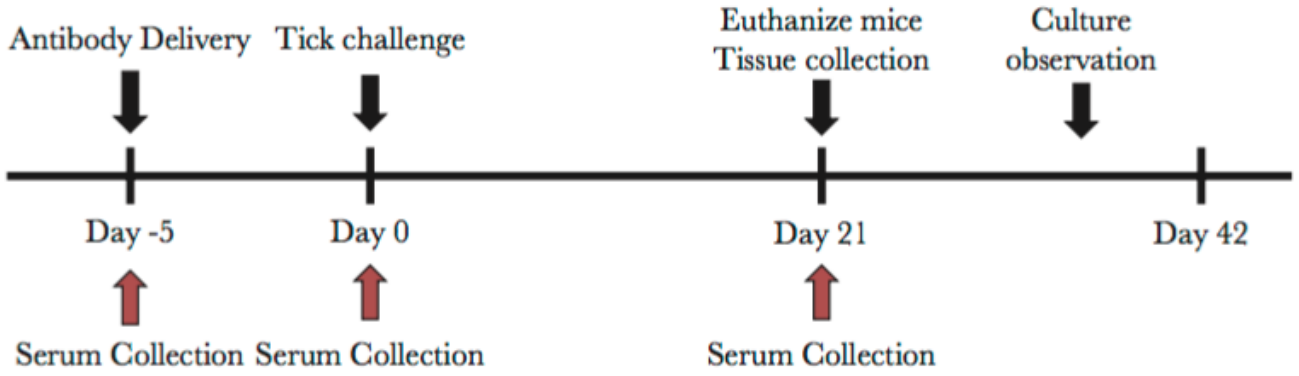
- Valneva vaccine candidate VLA15
  - Targets OspA
  - Phase 1 study completed
    - No safety concerns in any treatment groups
    - Immunogenic with good OspA IgG responses against OspA serotypes
    - Phase 2 study (2 sites in US in U.S.) started recruiting in December 2018

Data not yet published

UPSTATE MEDICAL UNIVERSITY | Center for Global Health and Translational Science

Prevention

A



B

Antibody Group	Average Concentration (µg/mL)	Protection (Mice)	
319-44 WT DMAb	12.86 ± 1.51*	10/13	77%#
319-44 Mod1 DMAb	12.68 ± 1.36*	12/13	92%#
319-44 WT HuMAb	9.29 ± 1.71	3/4	75%#
Irrelevant IgG DMAb Control	NA	0/9	0%

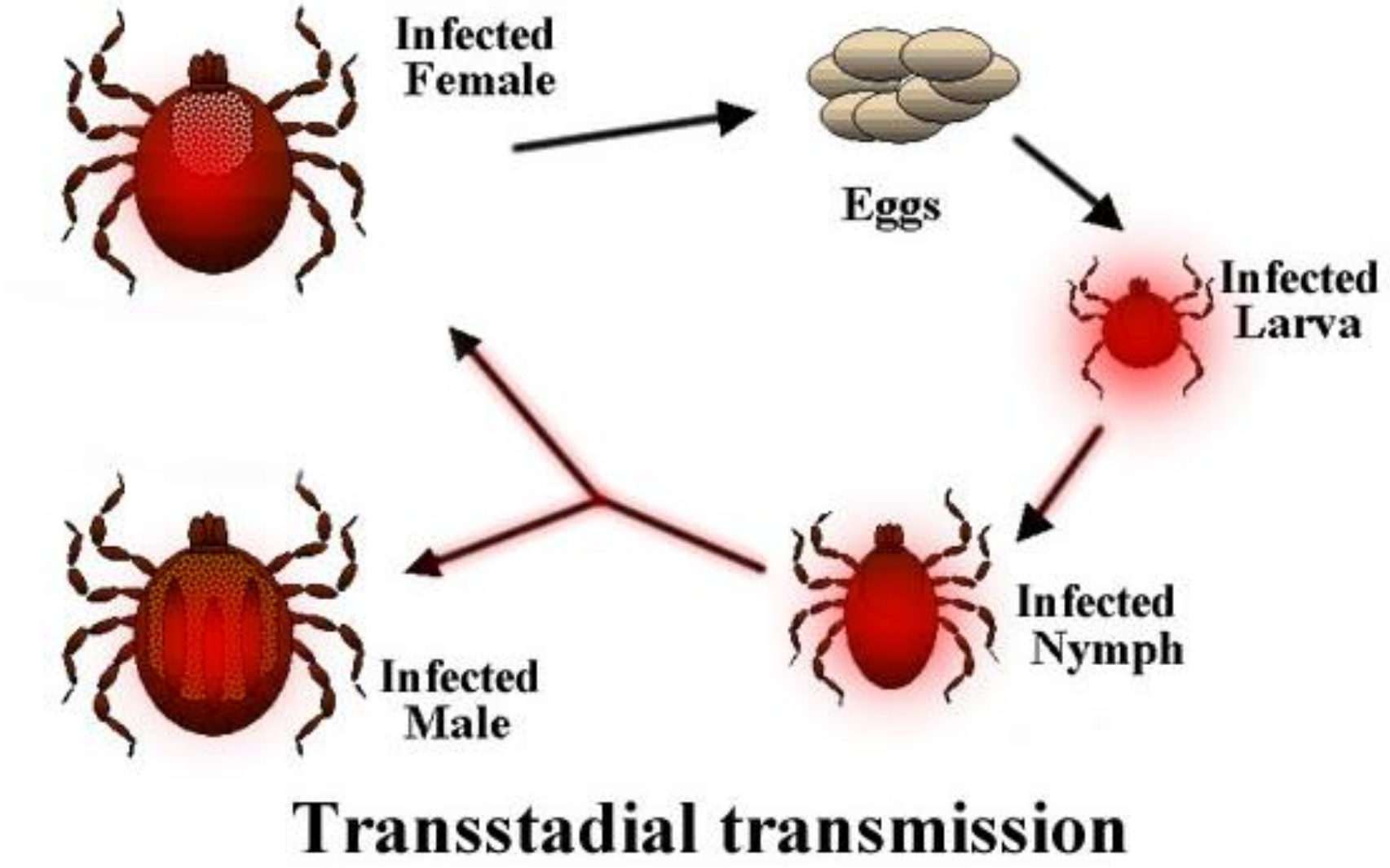
J Infect Dis 2018 Nov 21 (Epub ahead of print)

UPSTATE MEDICAL UNIVERSITY | *Center for Global Health and Translational Science*


And now
for something
completely different...

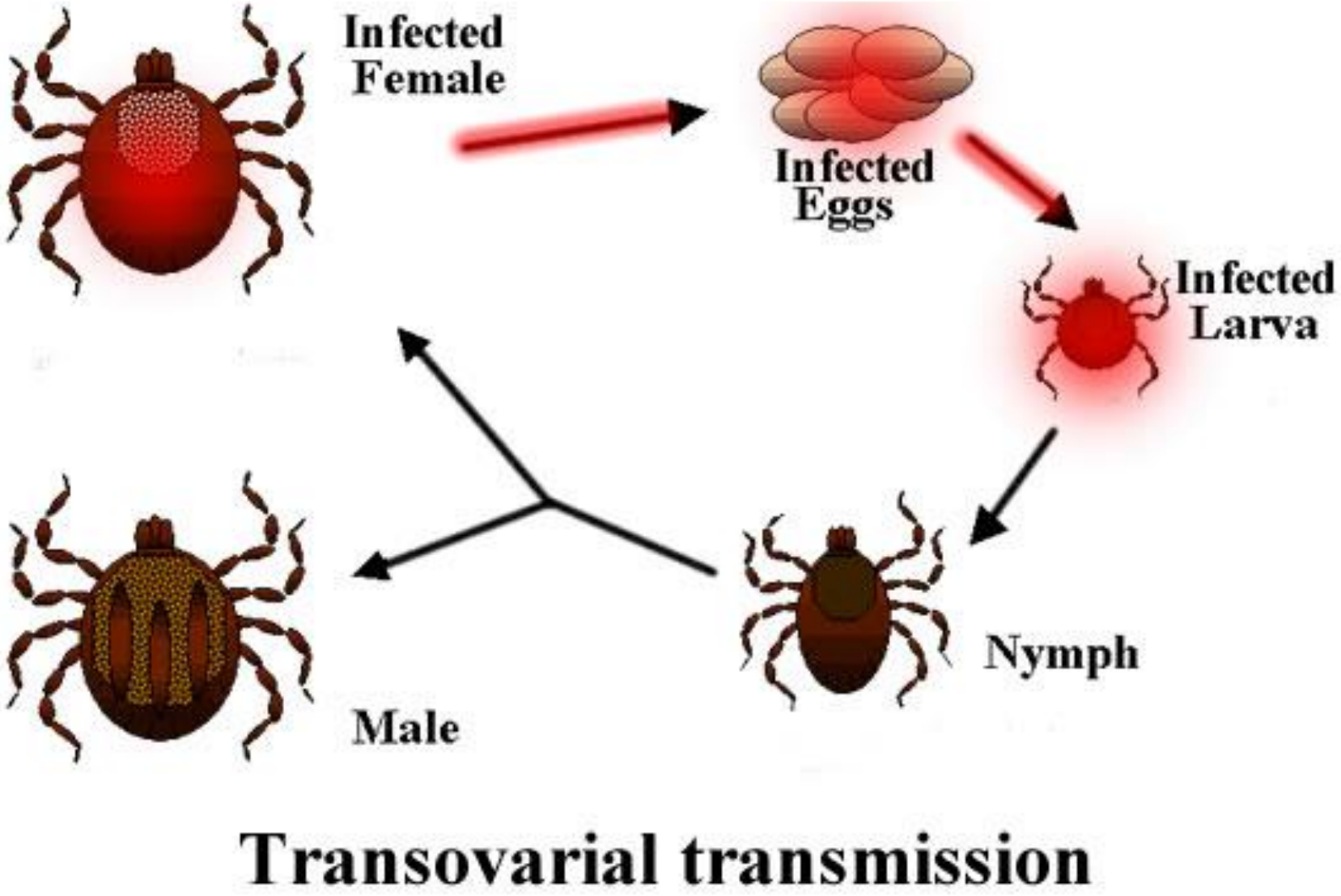
Borrelia miyamotoi

- Spread by *Ixodes* species ticks
- Genetically related to relapsing fever species
- First human cases reported in Russia 2011; U.S. 2013
- Presents with “viral like illness”
  - Neurologic symptoms may be more common in immunocompromised
- Generally treated with 2-4 weeks of doxycycline
  - Jarisch-Herxheimer reaction has been described
- PCR testing and serology is available
  - Blood smear also possible



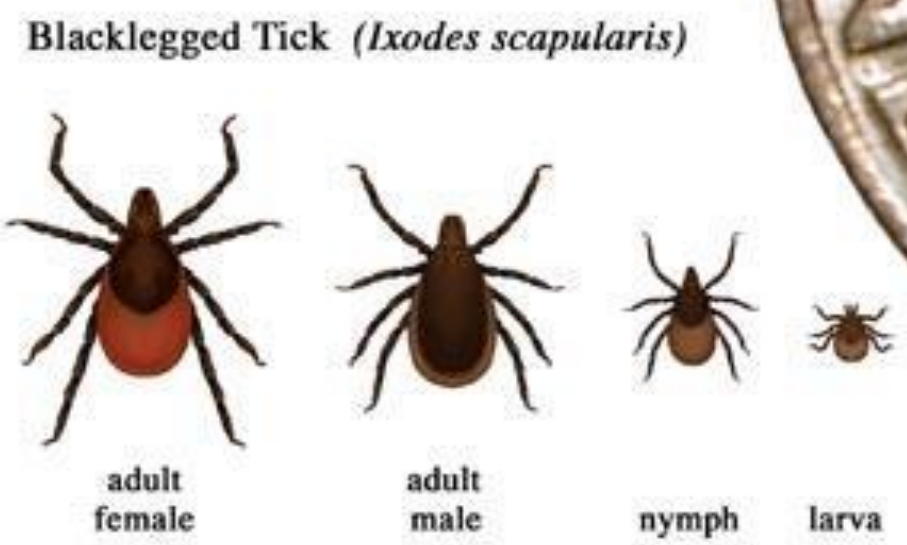
Lyme

wikipedia



B. miyamotoi

wikipedia



Local unpublished reports indicate a 4-5% tick infection rate

Blacklegged tick

Borrelia miyamotoi

The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Meningoencephalitis from *Borrelia miyamotoi* in an Immunocompromised Patient

Joseph L. Gugliotta, M.D., Heidi K. Goethert, Sc.D., Victor P. Berardi, B.S., and Sam R. Telford III, Sc.D.

N ENGL J MED 368;3 NEJM.ORG JANUARY 17, 2013

UPSTATE MEDICAL UNIVERSITY | *Center for Global Health and Translational Science*

Table 1. Clinical Features of the 51 Case Patients With BMD

Feature	Value*
Mean age (range), *y*	55 (12–82)
Male	29 (57)
Fever/chills	49 (96)
Headache†	49 (96)
Myalgia	42 (84)
Arthralgia	39 (76)
Malaise/fatigue	42 (82)
Rash	4 (8)
Gastrointestinal symptoms‡	3 (6)
Cardiac/respiratory symptoms§	3 (6)
Neurologic symptoms‖	4 (8)

BMD = *Borrelia miyamotoi* disease.
* Number (percentage) unless otherwise indicated.
† Severe in most patients.
‡ Nausea, abdominal pain, diarrhea, and anorexia.
§ Dyspnea.
‖ Dizziness, confusion, and vertigo.

Table 1. Serologic and Clinical Characteristics of *Borrelia miyamotoi* Infection in Study Patients.*

Group, Patient No., and Serum Phase†	Assay Method			Coinfection‡	No. of Symptoms
	ELISA	Western Blot			
		IgM	*IgG*		
Group 1					
Patient 1	Positive at 1:320 dilution	Positive	Positive	None	None
Patient 2	Positive at 1:320 dilution	Positive	Negative	None	None
Patient 3	Positive at 1:320 dilution	Positive	Positive	None	None
Patient 4	Positive at ≥1:320 dilution§	Not done	Positive	None	None
Patient 5	Positive at ≥1:320 dilution§	Not done	Positive	None	None
Patient 6	Positive at 1:320 dilution	Positive	Positive	None	None
Group 2					
Patient 7	Positive at ≥1:320 dilution§	Not done	Positive	None	5
Patient 8	Positive at 1:320 dilution	Negative	Positive	None	9
Patient 9	Positive at 1:320 dilution	Negative	Positive	None	8
Patient 10	Positive at ≥1:320 dilution§	Not done	Positive	None	6
Patient 11	Positive at ≥1:320 dilution§	Not done	Positive	None	3
Patient 12	Positive at 1:1280 dilution	Negative	Positive	Lyme disease	4
Patient 13	Positive at 1:320 dilution	Negative	Positive	Lyme disease	Uncertain
Patient 14	Positive at 1:320 dilution	Positive	Positive	Lyme disease	Uncertain
Patient 15					
Acute	Negative at 1:160 dilution	Negative	Negative	Babesiosis	12
Convalescent	Positive at 1:1280 dilution	Positive	Positive		
Group 3					
Patient 16	Positive at 1:1280 dilution	Positive	Positive	None	5
Patient 17					
Acute	Negative at 1:80 dilution	Positive	Negative	None	10
Convalescent	Positive at 1:320 dilution	Positive	Positive		
Patient 18					
Acute	Negative at 1:80 dilution	Positive	Positive	Lyme disease	12
Convalescent	Positive at 1:320 dilution	Negative	Positive		

SEROPREVALENCE

Group 1: 1%
Group 2: 3.2%
Group 3: 21%

NEJM 2013; 368: 291-3.

UPSTATE MEDICAL UNIVERSITY | *Center for Global Health and Translational Science*

Clinical Infectious Diseases

MAJOR ARTICLE

Seroreactivity to the C6 Peptide in *Borrelia miyamotoi* Infections Occurring in the Northeastern United States

Phillip J. Molloy,[1] Karen E. Weeks,[1] Brittany Todd,[1] and Gary P. Wormser[2]

[1]IMUGEN, Norwood, Massachusetts; and [2]Division of Infectious Diseases, New York Medical College, Valhalla

Background. There are no US Food and Drug Administration (FDA)–approved diagnostic tests for *Borrelia miyamotoi* infection, an emerging tick-borne illness in the United States. The purpose of this study was to evaluate whether the FDA-approved C6 peptide enzyme-linked immunosorbent assay (ELISA) currently used to diagnose Lyme disease may potentially serve as a diagnostic test for *B. miyamotoi* infections.

Methods. Serum specimens from 30 patients from the northeastern United States with *B. miyamotoi* infection established by a polymerase chain reaction assay of a blood specimen were tested using the C6 ELISA. To reduce confounding with *Borrelia burgdorferi* coinfection, 6 sera were excluded: 3 from patients with a positive Western immunoblot for antibodies to *B. burgdorferi* and 3 from patients for whom immunoblot testing had not been performed.

Results. Twenty-two of 24 (91.7% [95% confidence interval, 73.0%–98.8%]) evaluable *B. miyamotoi* patients were C6 ELISA reactive, principally on a convalescent-phase serum specimen. C6 ELISA index values were often well above the positive cutoff value of 1.1, exceeding 4 in 11 of the 22 (50.0%) C6 ELISA-reactive patients.

Conclusions. Although previously regarded as a highly specific test for Lyme disease, the C6 ELISA is also regularly reactive on convalescent-phase serum samples of patients from the northeastern United States with *B. miyamotoi* infection.

Keywords. Lyme disease; Lyme serology; C6 Lyme test; Borrelia; *Borrelia miyamotoi*.

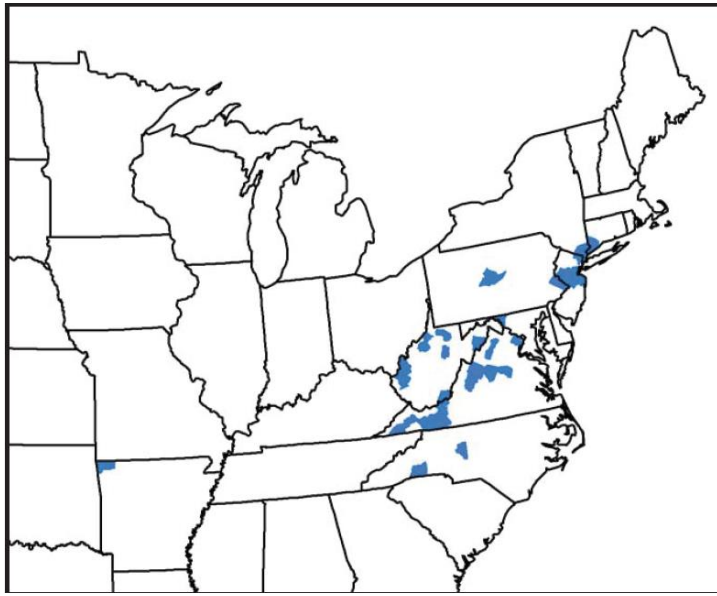
Clinical Infectious Diseases® 2018;66(9):1407–10

UPSTATE MEDICAL UNIVERSITY | *Center for Global Health and Translational Science*

One more thing…

Multistate Infestation with the Exotic Disease–Vector Tick *Haemaphysalis longicornis* — United States, August 2017–September 2018

H. longicornis is native to eastern China, Japan, the Russian Far East, and Korea. It is an introduced, and now established, exotic species in Australia, New Zealand, and several island nations in the western Pacific Region. Where this tick exists, it is an important vector of human and animal disease agents. In China and Japan, it transmits the severe fever with thrombocytopenia syndrome virus (SFTSV), which causes a human hemorrhagic fever (*2*), and *Rickettsia japonica,* which causes Japanese spotted fever (*3*). Studies in Asia identified ticks infected with various species of *Anaplasma*, *Babesia*, *Borrelia*, *Ehrlichia*, and *Rickettsia*, and all of these pathogen groups circulate zoonotically in the United States (*4*,*5*). In addition, parthenogenetic reproduction, a biologic characteristic of this species, allows a single introduced female tick to generate progeny without mating, thus resulting in massive host infestations. In some regions of New Zealand and Australia,



Questions?