Lyme and Tick-Borne Diseases

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No disclosures

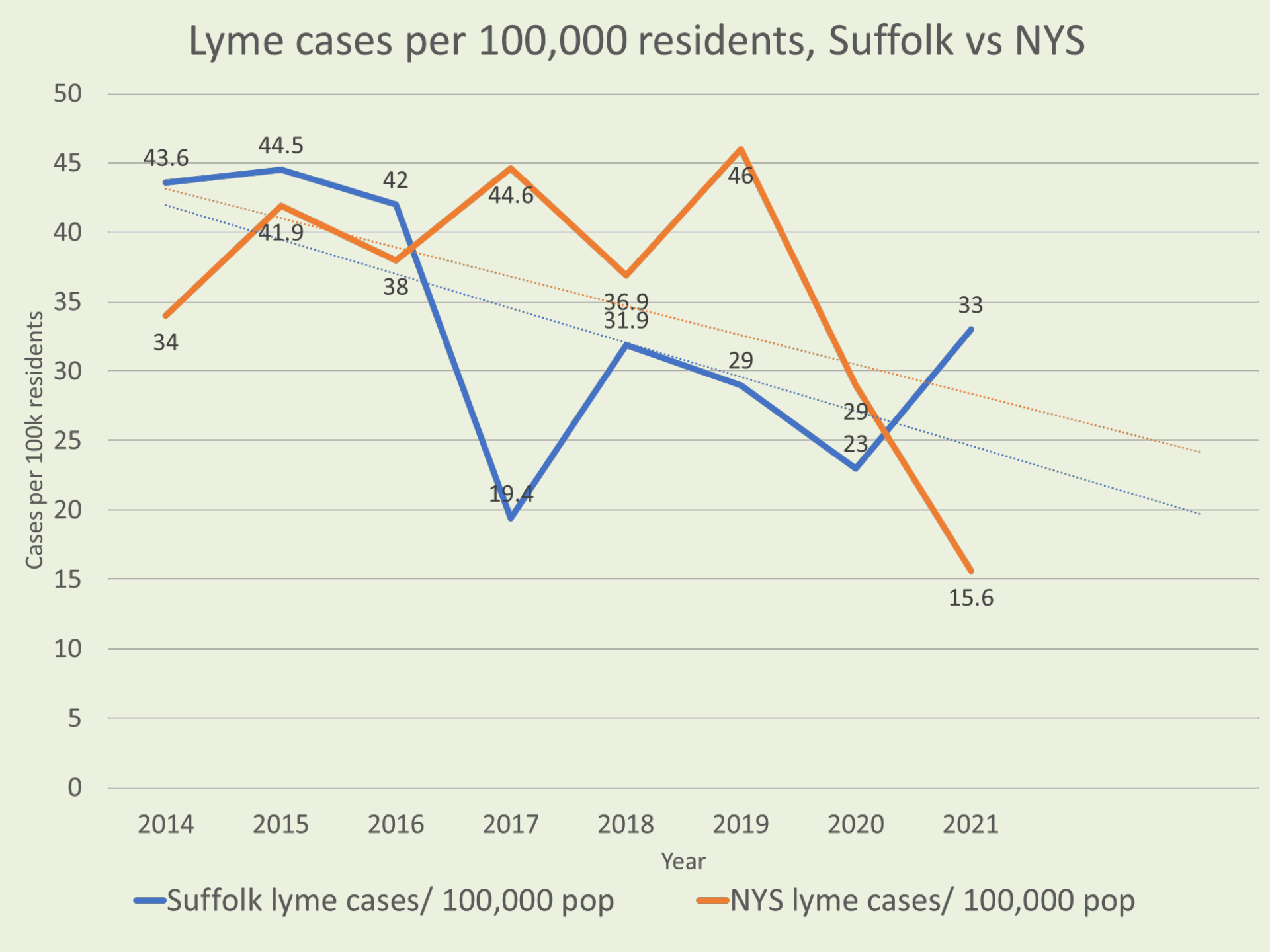
Grants from Department of Defense on Babesia and Lyme disease 2022-2026

* 2022-2023 Member for Tick-Borne Disease Committee at NYS

- 2021 Member for SubCommitte Tick-Borne Disease Committee, Lyme Treatment (HHS)

OUTLINE

- Know your ticks
- New York: Epicenter of LD
- Erythema migrans
- LD can cause a chronic infection
- Post-Treatment LD Syndrome


Lyme cases per 100,000 residents, Suffolk vs NYS
Cases per 100k residents
50
45
40
35
30
25
20
15
10
5
0
43.6
44.5
42
19.4
31.9
29
23
33
34
41.9
38
44.6
36.9
46
29
15.6
2014
2015
2016
2017
2018
2019
2020
2021
Year
Suffolk lyme cases/ 100,000 pop
NYS lyme cases/ 100,000 pop

LESSON 1

KNOW YOUR TICKS

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TICKS OF NEW YORK

Deer tick (*Ixodes scapularis*)

- *Borrelia burgdorferi* and *B. mayonii* (which cause Lyme disease)
- *Anaplasma phagocytophilum* (anaplasmosis),
- *B. miyamotoi* disease (a form of relapsing fever)
- *Ehrlichia muris eauclairensis* (ehrlichiosis)
- *Babesia microti* (babesiosis)
- Powassan virus (Powassan virus disease).

Lone start tick (*Amblyomma americanum)*

- *Ehrlichia chaffeensis* and *E. ewingii* (which cause human ehrlichiosis)
- *Francisella tularensis* (tularemia)
- Heartland virus (Heartland virus disease)
- Bourbon virus (Bourbon virus disease)
- Southern tick-associated rash illness (STARI).

American Dog tick (*Dermacentor variabilis)*

- *Francisella tularensis* (tularemia)
- *Rickettsia rickettsii* (Rocky Mountain spotted fever).


IN GOD WE TRUST
LIBERTY
1977
D

100x Microscope

For Smartphone

Zoom 100x

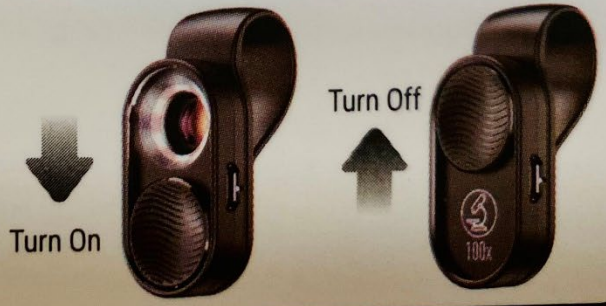
Exempt Driver

High-Resolution

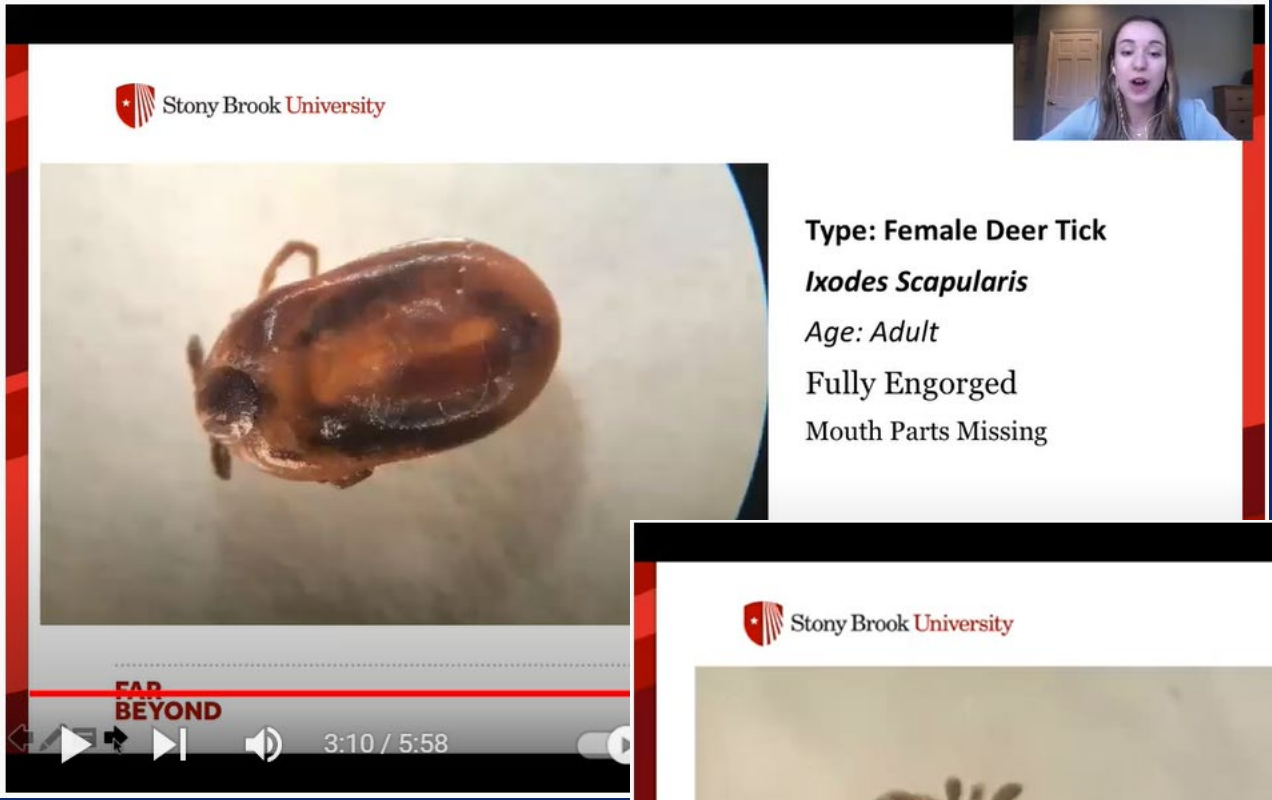
Instant Sharing

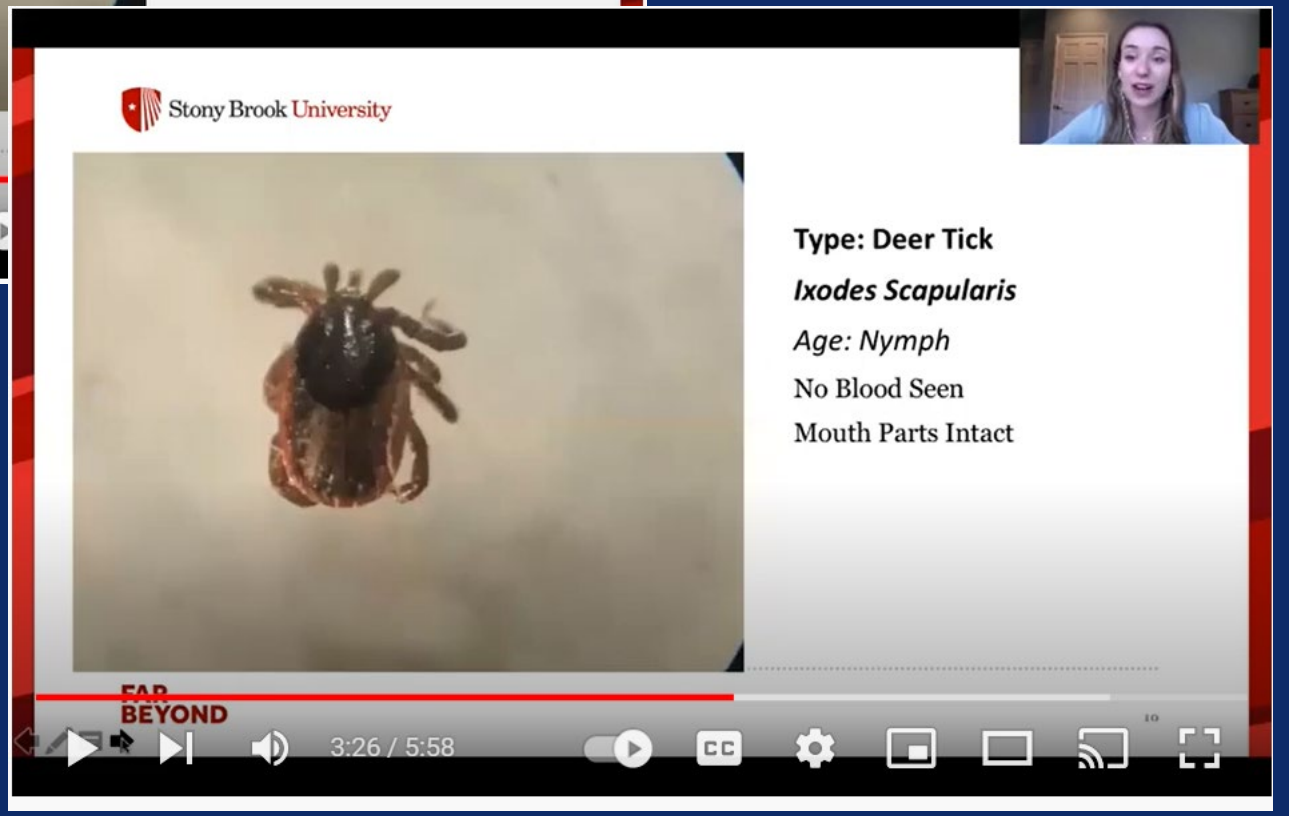
Easy Operation

switch cover slide down to turn on, slide up to turn off.



ID DIVISION WEBSITE, STONY BROOK UNIVERSITY





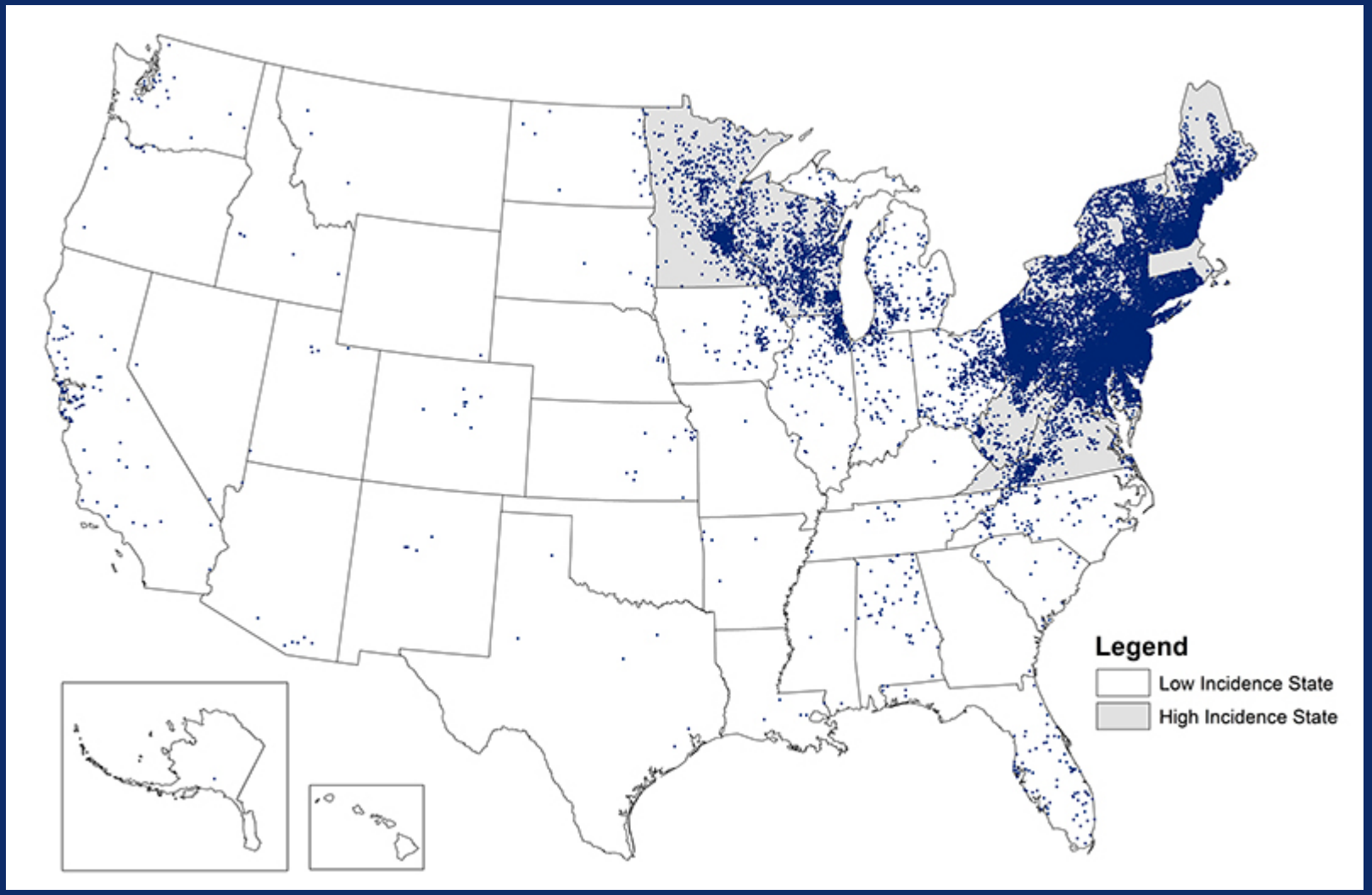
Lesson learnt: Know your ticks

https://www.youtube.com/watch?v=tut-3G4WcHk

LESSON 2

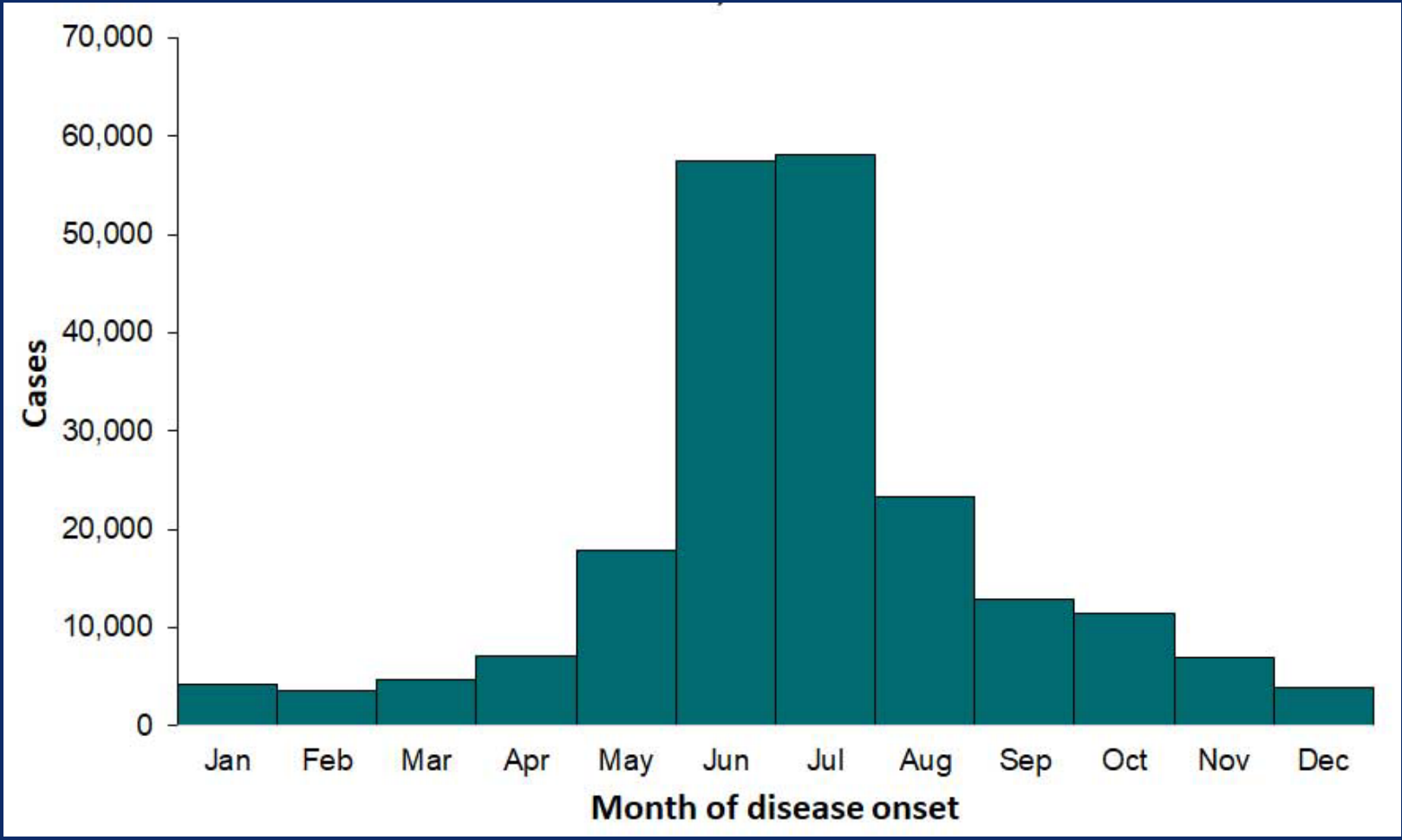
WE LIVE IN THE EPICENTER OF LYME DISEASE IN THE US

Reported Cases of Lyme Disease — United States, 2019



Source: CDC. Incidence in NY: 14.6 / 100,000 population. Absolute: 2847 confirmed cases, second in the country.

Confirmed Cases of Lyme Disease in the US by Month of Disease Onset, 2008-2018



Source: https://www.cdc.gov/lyme/datasurveillance/charts-figures-recent.html

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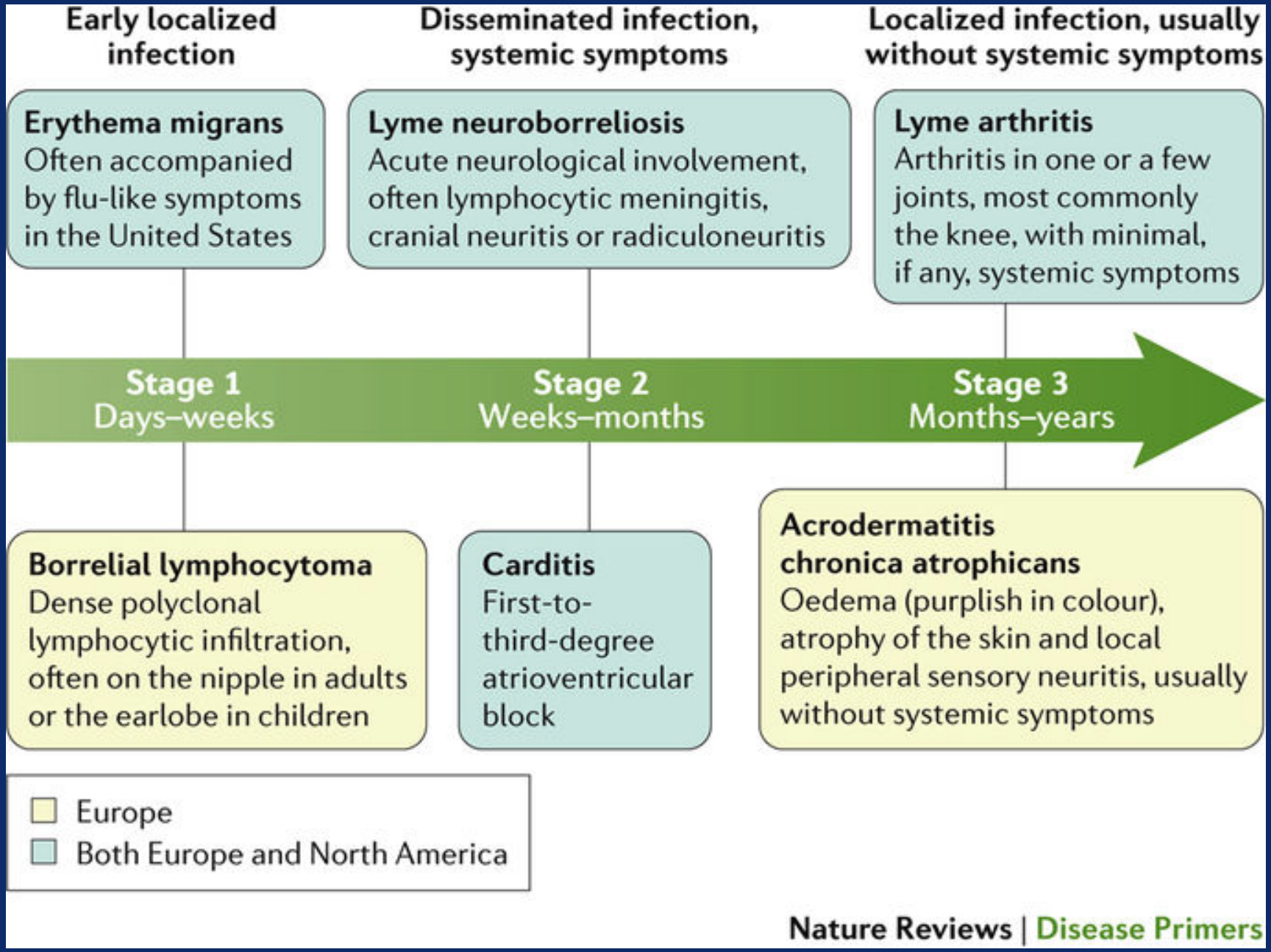
Courtesy: Dr. Jorge Benach, SBU

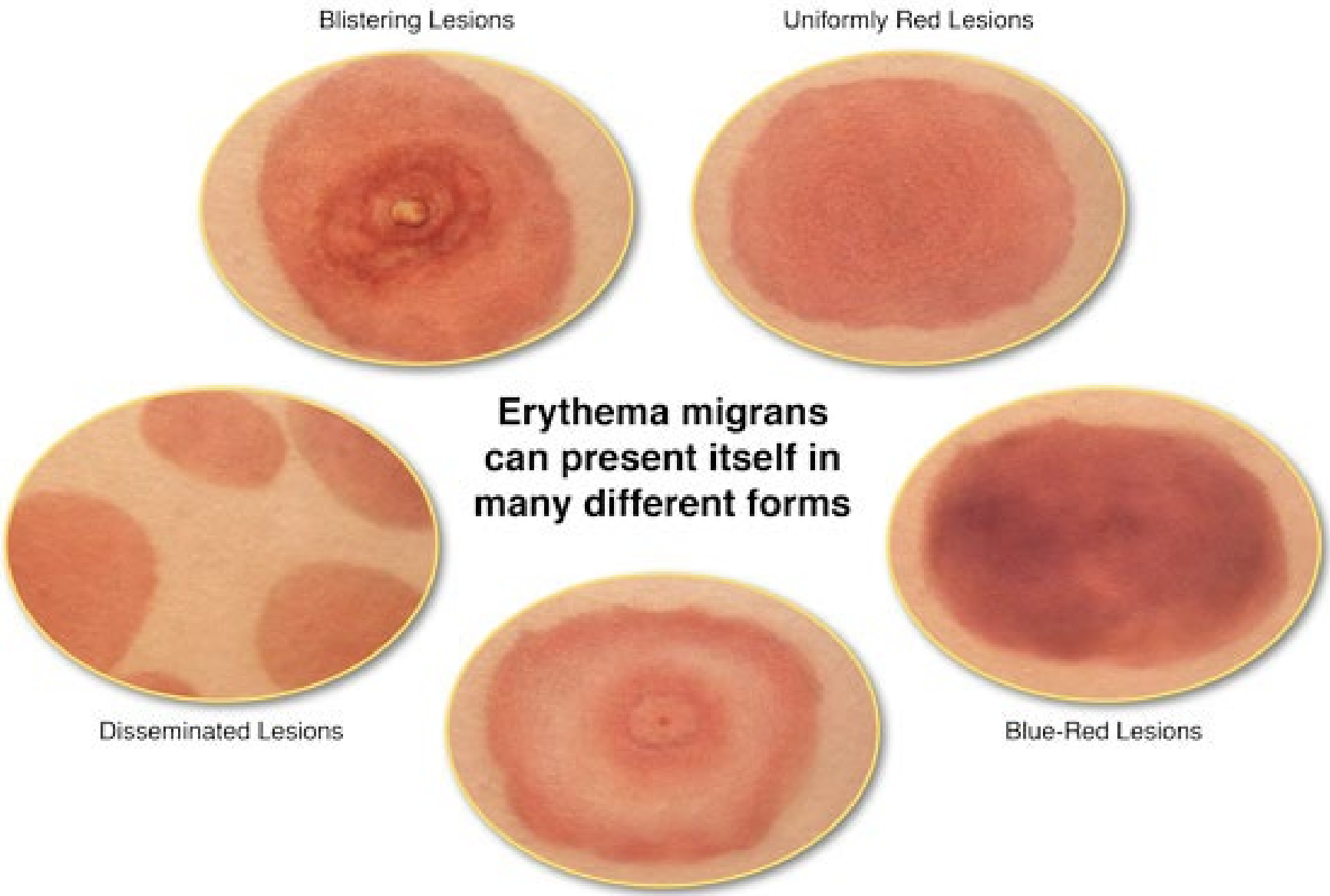
LESSON 3

ERYTHEMA MIGRANS



Steere, A., *et al.* Lyme borreliosis. *Nat Rev Dis Primers* (2016)

Erythema migrans




06/27/2018

Atypical erythema migrans due to use of steroids topical cream

STARI OR LYME?

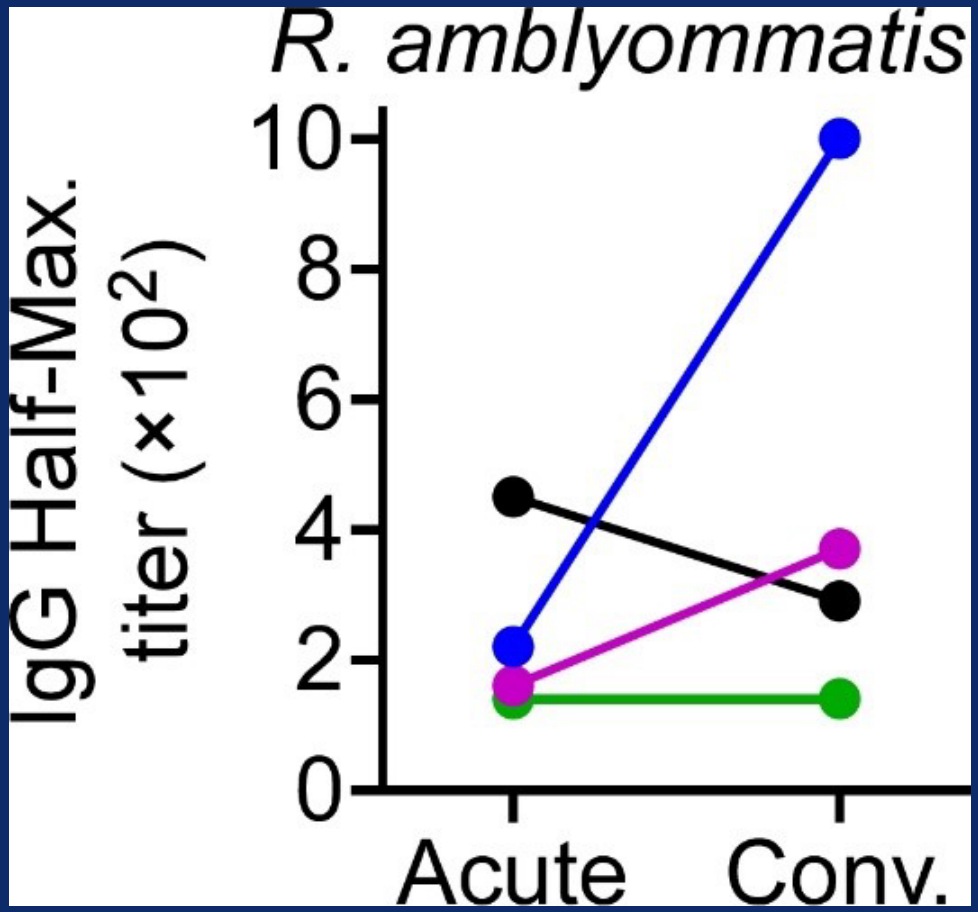
"Many people, even health care providers, can be confused about whether the lone star tick causes Lyme disease. It does not. Patients bitten by lone star ticks will occasionally develop a circular rash similar to the rash of early Lyme disease. The cause of this rash has not been determined". **CDC**

STARI: southern tick-associated rash illness.
Symptoms: fatigue, headache, fever, and muscle pains
STARI has not been linked to arthritis, neurologic disease, or chronic symptoms. Researchers once hypothesized that STARI was caused by the spirochete, *Borrelia lonestari,* however other studies did not support this finding.

The cause of STARI remains unknown.

Rickettsia amblyommatis infection transmitted by *Amblyomma americanum* in New York

Figure 1. Human patients elicit *R. amblyommatis*-specific IgG responses after *A. americanum* bite.



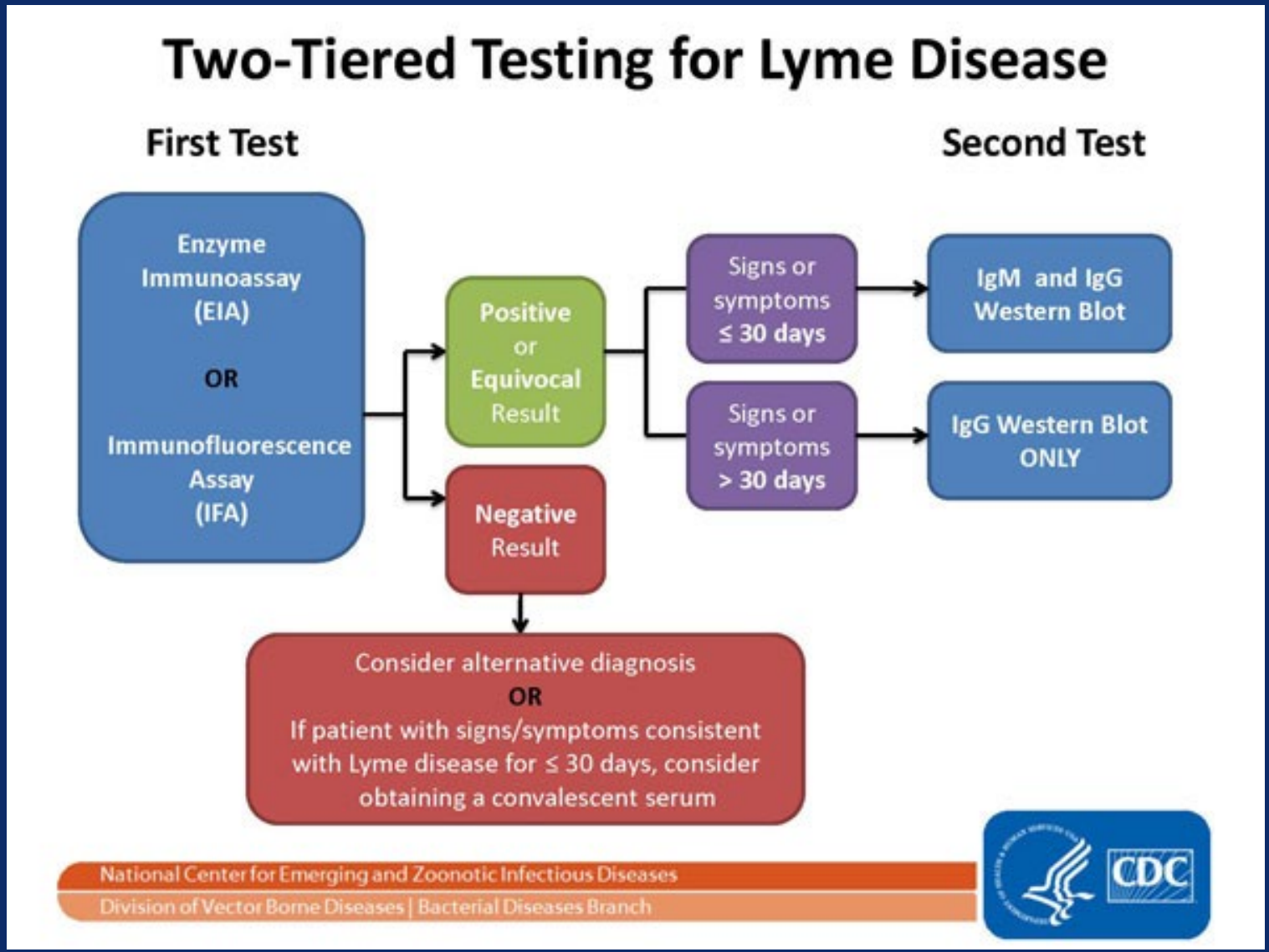
R. amblyommatis may cause RMSF serology positive, be aware!

Funding: DOM, SBU. PI: Marcos LA. Co-PI: Kim H.

LESSON 4

LYME DISEASE CAN LEAD TO A CHRONIC INFECTION

Serology


Two-Tiered Testing for Lyme Disease
First Test
Second Test
Enzyme Immunoassay (EIA)
OR
Immunofluorescence Assay (IFA)
Positive or Equivocal Result
Negative Result
Signs or symptoms ≤ 30 days
Signs or symptoms > 30 days
IgM and IgG Western Blot
IgG Western Blot ONLY
Consider alternative diagnosis
OR
If patient with signs/symptoms consistent with Lyme disease for ≤ 30 days, consider obtaining a convalescent serum
National Center for Emerging and Zoonotic Infectious Diseases
Division of Vector Borne Diseases | Bacterial Diseases Branch
CDC

AMERICAN SOCIETY FOR MICROBIOLOGY | Journal of Clinical Microbiology®

COMMENTARY

Revisiting the Lyme Disease Serodiagnostic Algorithm: the Momentum Gathers

Adriana R. Marques[a]

TABLE 1 Sensitivity of MTT algorithm versus that of the STT algorithm in acute-phase samples from patients with erythema migrans

	MTT algorithm[a]		STT algorithm[b]	
Reference(s) (no.)	Test program[c]	Acute-phase EM sensitivity (%)	Test program	Acute-phase EM sensitivity (%)
Branda et al. (16)	WCS Vidas f/b C6 EIA	52.6	WCS Vidas f/b WB	42.1
Branda et al. (27)	WCS W EIA f/b C6 EIA	38.2	C6 EIA f/b WB	36.4
	WCS W EIA f/b VlsE CLIA	36.4	VlsE CLIA f/b WB	34.5
	VlsE CLIA f/b C6 EIA	54.5	WCS W f/b WB	25.4
Molins et al. (28)[d]	WCS Vidas f/b C6 EIA	50	WCS Vidas f/b WB	47.5
Molins et al. (29)[d]	WCS Vidas f/b C6 EIA	50	LYM/G Vidas f/b WB	42.5
	LYM/LYG f/b C6 EIA	55	WCS Vidas f/b WB	47.5
Pegalajar-Jurado et al. (4)[d]	WCS Captia f/b C6 EIA	55	WCS Captia f/b WB	50
	WCS Captia f/b VlsE CLIA	57.5	VlsE CLIA f/b WB	42.5
	VlsE CLIA f/b C6 EIA	50	C6 EIA f/b WB[e]	42.5
Wormser et al. (11, 25)	WCS EIA f/b C6 EIA[f]	58.4	C6 EIA f/b WB	37.6
			WCS f/b WB	38.3

MTT SENSITIVITY = 58%; STT SENSITIVITY = 45%

CLINICAL AND VACCINE IMMUNOLOGY, May 2011, p. 851–859 Vol. 18, No. 5
1556-6811/11/$12.00 doi:10.1128/CVI.00409-10

Multiplex Immunoassay for Lyme Disease Using VlsE1-IgG and pepC10-IgM Antibodies: Improving Test Performance through Bioinformatics[▽]

TABLE 3. Sensitivity of Western blotting versus multiplex assay by disease stage

Stage (no. of cases)	Sensitivity (no. [%] of positive samples)				
	IgG blotting	IgM blotting	Either IgG or IgM blotting	2-Tier blotting[a]	Multiplex assay[b]
Early acute phase (79)	6 (7.6)	29 (36.7)	31 (39.2)	31 (39.2)	36 (45.7)
Early convalescent phase (82)	17 (20.7)	60 (73.2)	63 (76.8)	56 (68.3)	73 (89.0)[c]
Stages II and III combined[d] (47)	39 (83.0)	32 (68.1)	45 (95.7)	43 (91.5)	47 (100)
Neuro/carditis[e] (stage II) (18)	11 (61.1)	13 (72.2)	16 (88.8)	15 (83.3)	18 (100)
Arthritis (stage III) (29)	28 (96.6)	19 (65.5)	29 (100)	28 (96.6)	29 (100)
Posttreatment[f] stages II and III (16)	13 (81.25)	4 (25)	13 (81.3)	13 (81.3)	16 (100)
Posttreatment[f] stage I (18)	4 (22.2)	9 (50.0)	10 (55.6)	4 (22.2)	11 (61.1)[g]

- EM: history and visual inspection of the skin lesion. Laboratory testing not needed or recommended.
- Tests are not sensitive in very early disease
- Avoid overtesting for Lyme for unspecific chronic symptoms (especially avoid IgM testing)

	June '21	Dec '21	Mar '22	Apr '22	Oct '22	Jul '23	Jan '24	Feb '24	Aug '24
Lyme AB Screen (Quest)	4.55			4.06	3.49	2.94	3.97	3.97	3.43
Lyme VISE IgG/IgM Ab (Northwell Labs)		4.33 Positive A							↗ also Lyme AB Screen 1.18?
Lyme IgG Ab chemiluminescent Immunoassay (Northwell Labs) (Quest)		7.17 Positive A							1.02 LY?
Lyme IgM Ab chemiluminescent Immunoassay (Northwell Labs) (Quest)		3.09 Positive A							<.90 (assume its 0.1<)
Lyme Disease antibodies (IGG/IGM) Immunoblot (Quest) * reflects reactive Bands	IGG Blot Neg. IGM Blot Neg. 58 kD IGG 23 kD IGM			IGG Blot Neg. IGM Blot Neg. 23 kD IGM	IGG Blot Neg. IGM Blot Neg. 23 kD IGM	IGG Blot Neg. IGM Blot Neg. 58 kD IGG 23 kD IGM	IGG Blot Neg. IGM Blot Neg. 58 kD IGG 23 kD IGM	IGG Blot Neg. IGM Blot Neg. 58 kD IGG 23 kD IGM	IGG Blot Neg. IGM Blot Neg. 58 kD IGG 23 kD IGM
AST (average 27.5 since 2015) - June 2021	23		36	26		43	40	27	28
ALT (avege 23 since 2015) - June 2021	17		33	26		55	49	31	39
Doxycycline 100mg (100 mg per pill; 42 pills/21 days)		* Jul '21	* Dec '21				* Feb '24		

TREATMENT

- **Early, localized and disseminated, Lyme disease**
  - EM: doxycycline, 100 mg BID for 10 days
  - Meningitis or Neuropathy: Ceftriaxone 2gr IV daily or cefotaxime 2gr IV q8h or doxycycline 100 mg BID for 14 -21 days
  - Cardiac disease: All above or cefuroxime 500mg PO BID x 14 days

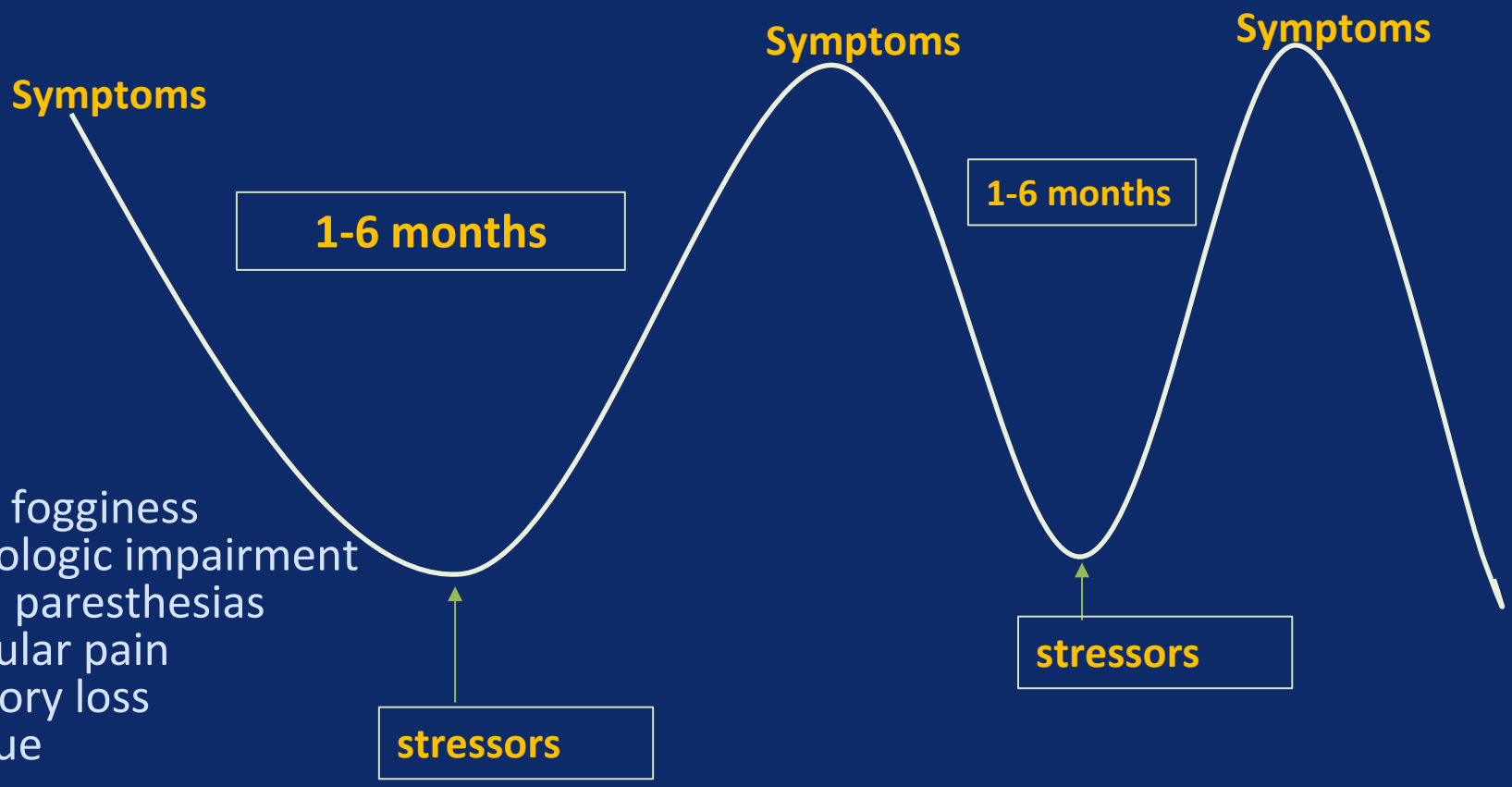
- **Late Lyme disease**
  - Arthritis: PO regimen for 28 days
  - Recurrent arthritis: IV ceftriaxone for 14-28 days (but refractory arthritis does not respond to ATB)
  - Neurological Lyme disease: IV regimen for 14-28 days

IDSA LYME GUIDELINES 2021

LESSON 5

POST TREATMENT LYME DISEASE SYNDROME

Chronic Symptoms on treated Lyme patients



Brain fogginess
Neurologic impairment
distal paresthesias
radicular pain
memory loss
Fatigue

Post Lyme disease syndrome

Renaissance School *of* Medicine
Stony Brook University

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 31, 2016 VOL. 374 NO. 13

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

Anneleen Berende, M.D., Hadewych J.M. ter Hofstede, M.D., Ph.D., Fidel J. Vos, M.D., Ph.D., Henriët van Middendorp, Ph.D., Michiel L. Vogelaar, M.Sc., Mirjam Tromp, Ph.D., Frank H. van den Hoogen, M.D., Ph.D., A. Rogier T. Donders, Ph.D., Andrea W.M. Evers, Ph.D., and Bart Jan Kullberg, M.D., Ph.D.

Antibiotics don't improve symptoms for long term symptoms attributed to Lyme Disease.

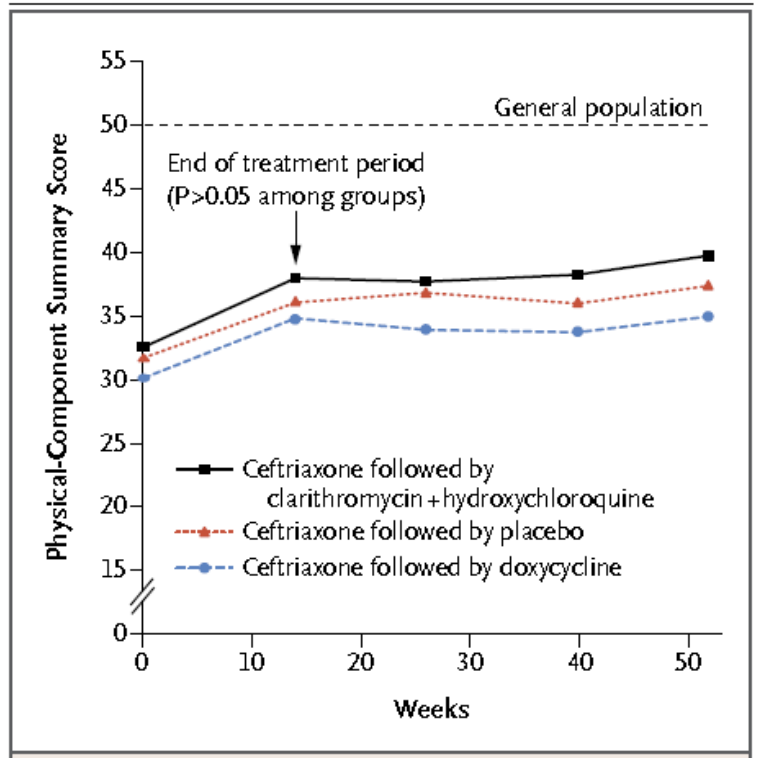


Figure 2. Physical-Component Summary Scores.

Randomized Controlled Trial > Neurology. 2019 Mar 26;92(13):e1447-e1455.
doi: 10.1212/WNL.0000000000007186. Epub 2019 Feb 22.

Effect of prolonged antibiotic treatment on cognition in patients with Lyme borreliosis

Anneleen Berende [1], Hadewych J M Ter Hofstede [2], Fidel J Vos [2], Michiel L Vogelaar [2],

Methods: Data were collected during the Persistent Lyme Empiric Antibiotic Study Europe (PLEASE) trial, a randomized, placebo-controlled study. Study participants passed performance-validity testing

Cognitive performance does not improve with longer antibiotic treatment compared to shorter-term treatment in patients with persistent symptoms attributed to Lyme borreliosis.

Conclusions: A 2-week treatment with ceftriaxone followed by a 12-week regimen of doxycycline or clarithromycin/hydroxychloroquine did not lead to better cognitive performance compared to a 2-week regimen of ceftriaxone in patients with Lyme disease-attributed persistent symptoms.

LESSON 6

NOT EVERYTHING IS LYME, WE HAVE 10 MORE TICK BORNE DISEASES IN NY

Annals of Internal Medicine

ORIGINAL RESEARCH

Borrelia miyamotoi Disease in the Northeastern United States

A Case Series

Philip J. Molloy, MD; Sam R. Telford III, ScD; Hanumara Ram Chowdri, MD; Timothy J. Lepore, MD; Joseph L. Gugliotta, MD; Karen E. Weeks, BS; Mary Ellen Hewins, BS; Heidi K. Goethert, ScD; and Victor P. Berardi

- Relapsing fever
- First case in the US, 2013
- *B. miyamotoi* may cause chronic meningitis in immunocompromised host
- *B. miyamotoi* can cause a summer illness without a rash
  - Clinical syndrome is different from Lyme disease

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)

Marcos et al. Ann Clin Microbiol Antimicrob (2020) 19:22
https://doi.org/10.1186/s12941-020-00364-0

Annals of Clinical Microbiology and Antimicrobials

SHORT REPORT Open Access

Presence of *Borrelia miyamotoi* infection in a highly endemic area of Lyme disease

Table 1 Demographics, clinical manifestations and laboratory results on patients with *Borrelia miyamotoi* PCR positive in the blood

Case	Age Gender	Co-infections	Clinical manifestations	Laboratory findings					
				WBC (/mm^3)	Hb (g/dL)	Platelets (/mm^3)	Creatinine (mg/dL)	AST (IU/L)	ALT (IU/L)
1	90/M	Negative	Fatigue, vomiting, fevers	4100 (90% N)	9.7	91,000	1.46	74	46
2	22/M	Negative	Headaches, fevers, abdominal pain, arthralgia	3200 (88% N)	14.7	99,000	0.8	73	117
3	26/M	Negative	Fevers, diarrhea, hematuria	5400 (40%N, 30%B)	16.3	127,000	1.05	51	68
4	74/M	Negative	Fatigue, arthralgia	4600 (63% N)	14.2	154,000	0.7	21	28
5	32/M	Negative	Fevers, muscle pain, fatigue	3000 (45%N, 9%B)	15.6	166,000	1.0	98	65
6	74/M	Negative	Fevers, myalgia, chills, vomiting	6800 (N37%, B17%)	15.6	51,000	3.1	212	165
7	68/M	Negative	Fever, myalgia, arthralgia, fatigue	Unknown	Unknown	Unknown	Unknown	20	18
8	67/F	Negative	Fevers, arthralgias, mylagias	5500 (N 64%)	14.7	260,000	0.8	33	23
9	60/M	Unknown	Unknown Fevers, arthralgia, myalgias, fatigue	7100 (N 60%)	14.8	Unknown	Unknown	Unknown	Unknown

Heartland Virus Transmission, Suffolk County, New York, USA

Alan P. Dupuis II,[1] Melissa A. Prusinski,[1] Collin O'Connor, Joseph G. Maffei, Kiet A. Ngo, Cheri A. Koetzner, Michael P. Santoriello, Christopher L. Romano, Guang Xu, Fumiko Ribbe, Scott R. Campbell, Stephen M. Rich, P. Bryon Backenson, Laura D. Kramer, Alexander T. Ciota

Heartland virus is here

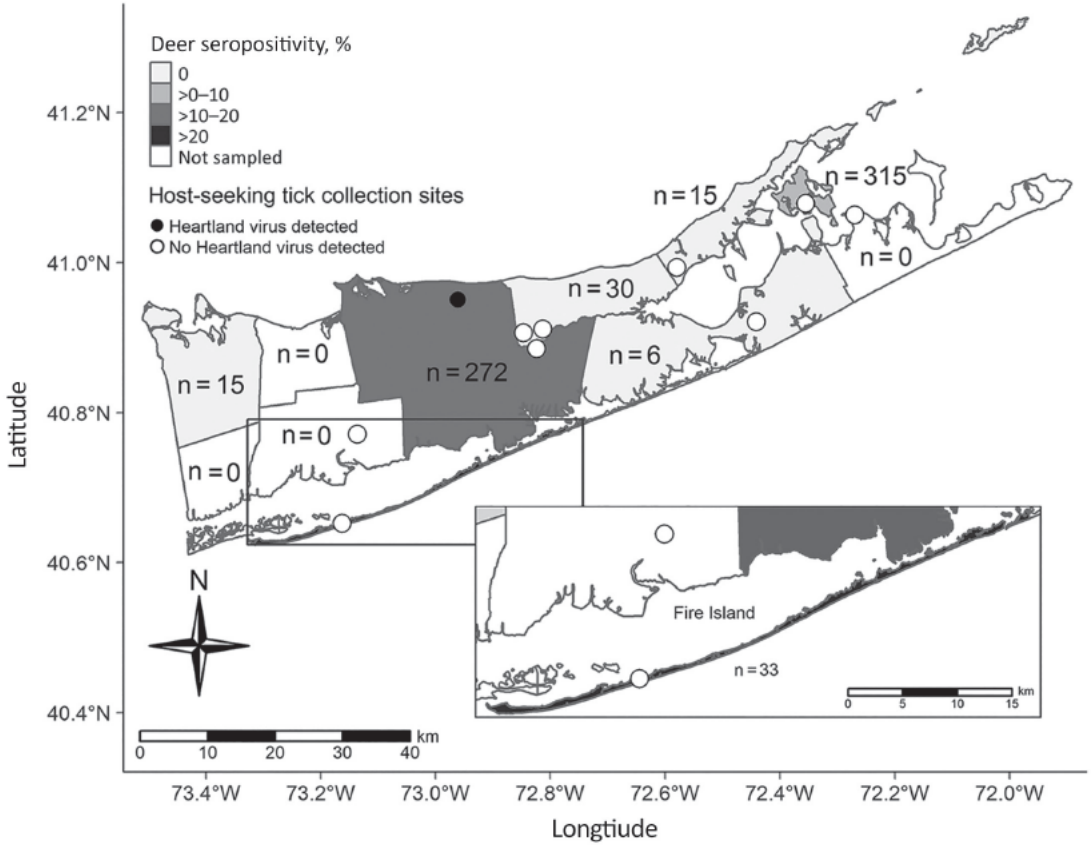


Figure 1. Tick collection sites in study of heartland virus transmission, Suffolk County, New York, USA. Numbers within townships indicate sample size of deer tested for neutralizing antibody.

U.S Data of TBD 1987-2013

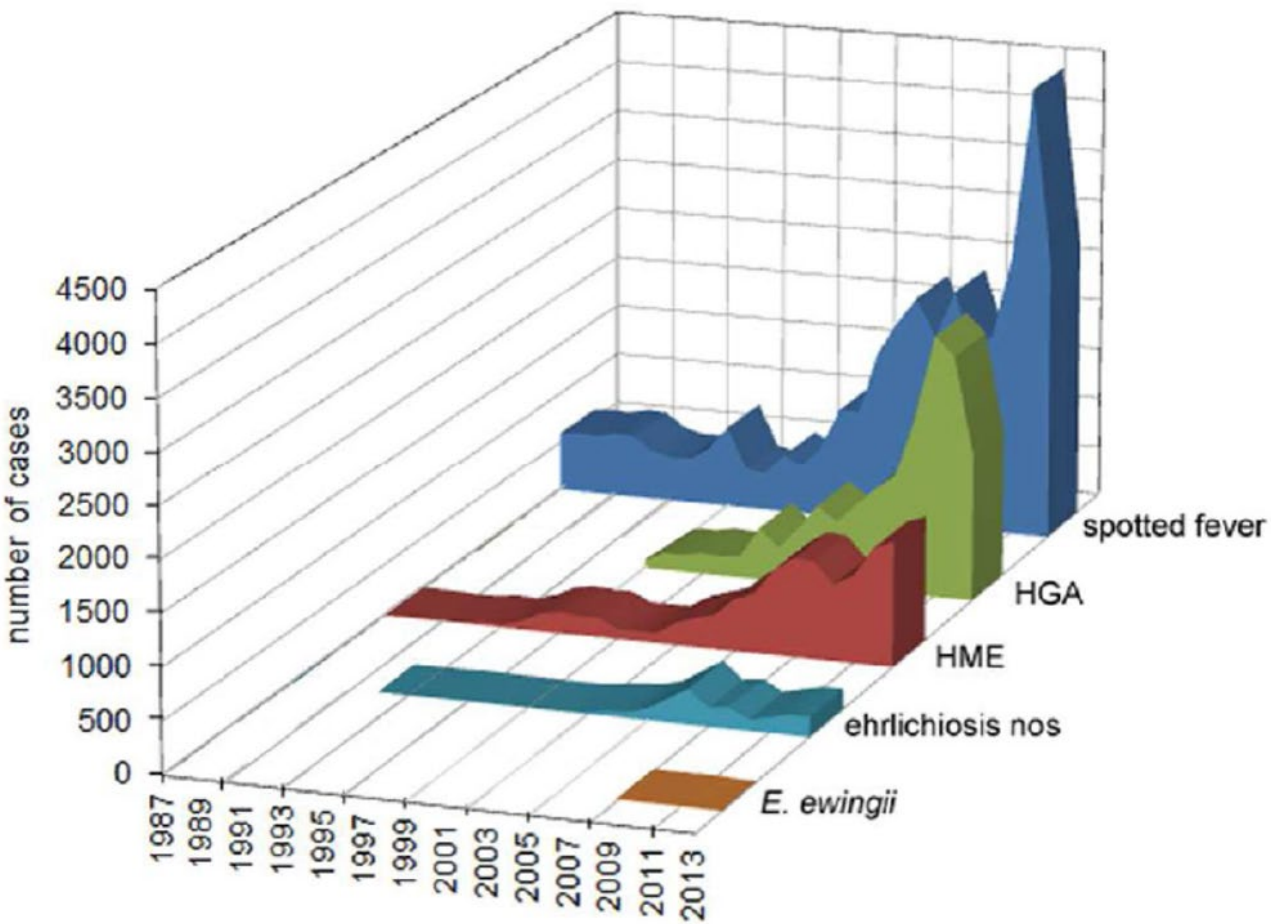


Figure 1

VECTOR-BORNE AND ZOONOTIC DISEASES
Volume 8, Number 5, 2008

DOI: 10.1089/vbz.2007.0271

Tick-Borne Diseases in North Carolina: Is "*Rickettsia amblyommii*" a Possible Cause of Rickettsiosis Reported as Rocky Mountain Spotted Fever?

TABLE 3. RESULTS OF DIAGNOSTIC TESTS OF PROBABLE RMSF PATIENTS. VALUES REPRESENT THE RECIPROCALS OF END-POINT DILUTIONS GIVING STRONG FLUORESCENCE IN IFA TESTS

	Sera drawn (days after onset)		*Rickettsia rickettsii antigens*				*"Rickettsia amblyommii" antigens*			
			IgM (mu)		*IgG (gamma)*		*IgM (mu)*		*IgG (gamma)*	
Patient	*acute*	*conv.*	*acute*	*conv.*	*acute*	*conv.*	*acute*	*conv.*	*acute*	*conv.*
1	0	24	28	128	<16	16	512	256	128	64
2	5	59	28	128	64	32	256	128	32	64
3	1	51	28	128	32	32	128	128	256	256
4	9	64	64	64	16	16	16	256	256	1024
5	1	14	28	128	16	64	256	256	<16	512
6	21	46	32	32	64	64	128	64	<16	512

RMSF IgG 1:64 is due to Ricketssia amblyommii?

TICK BORNE DISEASES

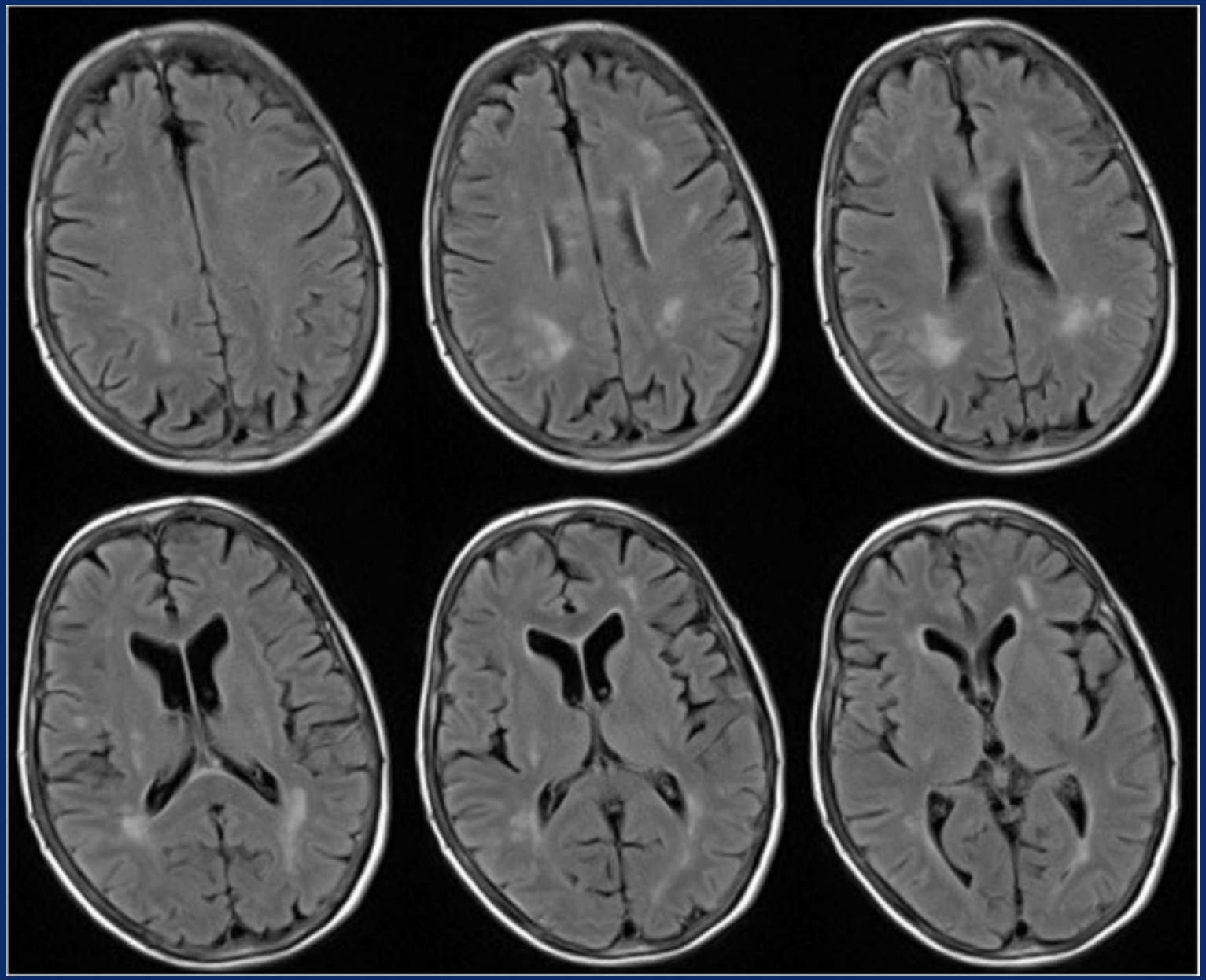
TICK BORNE DISEASES	Human Monocytic Ehrlichiosis (HME)	Human Granulocytic Anaplasmosis (HGA)	Babesiosis
Organism	*Ehrlichia chaffeensis*	*Anaplasma phagocytophilum*	*Babesia microti*
Vector	Lone star tick (Amblyomma americanum)	Deer tick (Ixodes scapularis)	Deer tick (Ixodes scapularis)
Clinical Manifestations	Fever, headache, rash, leukopenia, thrombocytopenia (95%) Transaminitis	Fever, headache, leukopenia, thrombocytopenia (70%) Transaminitis No rash	Thrombocytopenia (95%) Mild transaminitis Mild jaundice Dark urine Splenomegaly (pain)
Diagnosis	PCR in blood (test of choice) Convalescent titers (IgM is negative during first week). A titer above 256 is indicative of recent infection.	PCR in blood Convalescent titers 4-fold higher titers	Blood smear microscopy x 3 PCR in blood Convalescent titers
Treatment	Doxycycline 100mg PO BID x 7-14 days	Doxycycline 100mg PO BID x 7-14 days	Atovaquone 750mg PO BID and azithromycin (500mg loading dose, 250mg PO daily) x 7-10 days
Complications	Myocarditis, cholecystitis, mortality 2-5%	Small bowel perforation, mortatlity 1%	Severe anemia, acute respiratory distress syndrome, relapsing disease on immunocompromised patients

POWASSAN VIRUS

POWASSAN VIRUS INFECTION

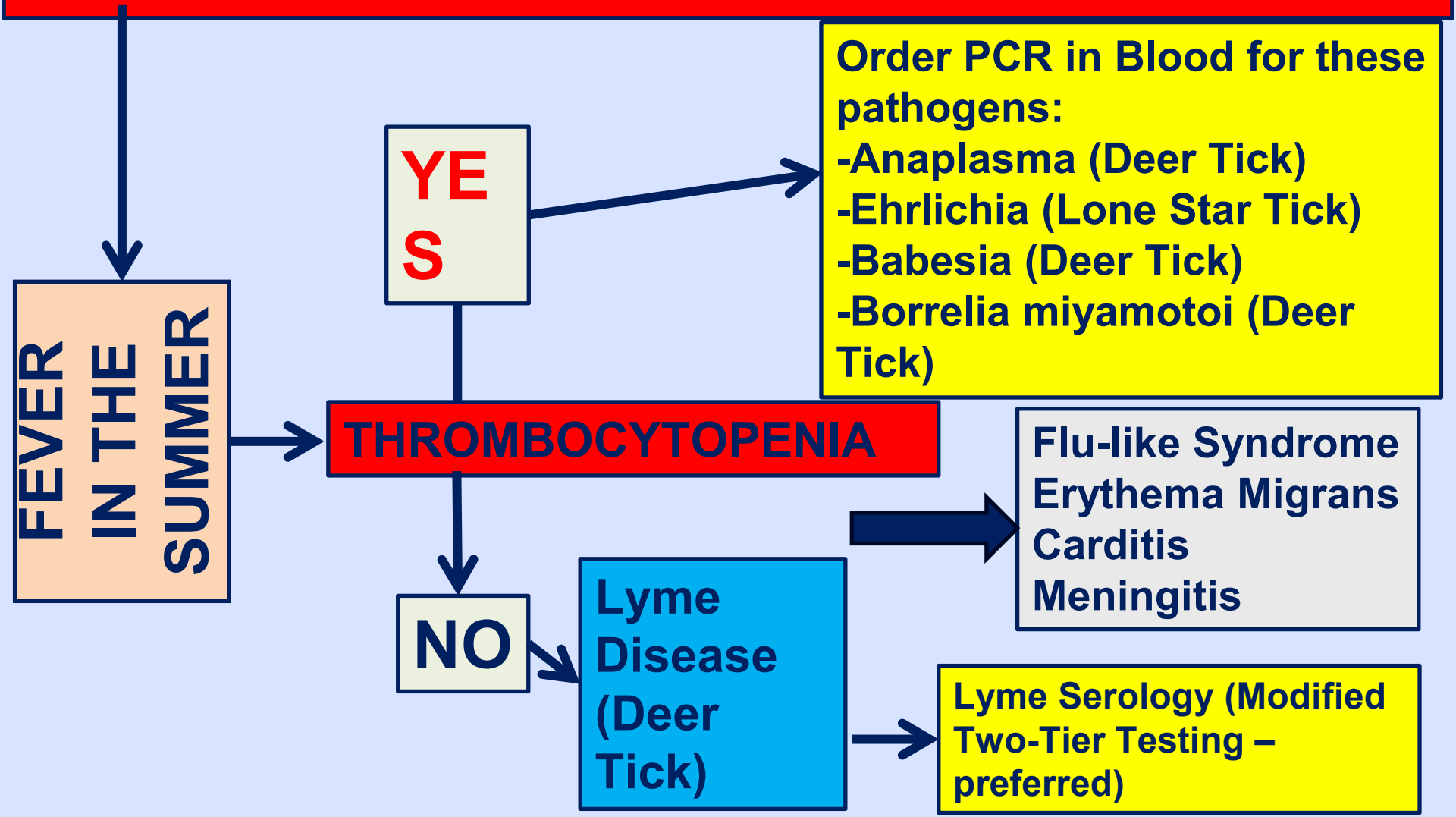
	1	2	3	4
Age **Gender**	70 y/o Man	53 y/o Woman	25 y/o Man	66 y/o Man
Fever **AMS**	104.7 F Yes	103 F Yes	101.3 F Yes	Afebrile Yes
CSF	40 white blood cells (WBCs)/mm^3 (normal: <4/mm^3) (87% lymphocytes) with elevated protein (96 mg/dL; normal: 20--50 mg/dL)	148 WBCs/mm^3 (46% neutrophils, 40% lymphocytes).	920 WBCs/mm^3 (74% lymphocytes) with elevated protein (77 mg/dL)	54 WBCs/mm^3 (95% lymphocytes) and elevated protein (67 mg/dL)
Serology	POW virus-specific IgM; neutralizing antibody (1:640 titer)	POW virus-specific IgM and neutralizing antibody (1:640 titer)	positive for POW virus-specific IgM antibody. The serum sample also had neutralizing antibody (1:80 titer) to POW virus	POW virus-specific IgM and neutralizing antibody (1:640 titer)
Outcome	unable to move his left arm or leg after three months	Nine months after onset of symptoms, she was walking and had regained her strength, but the ophthalmoplegia continued.	When discharged home 44 days later, the patient required assistance to stand and perform daily activities	When discharged home 11 days later, he could walk but had cognitive difficulties, including severe memory lapses.

Outbreak of Powassan Encephalitis --- Maine and Vermont, 1999—2001. MMWR 2001.



Brain MRI: T2/FLAIR white matter hyperintensity involving the deep and superficial periventricular white matter and corpus callosum

ALGORITHM FOR TICK-BORNE DISEASES IN NEW YORK



LYME ARTHRITIS USUALLY PRESENTS IN THE FALL OR WINTER

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1. NY Senate (2018-2019)
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