

Sun, Fun and Ticks: A Pre-Summer Lyme Disease Refresher



PHN Grand Rounds

5/25/23

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Pediatric Health Network



Disclosures

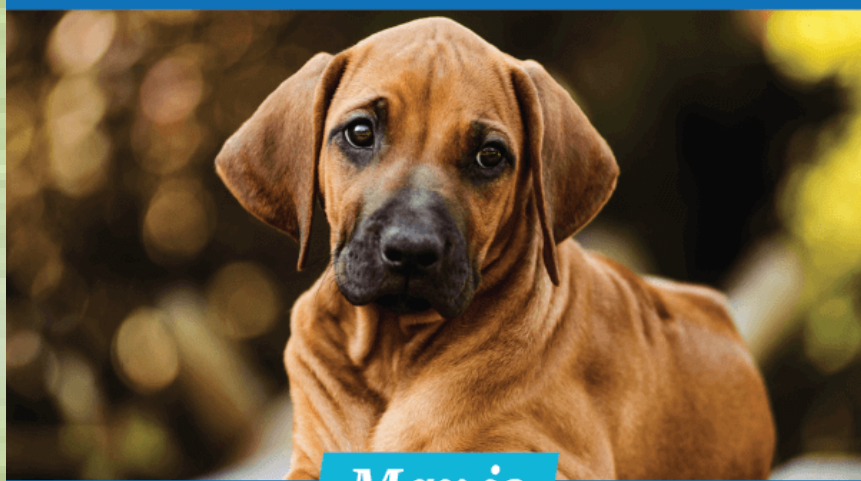
PI for PfizerVLA15 Lyme Vaccine Pediatric Clinical Safety Trial; my institution receives funding for conducting this trial

PI for multicenter, NIH funded Lyme meningitis comparative effectiveness study; my institution receives funding for this trial

Objectives

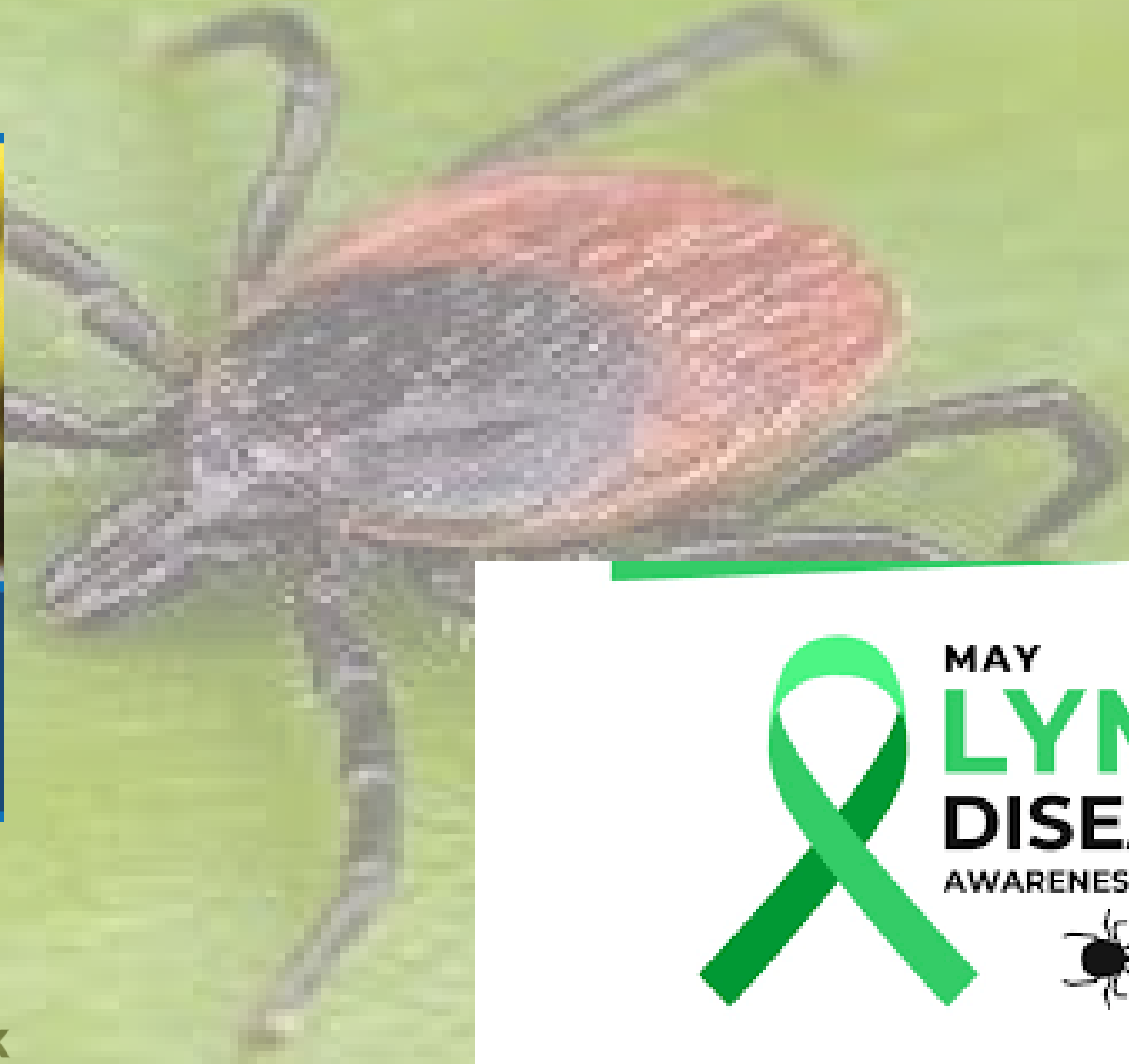
- Review epidemiology and recent up-**tick** in arthropod-borne illnesses
- Match Clinical Presentations of Lyme Disease...
 - Local, Early and Late (and a word about Post)
- ...and laboratory findings!
 - A tale of two assays
- Discuss treatment updates...
 - Doxy doxy doxy
- And future developments for lyme disease management and prevention
 - Lyme Vaccine
 - Lyme Meningitis Comparative Effectiveness Study

May is Lyme Disease Awareness Month



May is

**LYME DISEASE
AWARENESS MONTH**



Pediatric **Health** Network



Wide World of Ticks



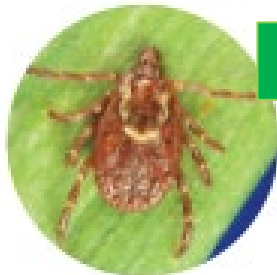
Ixodes scapularis- Blacklegged Tick

Lyme, Anaplasmosis,
Babesiosis, Ehrlichiosis,
Powassan Virus



Ixodes cookei-
Groundhog tick

Powassan Virus



Dermacentor-
American Dog Tick

Tularemia



Amblyomma americanum-
Lone Star Tick

Ehrlichiosis, Tularemia,
Heartland Virus, Bourbon Virus,
STARI, alpha-gal syndrome

Rickettsiosis

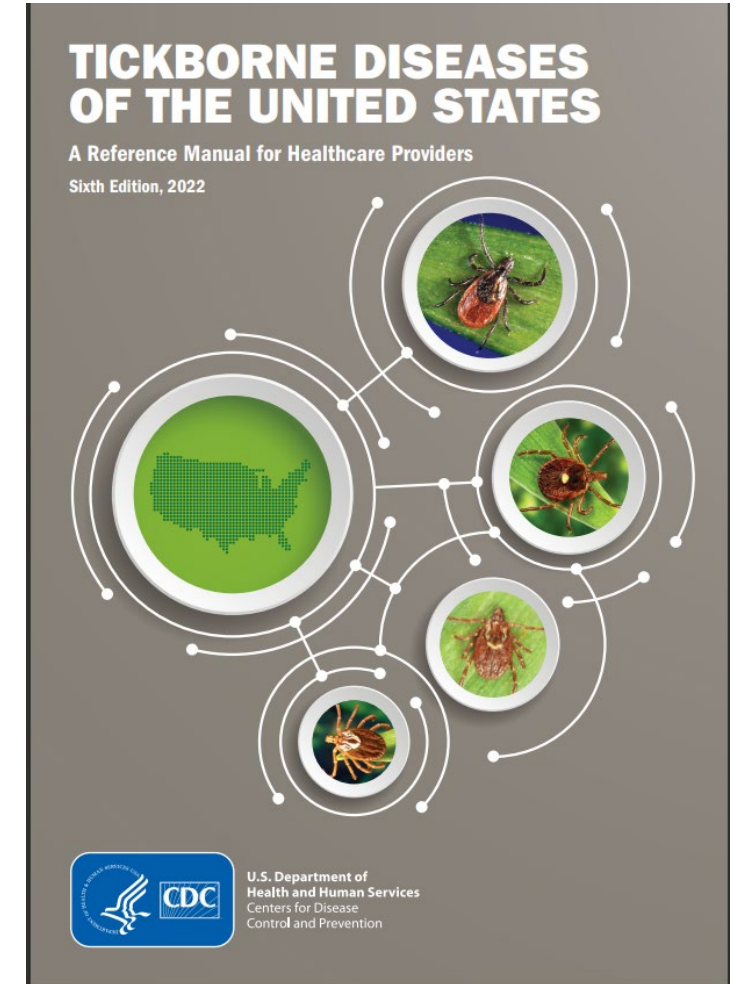


Amblyomma maculatum-
Gulf Coast Tick

RMSF

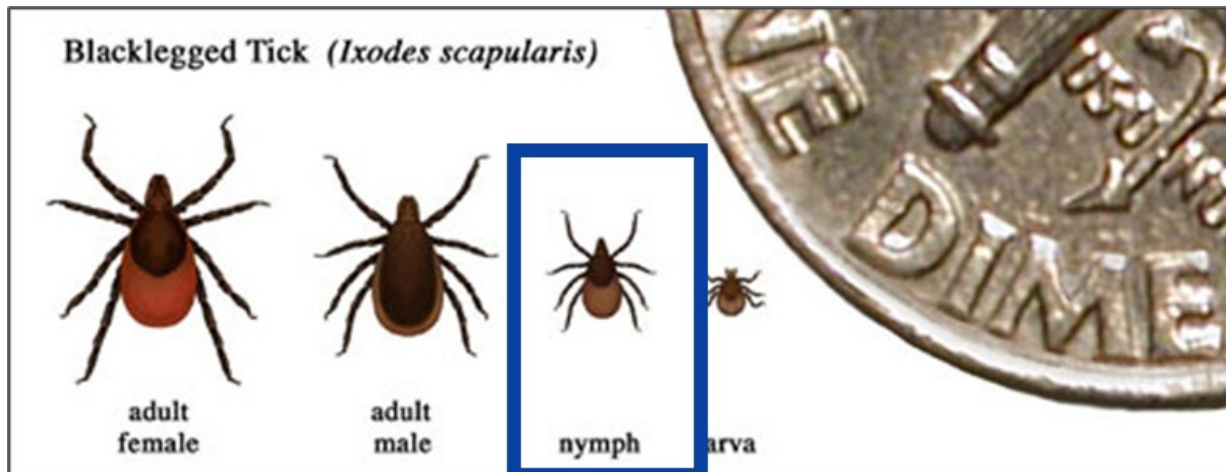


Rhipicephalus sanguineus-
Brown Dog Tick



<https://www.cdc.gov/ticks/tickbornediseases/TickborneDiseases-P.pdf>

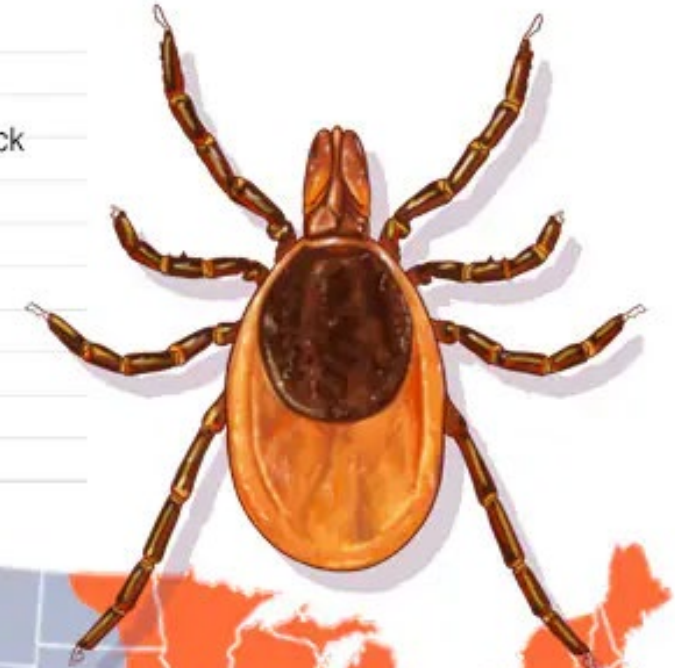
Ixodes scapularis



Types of ticks

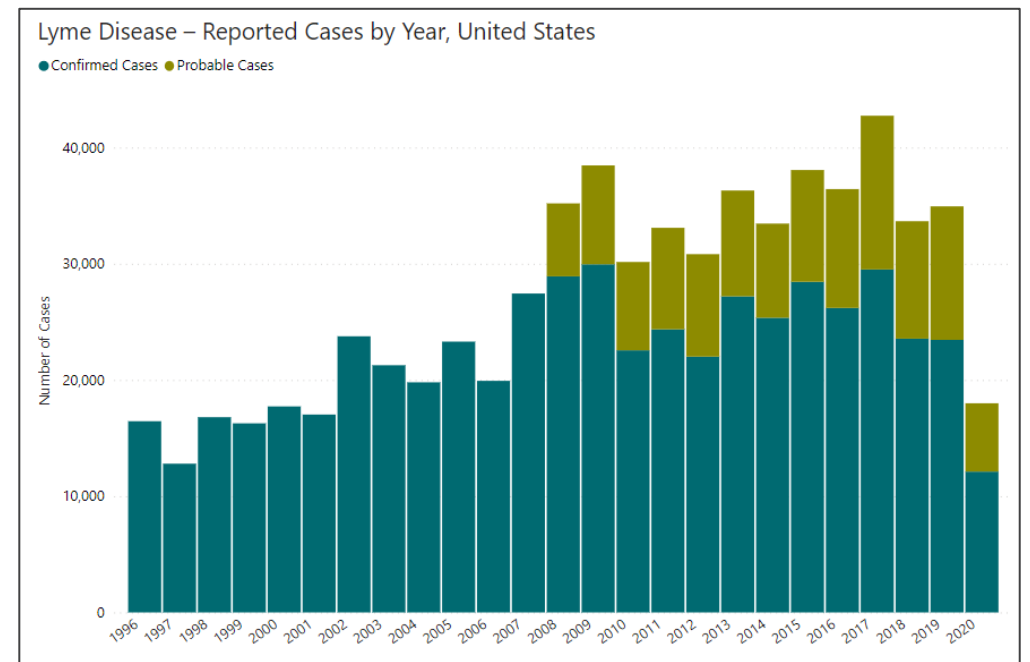
Blacklegged tick,
also known as deer tick
(female)

Millimeters



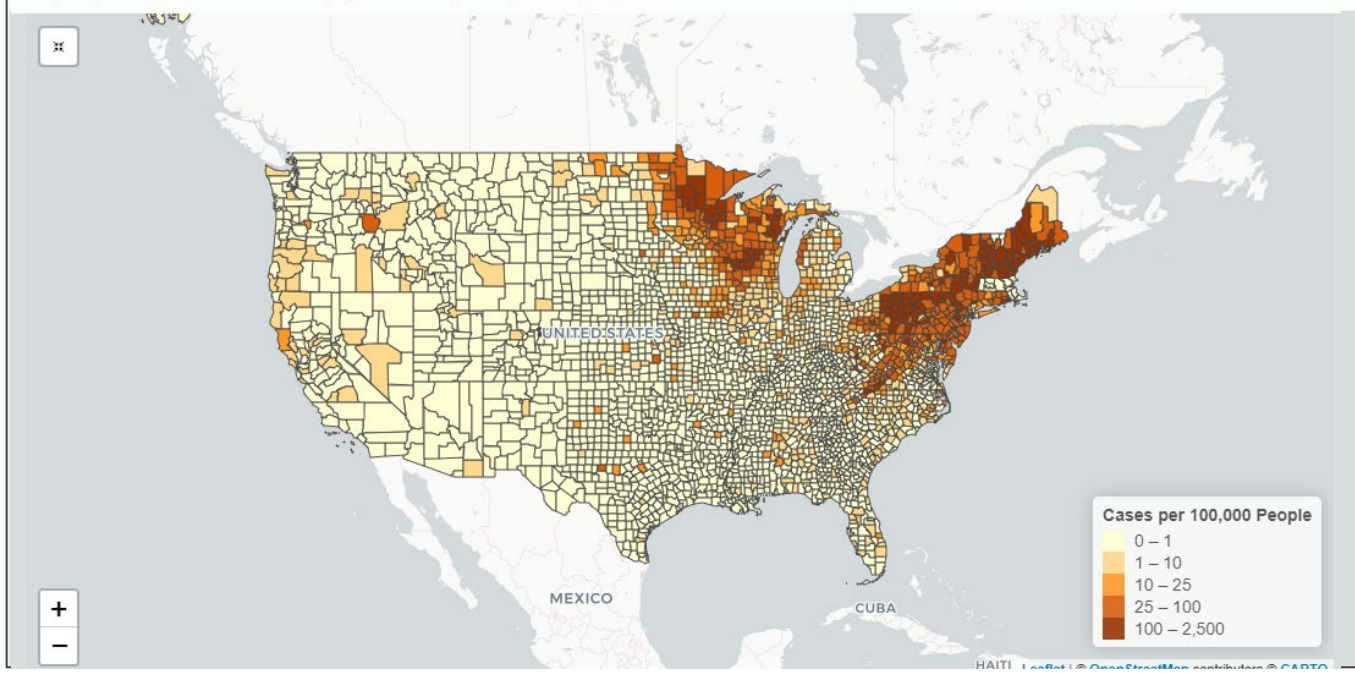
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Lyme Disease Epidemiology-CDC.gov



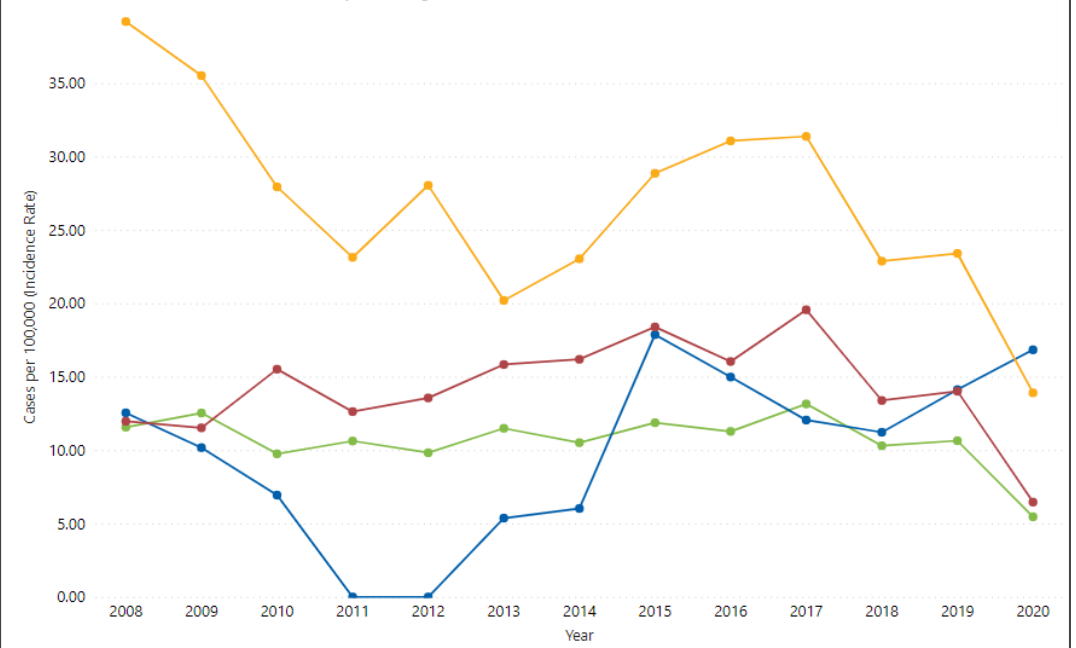
Johns Hopkins Lyme Tracker Dashboard

Map of Lyme Disease Incidence Rates (Reported Cases per 100,000 People)



Lyme Disease – Rates by Year, United States

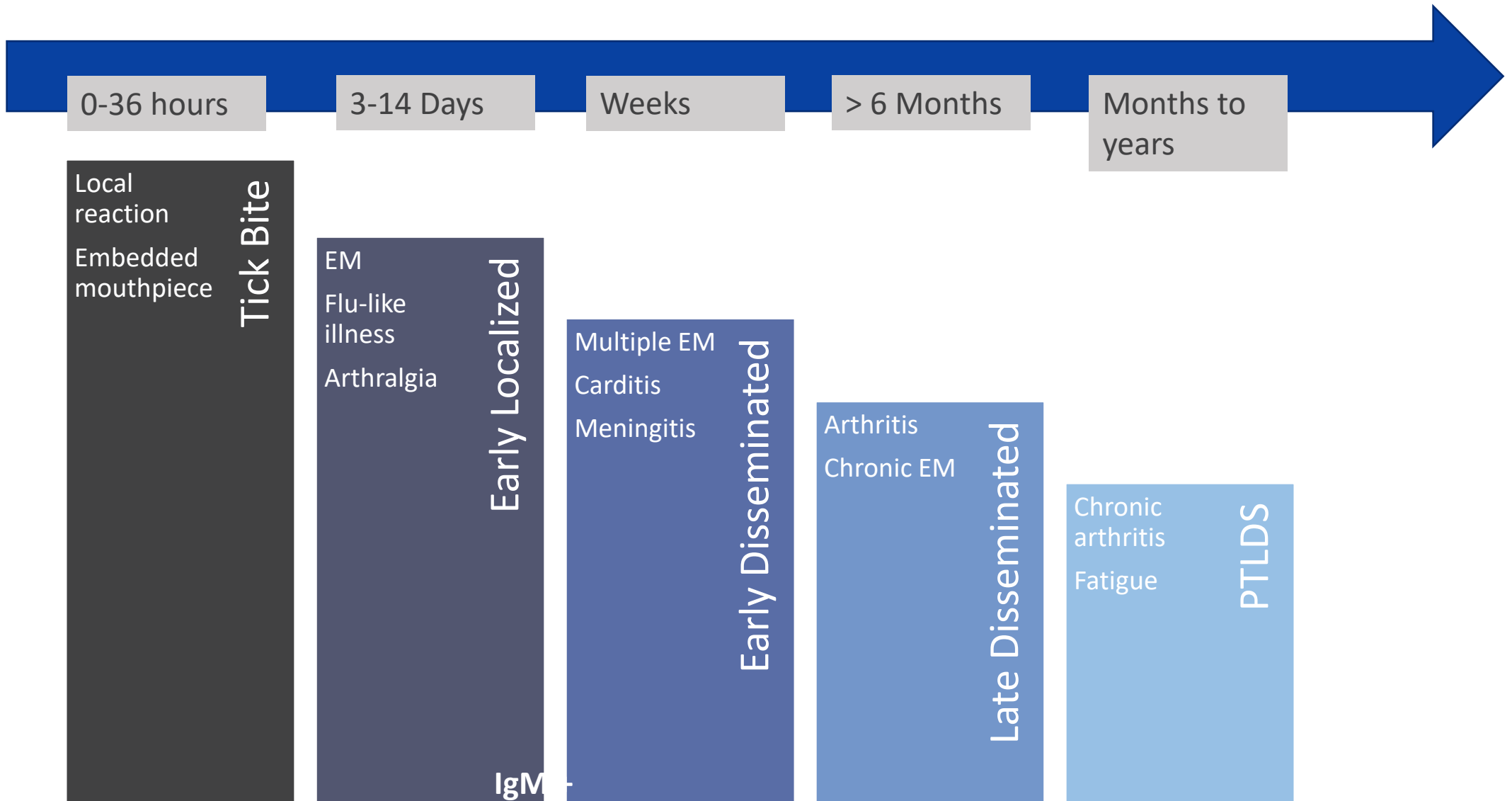
State U.S. Total District of Columbia Maryland Virginia



Lyme Disease Clinical Presentations

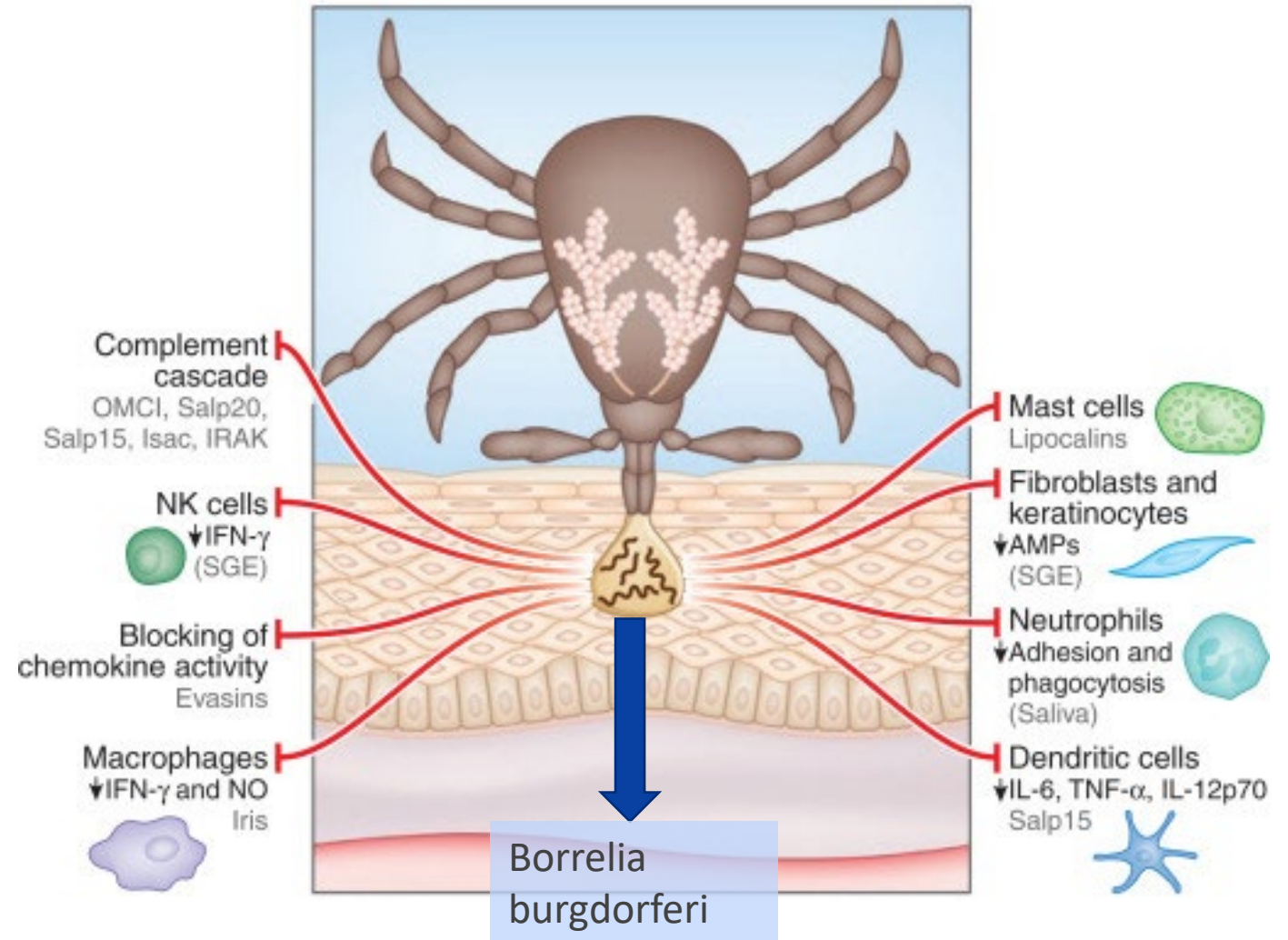


LD Clinical Presentation Timeline



Ixodes Tick Bite

- Tick saliva injected during blood meal
 - Can last up to 7 days
- Immunosuppressive
- Anesthetic
- Can develop allergic reaction



Erythema migrans

Early
Localized



Centers for Disease Control and Prevention, <http://phil.cdc.gov/phil/>

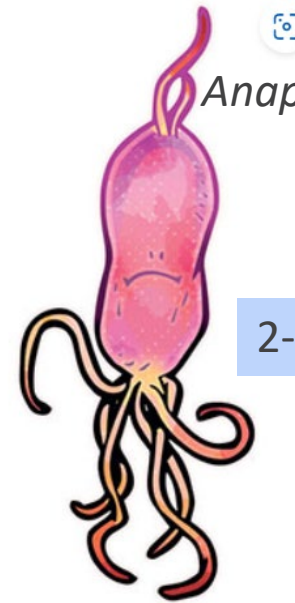
Early Localized- Erythema Migrans

- Local skin reaction to spirochete
- Variable appearance
- Site of tick bite
 - >72 hour blood meal required
- Affects 2/3 children with LD
- Slowly expands*
- Last 1-4 weeks*
- May disseminate *



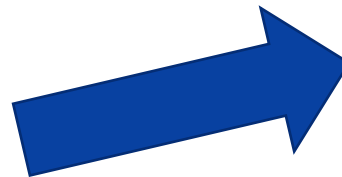
Early “localized” Lyme Disease...and co-infection

- “Influenza like illness”:
 - Up to 65% LD patient in US
 - Low grade fever
 - Myalgias
 - Neck stiffness
 - Headache
- Basic Laboratory Abnormalities
 - Transaminitis
 - Lymphopenia



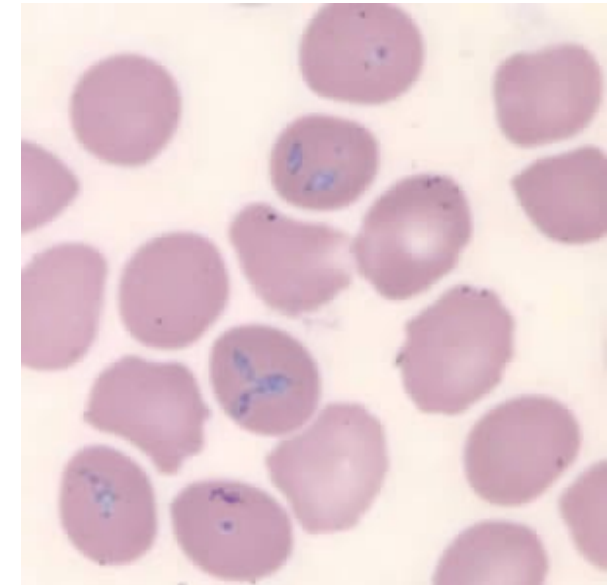
Anaplasma phagocytophilum

2-12% percent with co-infection



Leukopenia
Neutropenia
Thrombocytopenia
Anemia

Babesia microti



Early Disseminated

- Multiple EM Rash
- Early Lyme Neuroborreliosis (10-20%)
 - Meningitis
 - Cranial neuritis
 - Radiculopathy
- Carditis (1-16%)



Lyme Neuroborreliosis (CNS or PNS Lyme)

- Lyme Meningitis (2%)
 - Modest CSF pleocytosis (median- 160 cells/mL)
 - Elevated protein, normal glucose
 - Lymphocytic/monocytic
 - Indolent (>1 week symptoms)+/- LRFP (70%)
- Cranial Neuritis (Facial Nerve Palsy) (5%)
 - Resolves after months
- Radiculopathy (rare)
- Encephalopathy (rare)



Lyme Carditis (Early Disseminated)

- Variable incidence reported (1-16%)
- Costello et al
 - 207 children with early disseminated LD
 - 33 with carditis (15.9%)
 - 4 with depressed systolic function
 - 14 with heart block
 - 9 with complete heart block
 - Risk factors for carditis
 - **Age > 10**
 - **With arthralgias or cardiopulmonary symptoms**
 - Rhythms normalized within 3 days of antibiotics



Consider screening ECG!

Late Disseminated

Arthritis

- 50-60% of UNTREATED patients (↑children)
- Intermittent, recurrent joint swelling and pain
- Pauciarticular (knees)
- More “mild” than septic arthritis
 - Lower ESR, CRP, Synovial WBC and neutrophil %
 - Less likely to have high fever
- 10% require >1 course of antibiotic treatment
- 1-3% develop refractory inflammation



Thompson et al. Pediatrics. 2009.

Post Treatment Lyme Disease Syndrome (PTLDS)

- Post Infectious Syndrome
- Under researched chronic illness
- Etiology under investigation, possibly autoimmune
- **Cognitive dysfunction (“brain fog”)**
- Fatigue
- Pain (including joints)
- Long term antibiotics NOT effective and have potential for harm

Diagnostics

Standard Two-Tier Testing

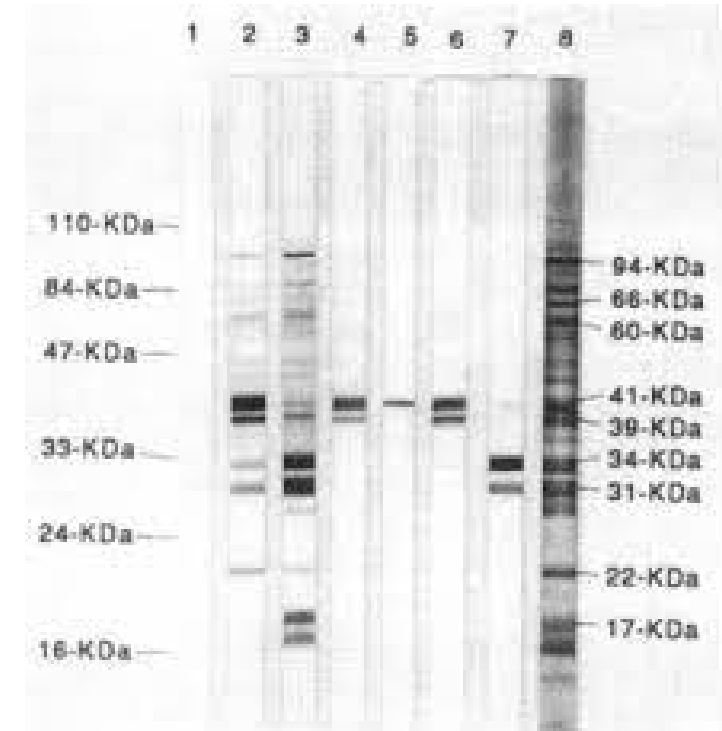
- Total Lyme IgG and IgM via EIA
- Reflex Western Blot (only if total elevated)
- ONLY Positive if:
 - **5/10 IgG bands positive**
 - **2/3 IgM bands positive**

Modified Two Tier Testing

- Two EIA tests
 - First IgM and IgG for VlsE/pepC10 antigens
 - Reflex whole cell sonicate antibody EIA

Borrelia PCR

- JOINT FLUID ONLY
- Poor sensitivity; adjunctive only



Lyme antibodies, especially IgG can remain positive FOR LIFE

Repeated positive **IgM** over time (esp if no EM rash) should prompt autoimmune evaluation

STTT Performance

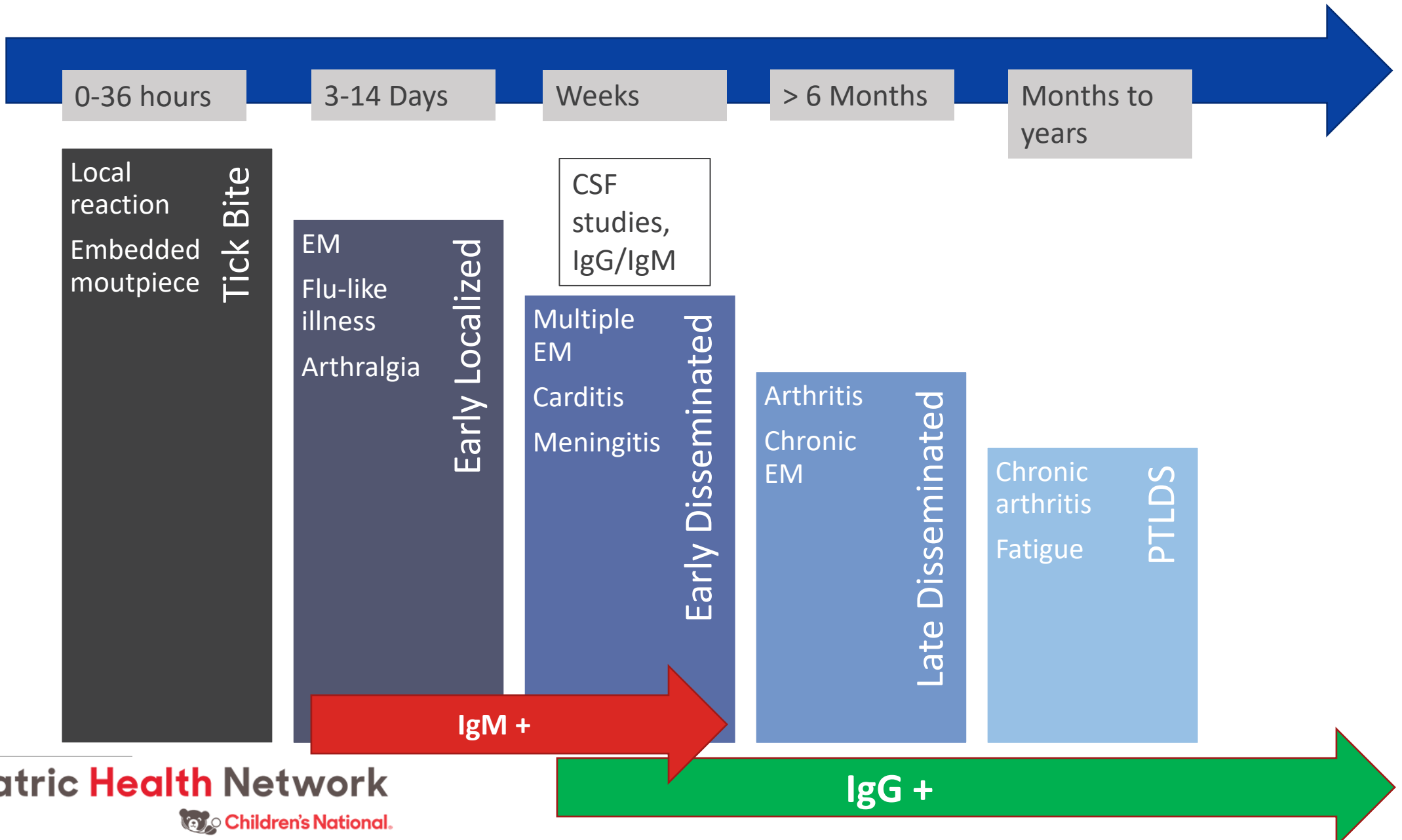
Stage of Lyme disease	Sensitivity (%)	Specificity (%)	Positive predictive value (%)	Negative predictive value (%)
Early localized				
Acute phase	17	98	75	26
Convalescent phase	53	98	90	83
Early disseminated				
Cardiac or neurologic manifestations	100	98	87	100
Multiple erythema migrans lesions	43	98	89	79
Late				
Arthritis or neurologic manifestations	100	98	94	100

NOTE: Data were calculated from 76 patients with erythema migrans and 86 healthy patients residing in a Lyme disease–endemic area. The accuracy may be overestimated because of the case-control design of the study.

Information from reference 26.

Steere AC, McHugh G, Damle N, Sikand VK. Prospective study of serologic tests for lyme disease. *Clin Infect Dis.* 2008;47(2):188-195.

LD Clinical Presentation Timeline



Treatment

IDSA Guidelines 2020

Clinical Infectious Diseases

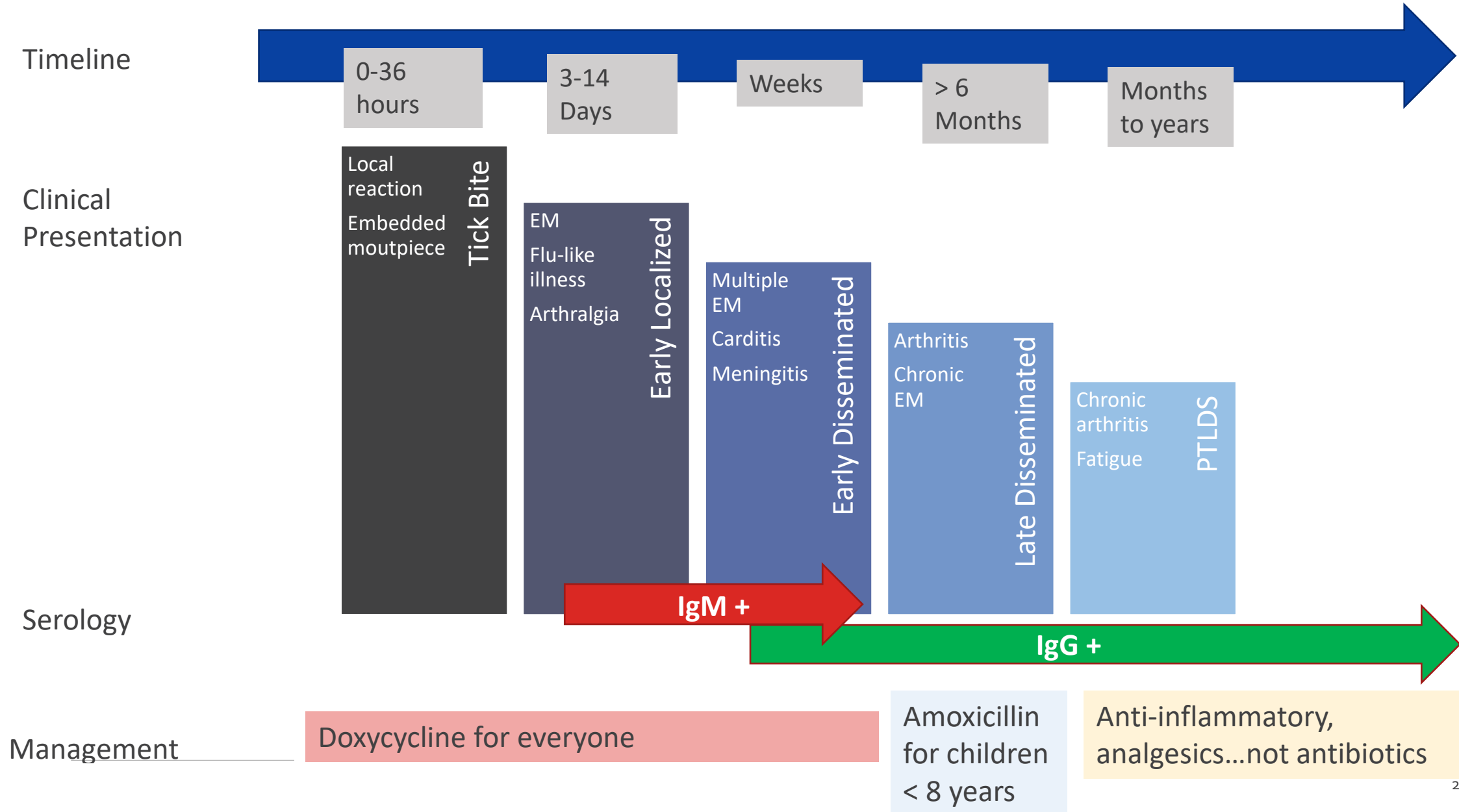
IDSA FEATURES



Clinical Practice Guidelines by the Infectious Diseases Society of America (IDSA), American Academy of Neurology (AAN), and American College of Rheumatology (ACR): 2020 Guidelines for the Prevention, Diagnosis and Treatment of Lyme Disease

Paul M. Lantos,¹ Jeffrey Rumbaugh,² Linda K. Bockenstedt,³ Yngve T. Falck-Ytter,⁴ Maria E. Aguero-Rosenfeld,⁵ Paul G. Auwaerter,⁶ Kelly Baldwin,⁷ Raveendhara R. Bannuru,⁸ Kiran K. Belani,⁹ William R. Bowie,¹⁰ John A. Branda,¹¹ David B. Clifford,¹² Francis J. DiMario Jr,¹³ John J. Halperin,¹⁴ Peter J. Krause,¹⁵ Valery Lavergne,¹⁶ Matthew H. Liang,¹⁷ H. Cody Meissner,⁸ Lise E. Nigrovic,¹⁸ James (Jay) J. Nocton,¹⁹ Mikala C. Osani,⁸ Amy A. Pruitt,²⁰ Jane Rips,²¹ Lynda E. Rosenfeld,³ Margot L. Savoy,²² Sunil K. Sood,²³ Allen C. Steere,¹¹ Franc Strle,²⁴ Robert Sundel,¹⁸ Jean Tsao,²⁵ Elizaveta E. Vaysbrot,⁸ Gary P. Wormser,²⁶ and Lawrence S. Zemel¹³

Lyme Disease Continuum



Treatment Duration by Indication

Doxycycline:

One time dose (4.4 mg/kg) for prophylaxis if tick on > 72 hours, engorged

Table 4. Treatment of Specific Manifestations of Lyme Disease

Disease Manifestation	Route	Medication	Duration, days (range) ^a
Erythema migrans^b	Oral	Doxycycline	10
		Amoxicillin or cefuroxime axetil	14
		Azithromycin ^c	7 (range: 5–10)
Meningitis or radiculopathy	Oral	Doxycycline	14–21
	IV ^d	Ceftriaxone	14–21
Cranial nerve palsy	Oral	Doxycycline	14–21
Carditis	Oral ^e	Doxycycline, amoxicillin, or cefuroxime axetil	14–21
	IV ^e	Ceftriaxone	14–21
Arthritis			
Initial treatment	Oral	Doxycycline, amoxicillin, or cefuroxime axetil	28
Recurrent or refractory arthritis	Oral	Doxycycline, amoxicillin, or cefuroxime axetil	28
	IV	Ceftriaxone	14 ^f
Acrodermatitis chronica atrophicans	Oral	Doxycycline, amoxicillin, Or cefuroxime axetil	21–28
Borrelial lymphocytoma	Oral	Doxycycline, amoxicillin, or cefuroxime axetil	14

Abbreviation: IV, intravenous.

Future Developments in Lyme Disease



Lyme Meningitis Comparative Effectiveness Study

- Multicenter, NIH funded
- PO doxycycline versus ceftriaxone
- Provider choice and logic
- Parental impressions
- Outcomes



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Pediatric **Health** Network



CME



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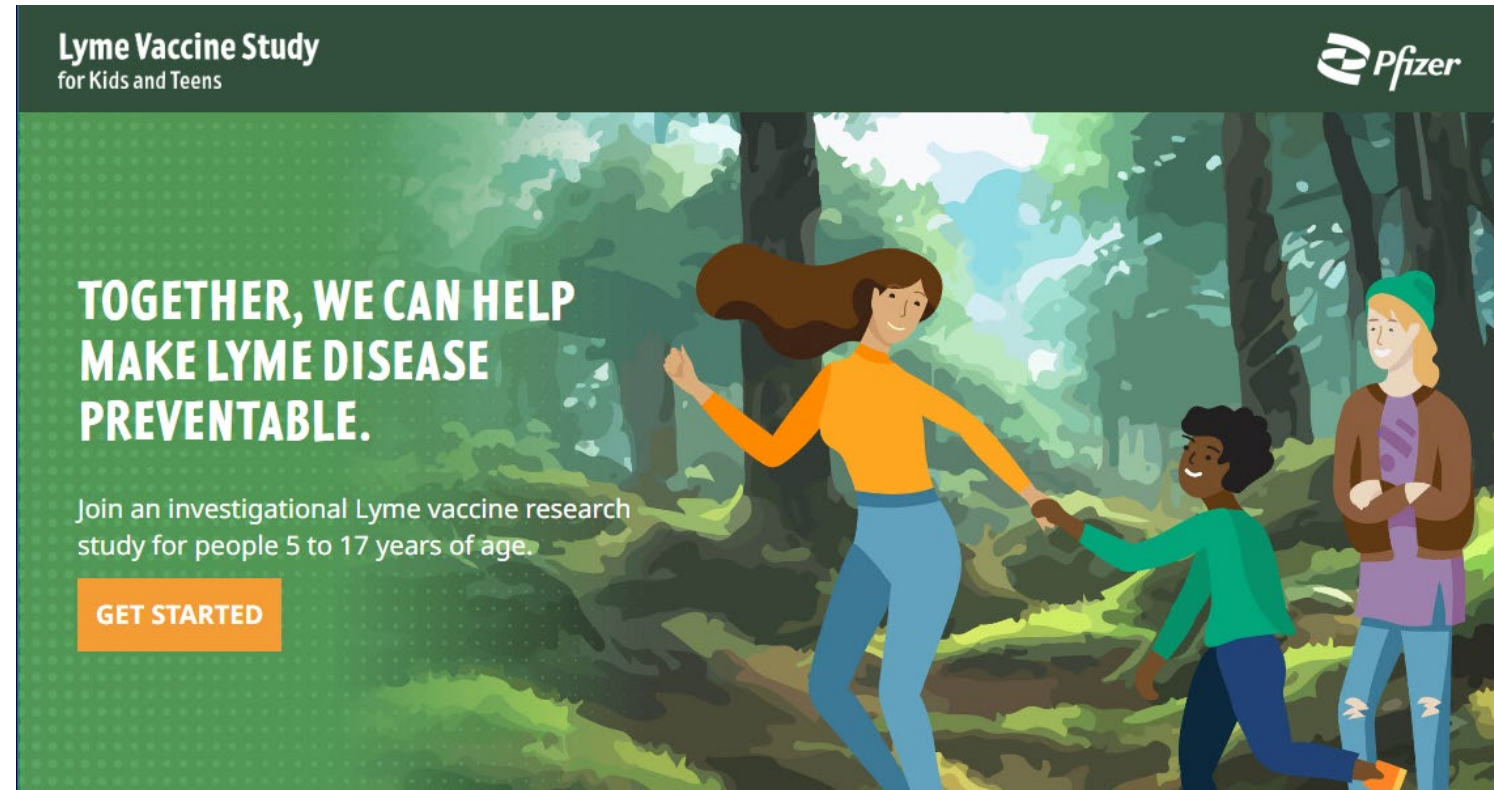
Questions? Please contact us at cme@inova.org.



Thank you

Lyme Vaccine Study (Pfizer C461012)

- Randomized, double blind, placebo-controlled SAFETY study
- vaccine VLA15 (6 valent OspA vaccine)
- Inclusion criteria
 - Ages 5-17
 - General healthy
 - Willing to attend 6 visits in person over 2 year at CNH and complete e-Diary regularly
- Enrolling through mid-June 2023



[Lyme Vaccine Study for Kids and Teens \(lymekidstudy.com\)](https://lymekidstudy.com)

Contact Info

- Email ayonts@childrensnational.org for both studies
- For Lyme Vaccine Trials:
- Pfizer Lyme Vaccine Clinical Trial website or Facebook
- Vaccinetrials@childrensnational.org

