



Tick, Tick...**BOOM**

The Emergence of Tick-borne Infections in
the Southeast

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Division of Infectious Diseases

Objectives

*By the end of this session, participants will be able to identify tickborne infections **endemic to the SE** and determine appropriate diagnostic and therapeutic **management in HIV** and non-HIV infected individuals.*

- Identify tickborne infection occurring in the SE
- Determine the most appropriate diagnostic test for tickborne infections
- Choose a therapeutic approach based on IDSA Guidelines and CDC recommendations

Disclosures

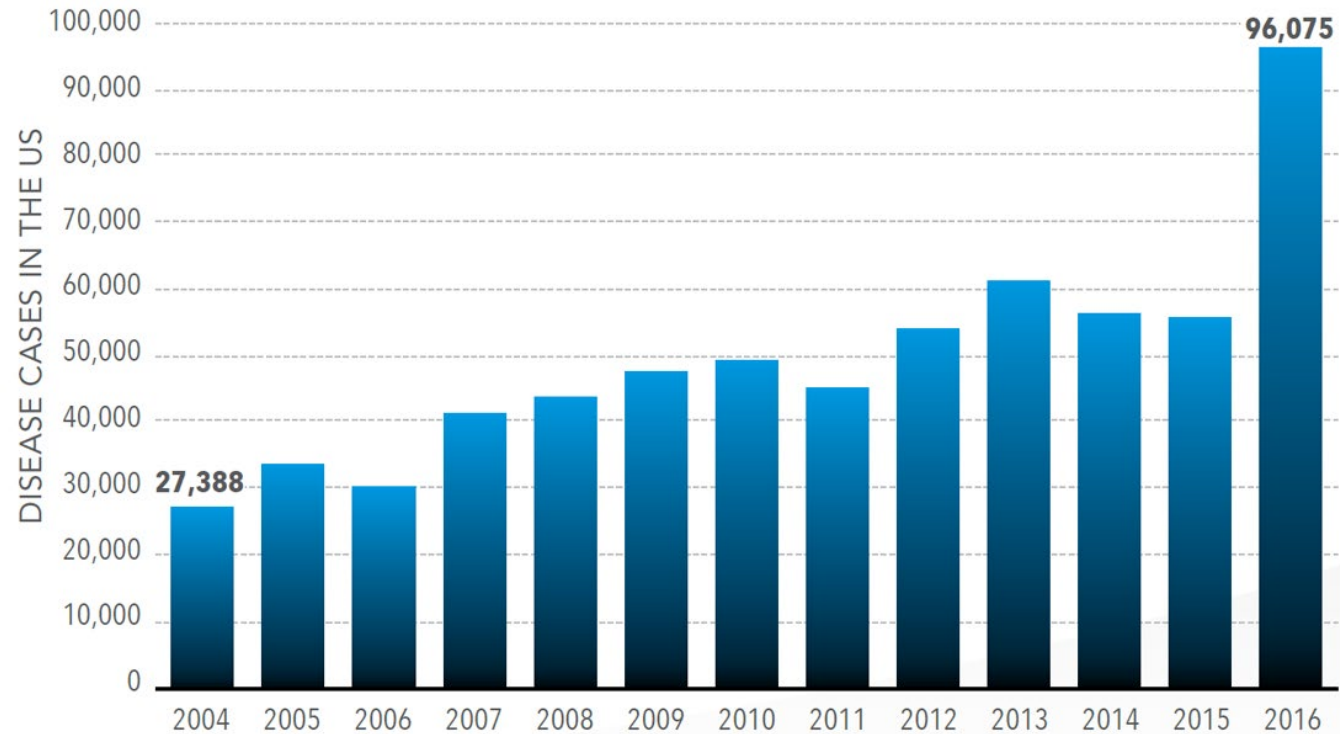
- *I have no financial disclosures*

- *This program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) under grant number U1OHA30535 as part of an award totaling \$4.2m. The contents are those of the author(s) and do not necessarily represent the official views of, nor an endorsement, by HRSA, HHS, or the U.S. Government. For more information, please visit [HRSA.gov](https://www.hrsa.gov).*

- *“Funding for this presentation was made possible by cooperative agreement U1OHA30535 from the Health Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.”*

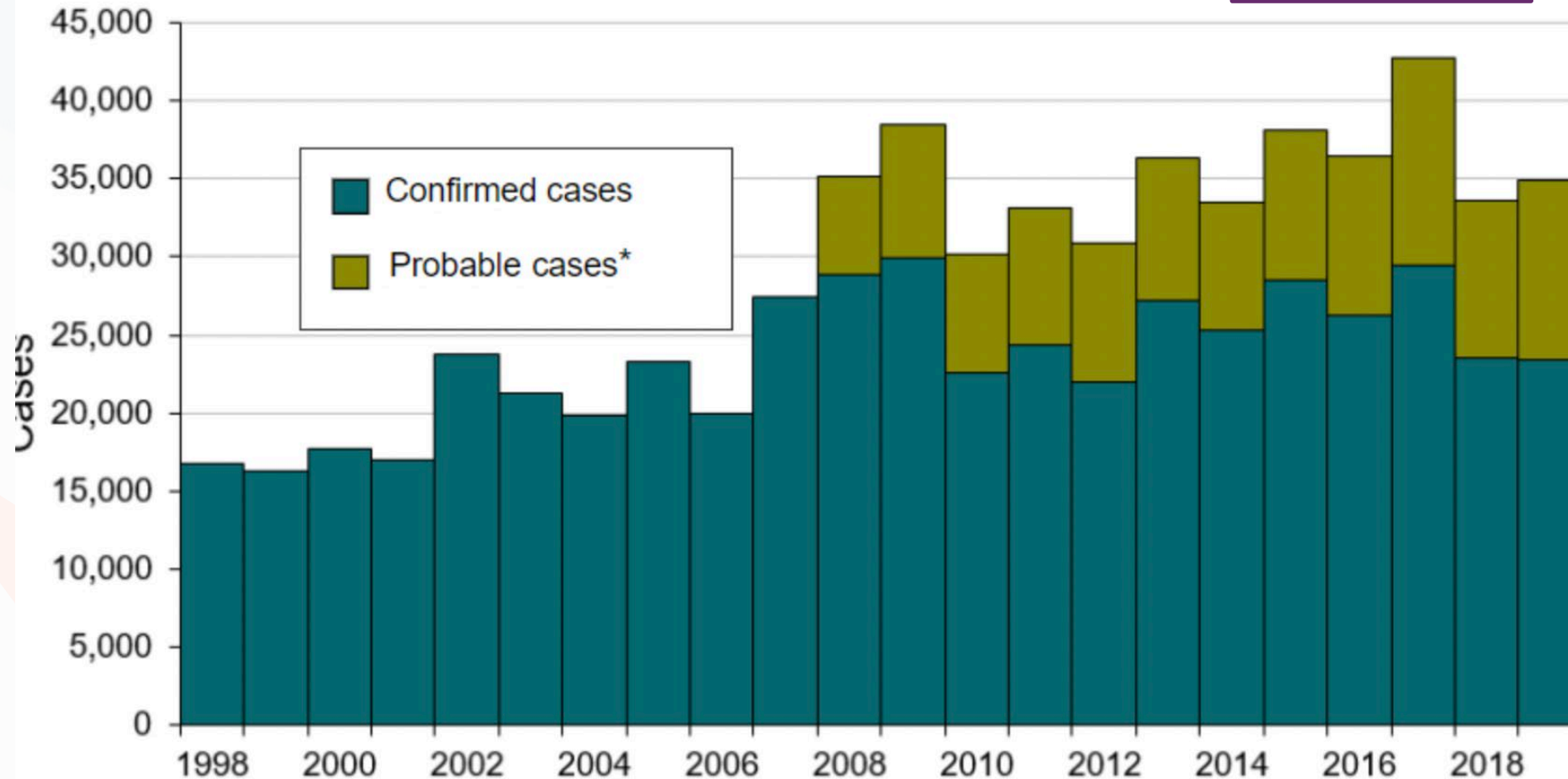
Invasion of the Ticks!

Disease cases from infected mosquitoes, ticks, and fleas have tripled in 13 years.

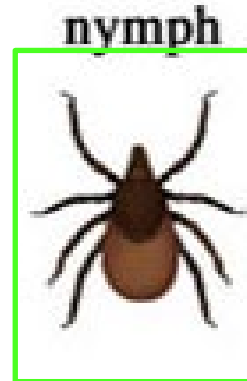
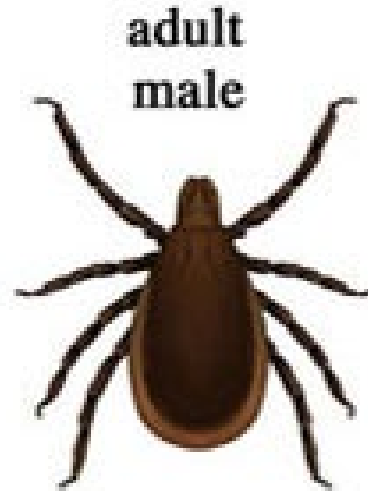


Reported Cases of Lyme Disease by Year, United States, 1998-2019

N=476,000/year



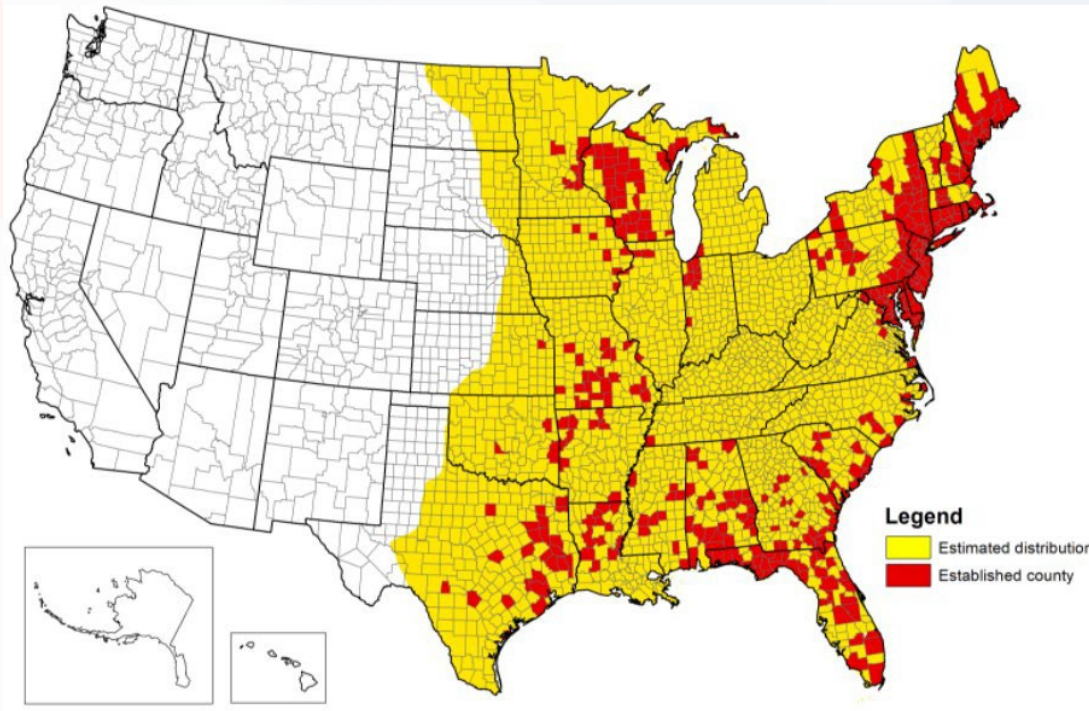
Blacklegged Tick (*Ixodes scapularis*)



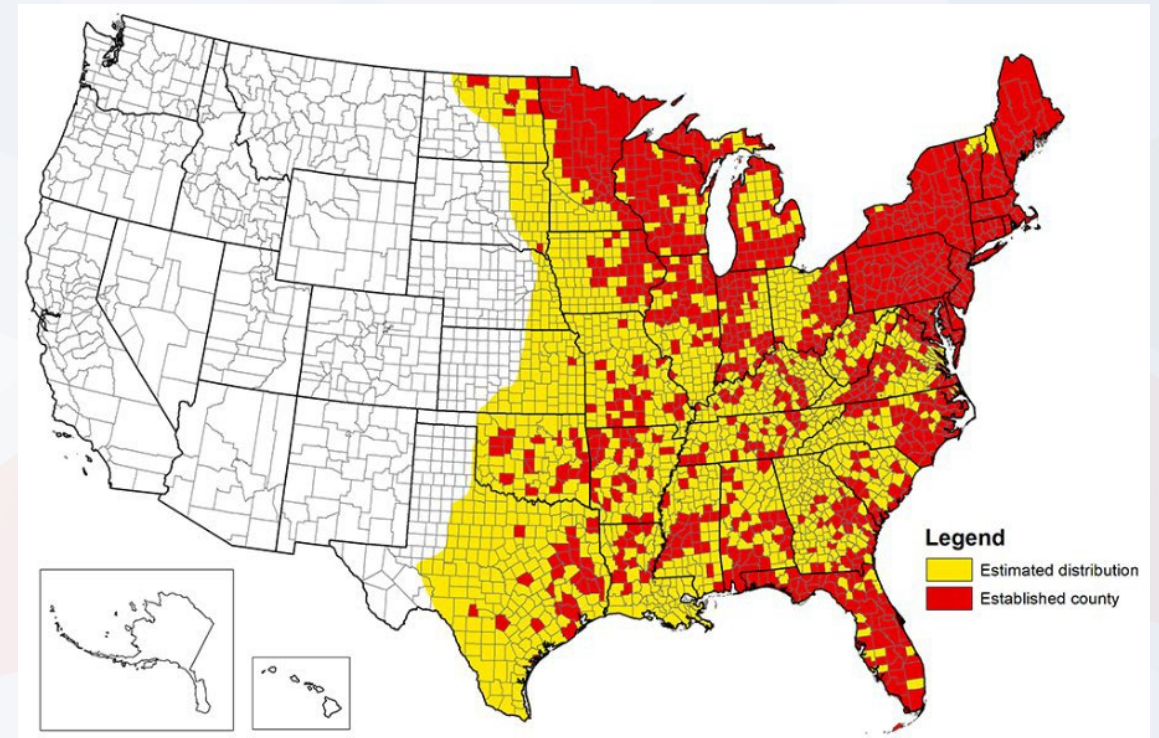
- *Ixodes* spp: Black-legged or Western Deer ticks
- Most cases transmitted by nymphs
- Less than 50% of patients with Lyme recall a tick bite
- **Attachment of >36 hours required for transmission**

Ixodes scapularis Distribution, 1996-2020

1996

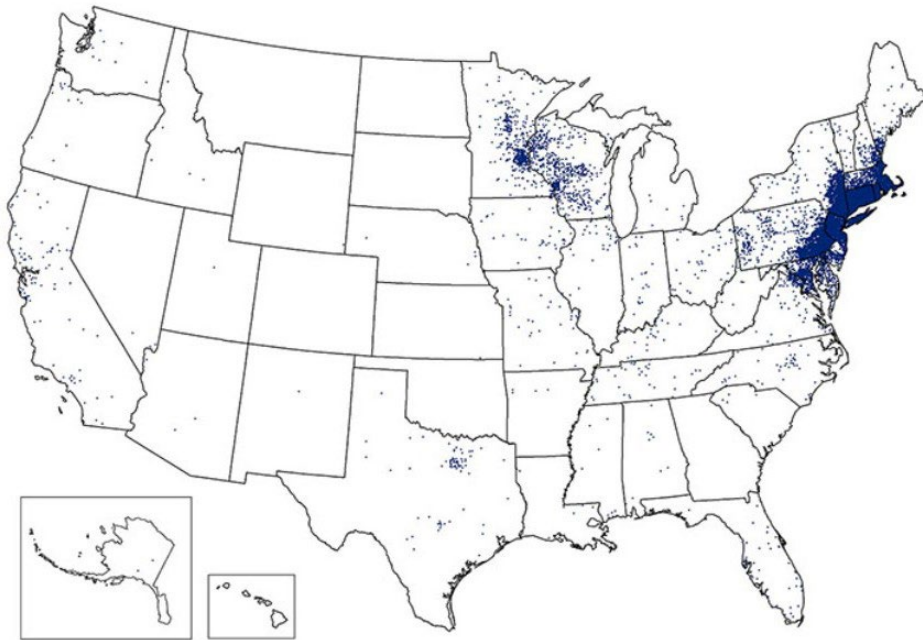


2020



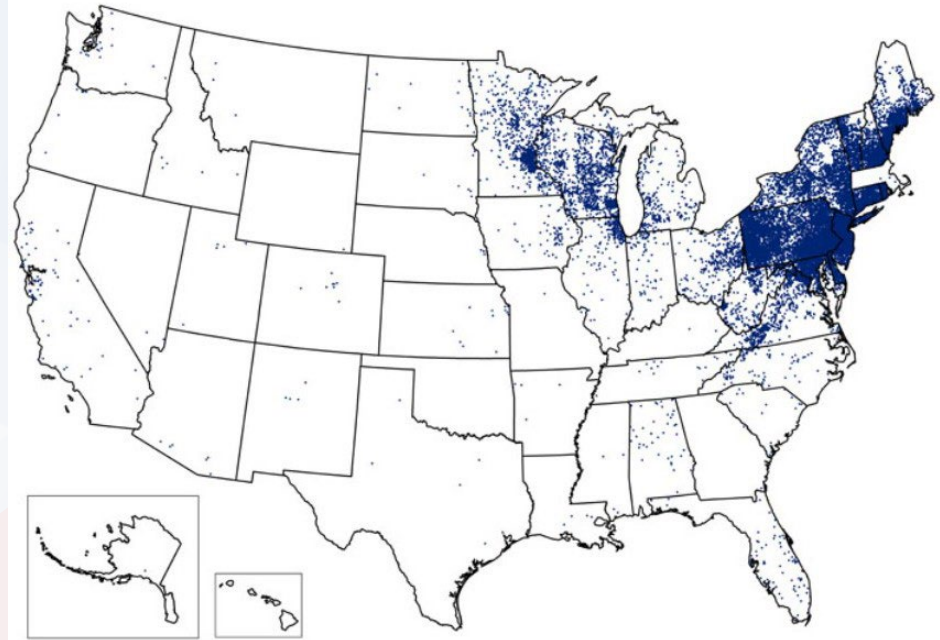
Lyme Incidence, 2001-2019

Reported Cases of Lyme Disease -- United States, 2001



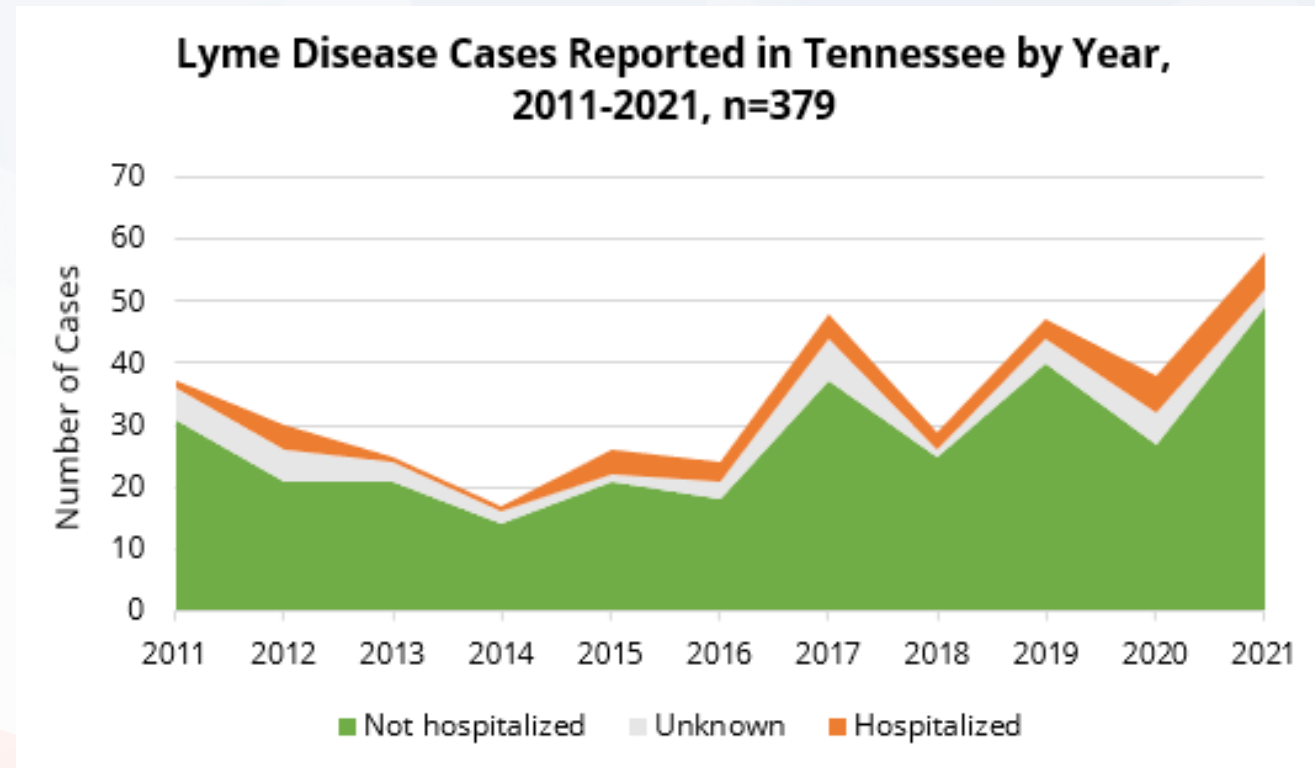
1 dot placed randomly within county of residence for each reported case

Reported Cases of Lyme Disease -- United States, 2019

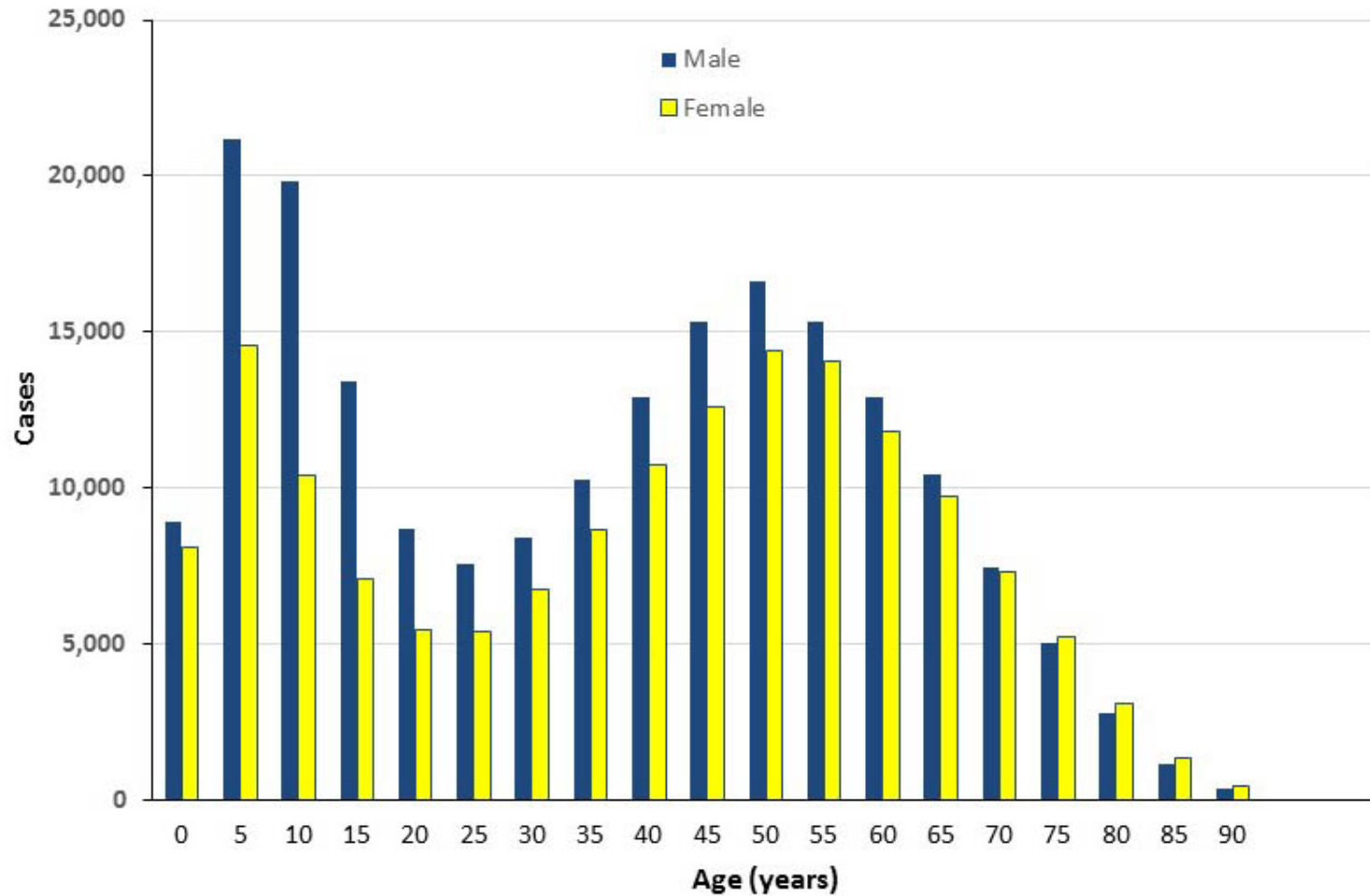


1 dot placed randomly within county of residence for each confirmed case

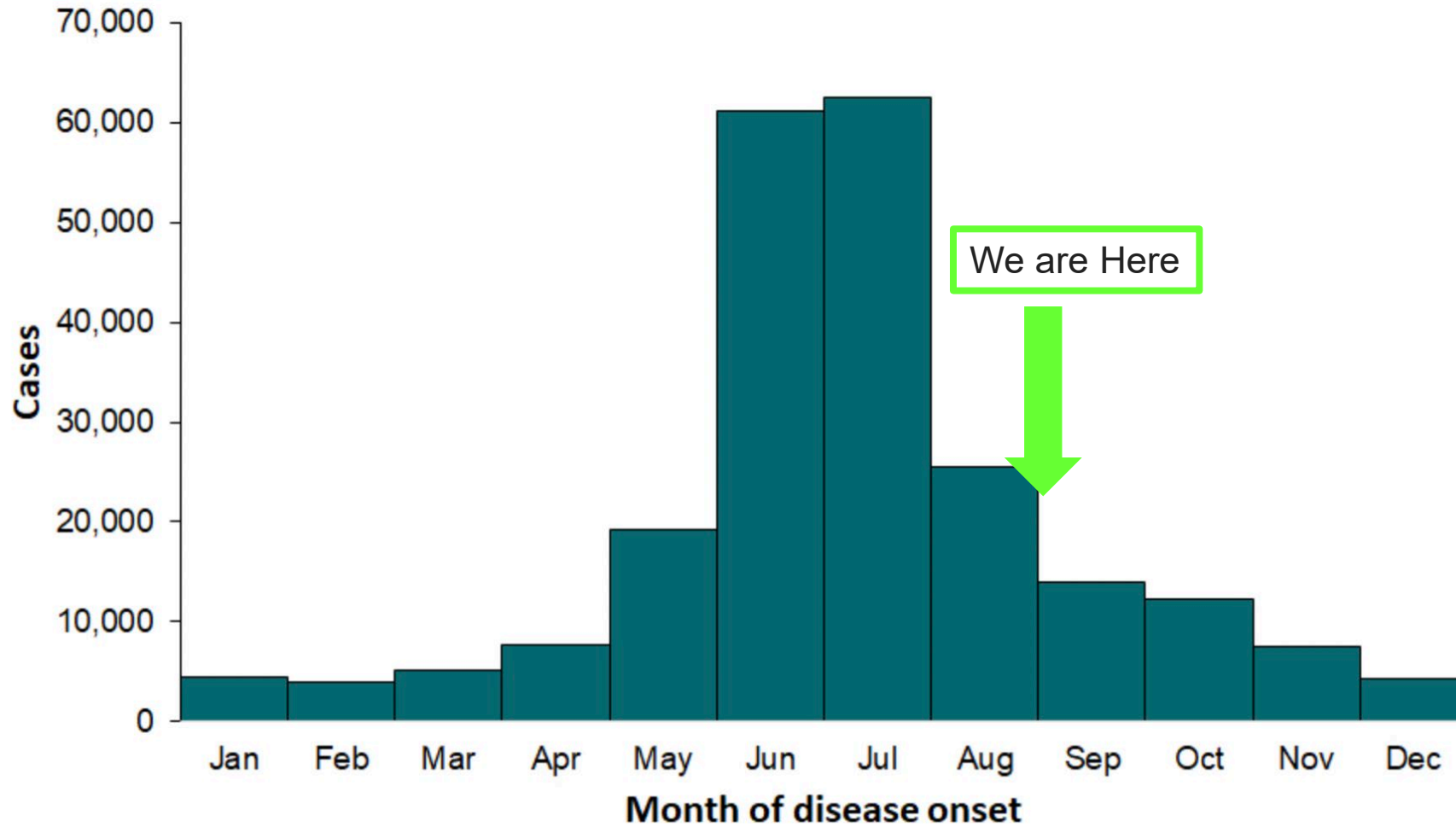
TN: Low incidence state
2021—**58** cases total (imported and locally acquired)



Lyme Disease Cases by Age and Sex—United States, 2001-2016



Confirmed Lyme disease cases by month of disease onset-- United States, 2008-2019



A Timely Talk...

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,¹⁸ Lise E. Nigrovic,¹⁹ James (Jay) J. Nocton,²⁰ Mikala C. Osani,²¹ Amy A. Pruitt,²² Jane Rips,²³ Lynda E. Rosenfeld,²⁴ Margot L. Savoy,²⁵ Sunil K. Sood,²⁶ 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



Case



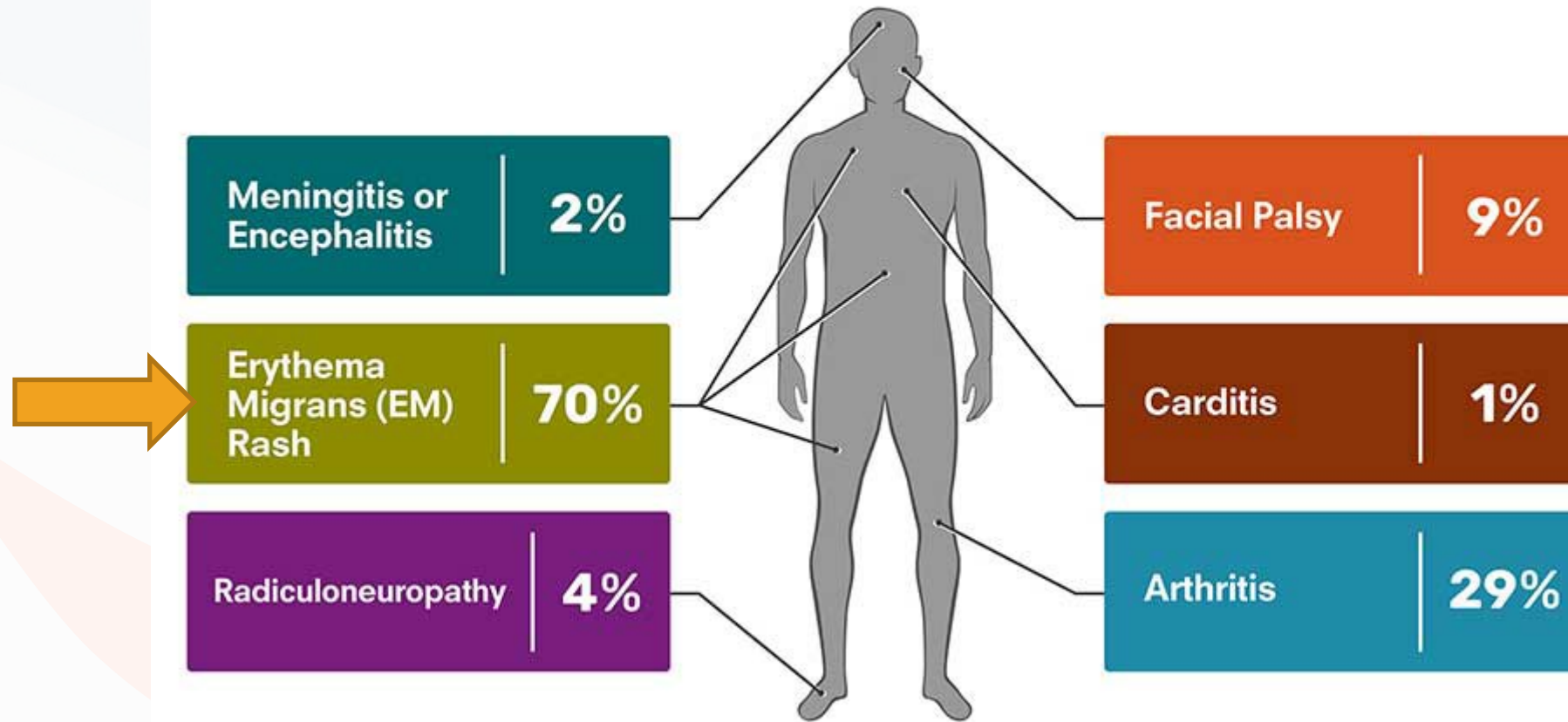
- A 25-year-old woman presents with a 1-day h/o rash
- Two weeks ago she was camping in the Smokies, but denies tick or mosquito bites
- She denies fevers or other constitutional symptoms

Is this Lyme Disease?

Clinical Manifestation of Lyme Disease at Diagnosis

LYME DISEASE

Relative frequency of clinical features among confirmed cases - United States, 2008-2018



Erythema migrans



- 7-14 days after attachment
- Expansile lesion ≥ 5 cm
- Bull's eye or target lesion
- Painless and nonpruritic
- Systemic symptoms rare
- Identified in **60-80%** of cases

Atypical Erythema Migrans is Typical

Variable	Patients, <i>n</i> (%)
Morphologic characteristics	
Predominant pattern	
Homogeneous	56 (59)
Central erythema	30 (32)
Central clearing	9 (9)
Punctum present	29 (31)
Vesicular or ulcerated	7 (7)
Blue center	2 (2)
Total	95 (100)



Erythema Migrans Mimickers

- Hypersensitivity to tick saliva
- Insect bite
- Nummular eczema
- Granuloma annulare
- Ringworm
- Cellulitis
- **STARI**



Southern Tick Associated Rash Illness (STARI)

- Associated with Lone Star Tick
- *B burgdorferi* serology and PCR negative
- No laboratory testing available
- Not associated with late sequelae
- Per CDC: It is not known whether antibiotic treatment is necessary or beneficial for patients with STARI. Nevertheless, **because STARI resembles early Lyme disease, physicians often treat patients with the same antibiotics recommended for Lyme disease.**



Case Revisited



- A 25-year-old woman presents with a 1-day h/o rash
- Two weeks ago she was camping in the Smokies, but denies tick or mosquito bites
- She denies fevers or other constitutional symptoms

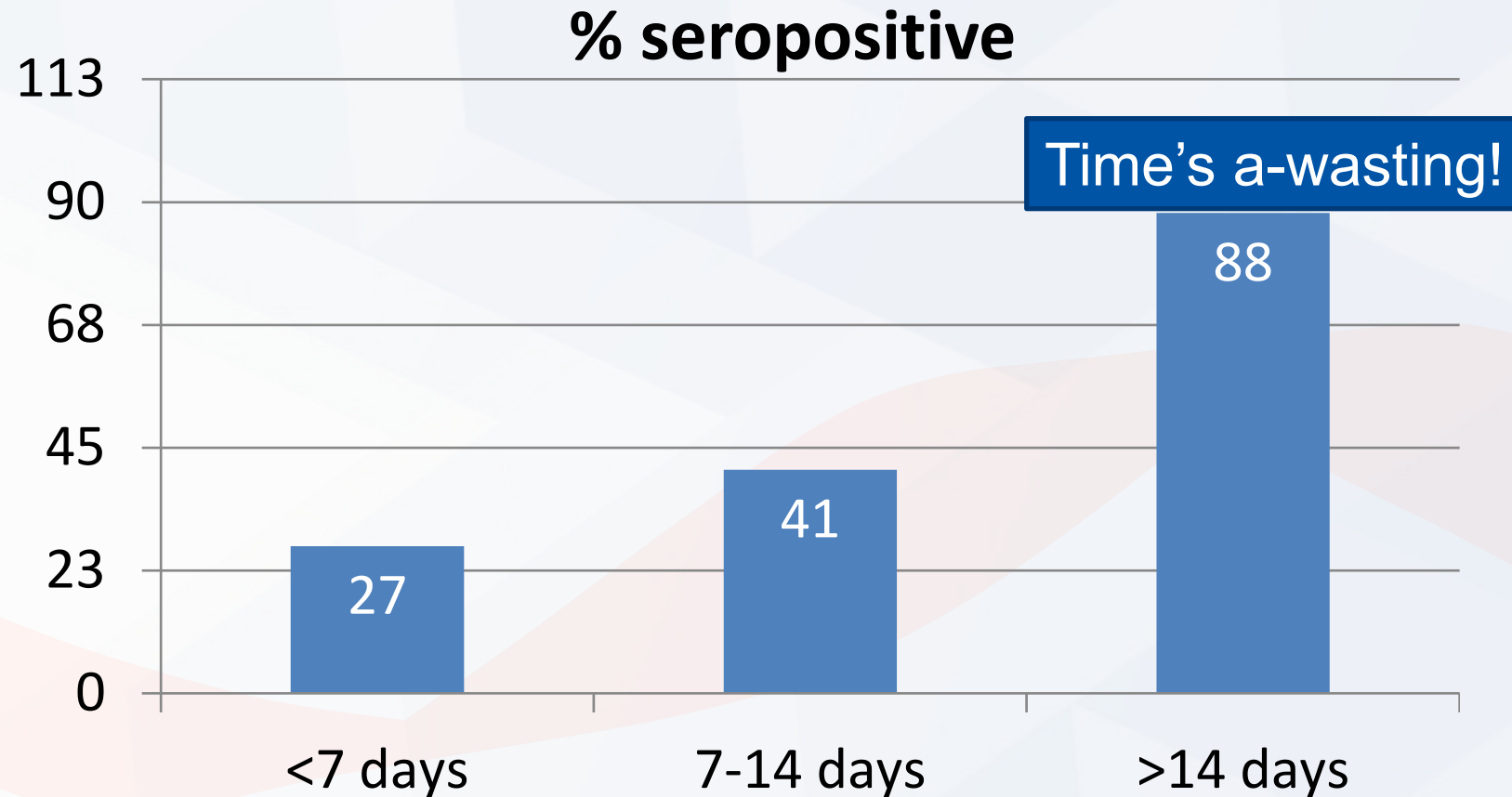
Is this Lyme Disease?

What is the Most Appropriate Diagnostic Test?



1. *B. burgdorferi* EIA total
2. *B. burgdorferi* Western blot IgM
3. Skin biopsy for PCR
4. *B. burgdorferi* Western blot IgG
5. No test needed

Detection of Antibodies in Early Localized Lyme Disease Following Onset of EM



Diagnostic Testing for EM

- Typical lesion (s), appropriate epidemiology: clinical dx **no lab testing needed** → treat
- Atypical lesion/Epi:
 - Treat, or
 - Acute (and if negative con) antibodies



Therapy for erythema migrans

IDSA Guidelines, 2006 → 2020

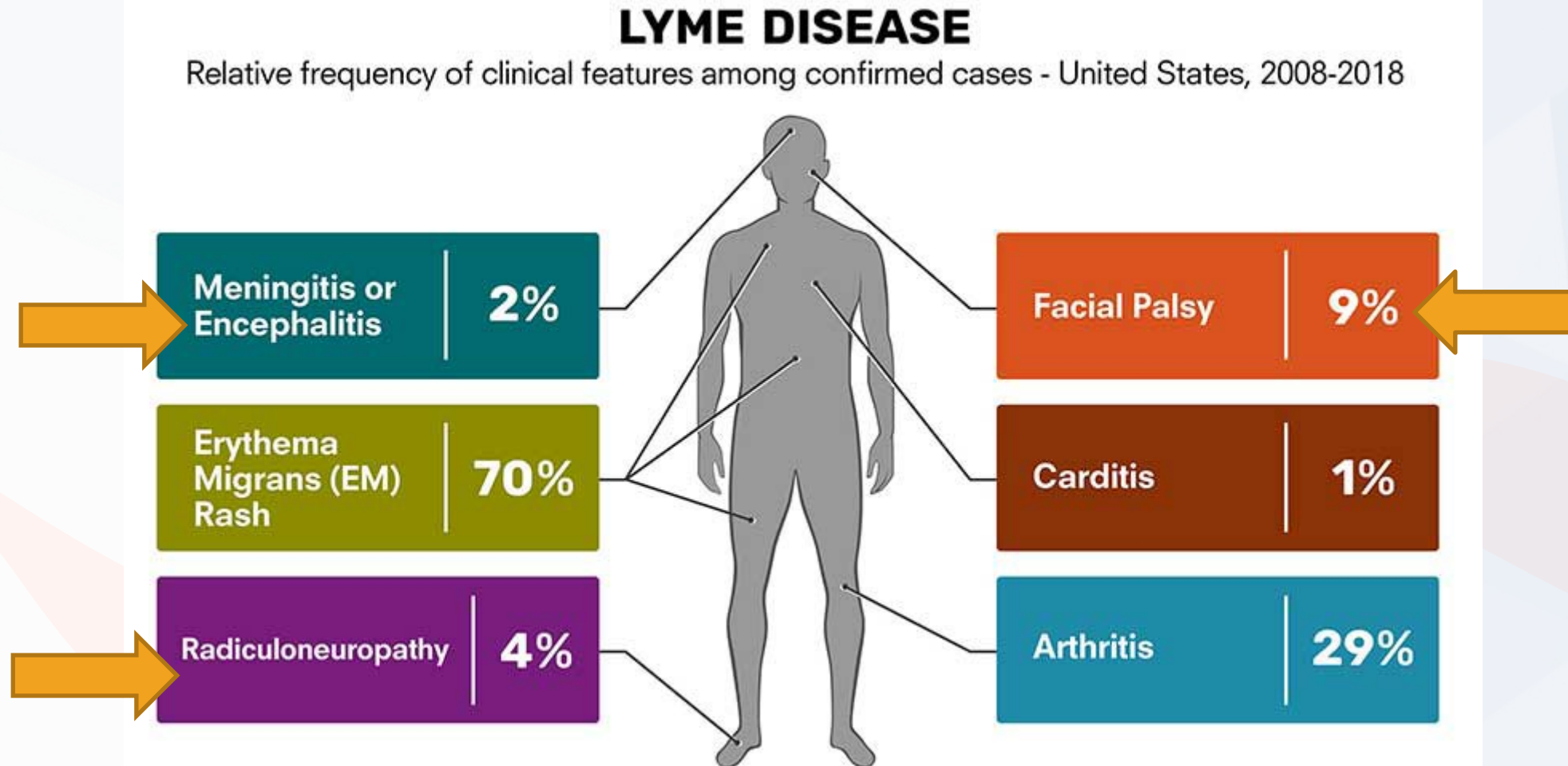
Treatment	Duration
Doxycycline	10- 21 days
Amoxicillin	14- 21 days
Cefuroxime axetil	14- 21 days

Doxycycline

- No interactions with ART
- Binds to Ca, Fe, Mg (incl MVI)
- Adverse effects:
 - GI upset (take with food)
 - Pill esophagitis (>30 degrees for 30 min)
 - Photosensitivity

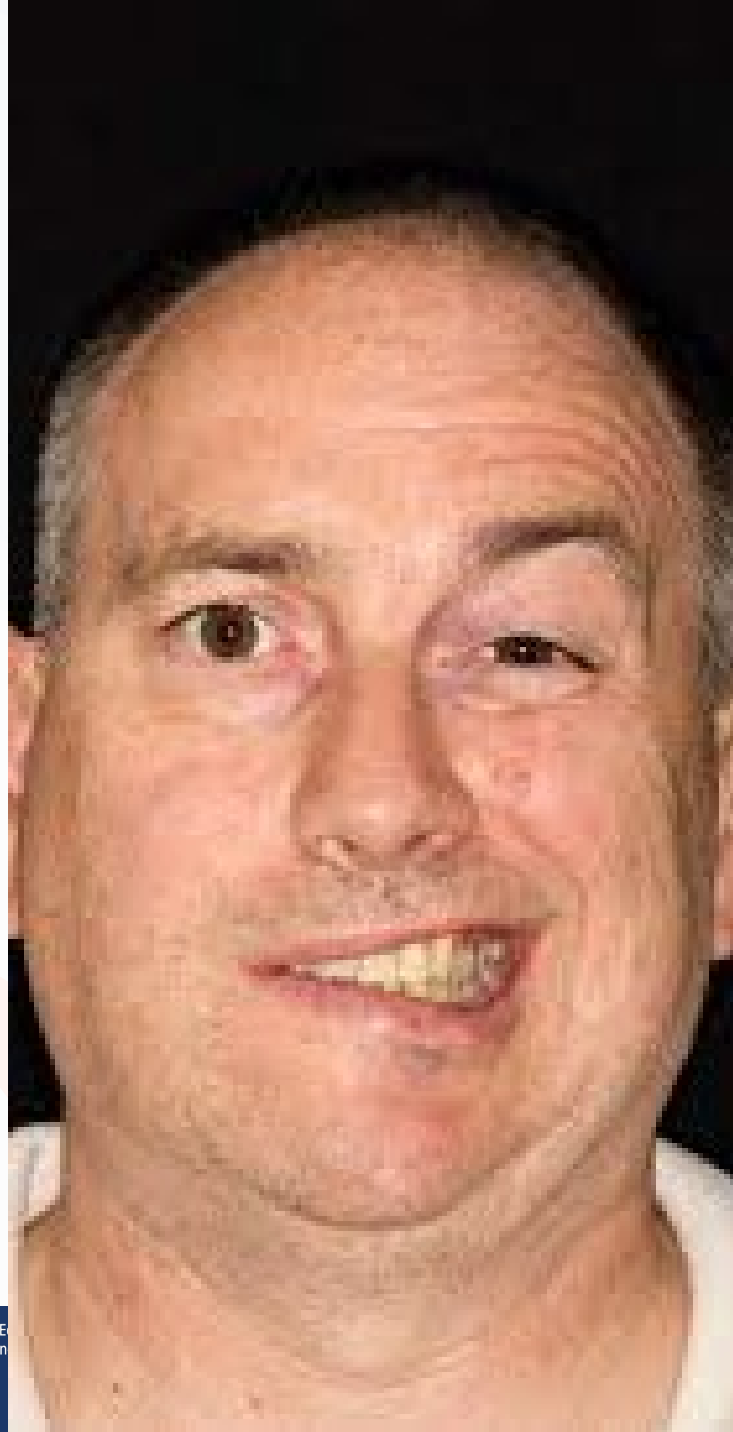


Clinical Manifestation of Lyme Disease at Diagnosis

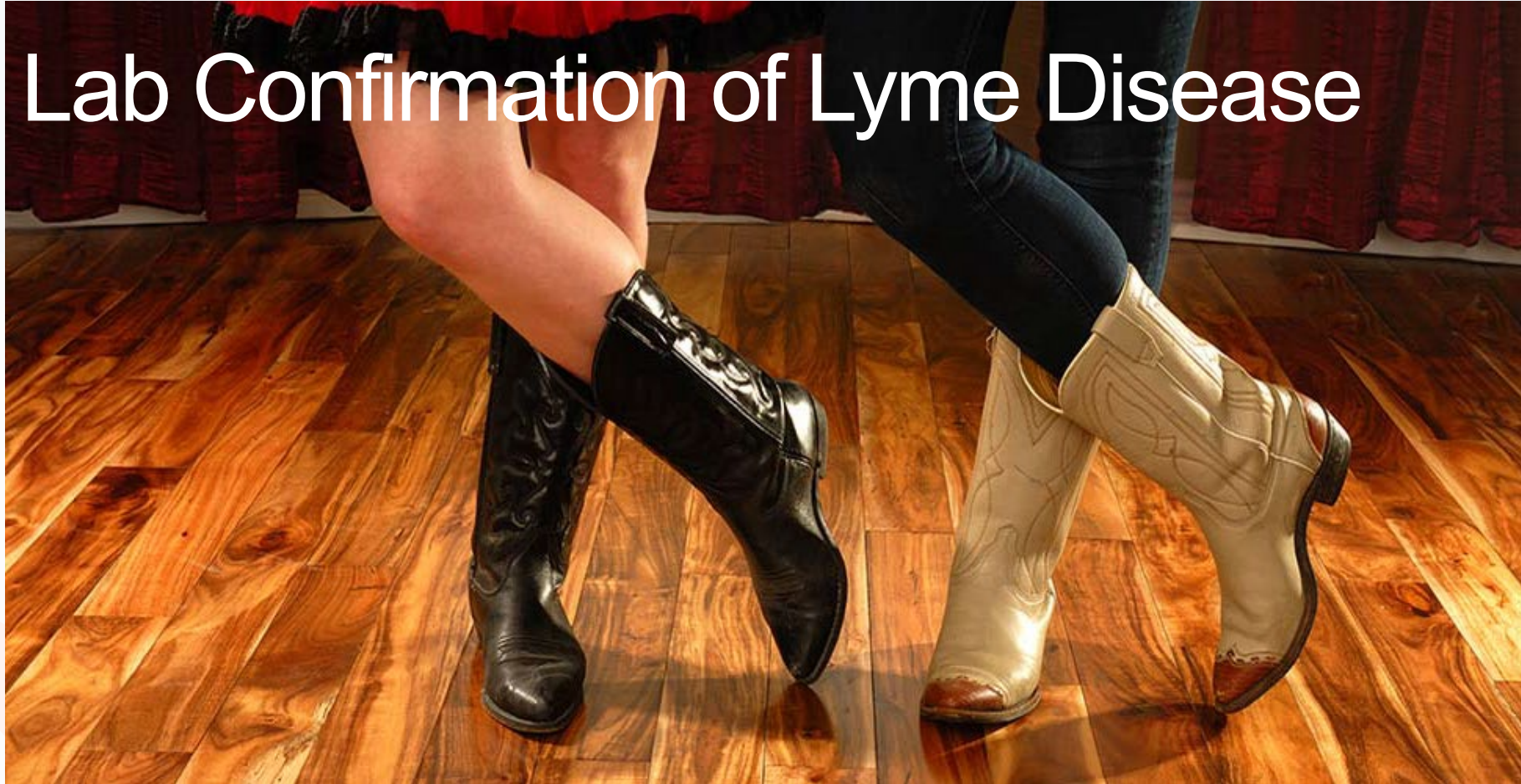


When to Consider Neuroborreliosis

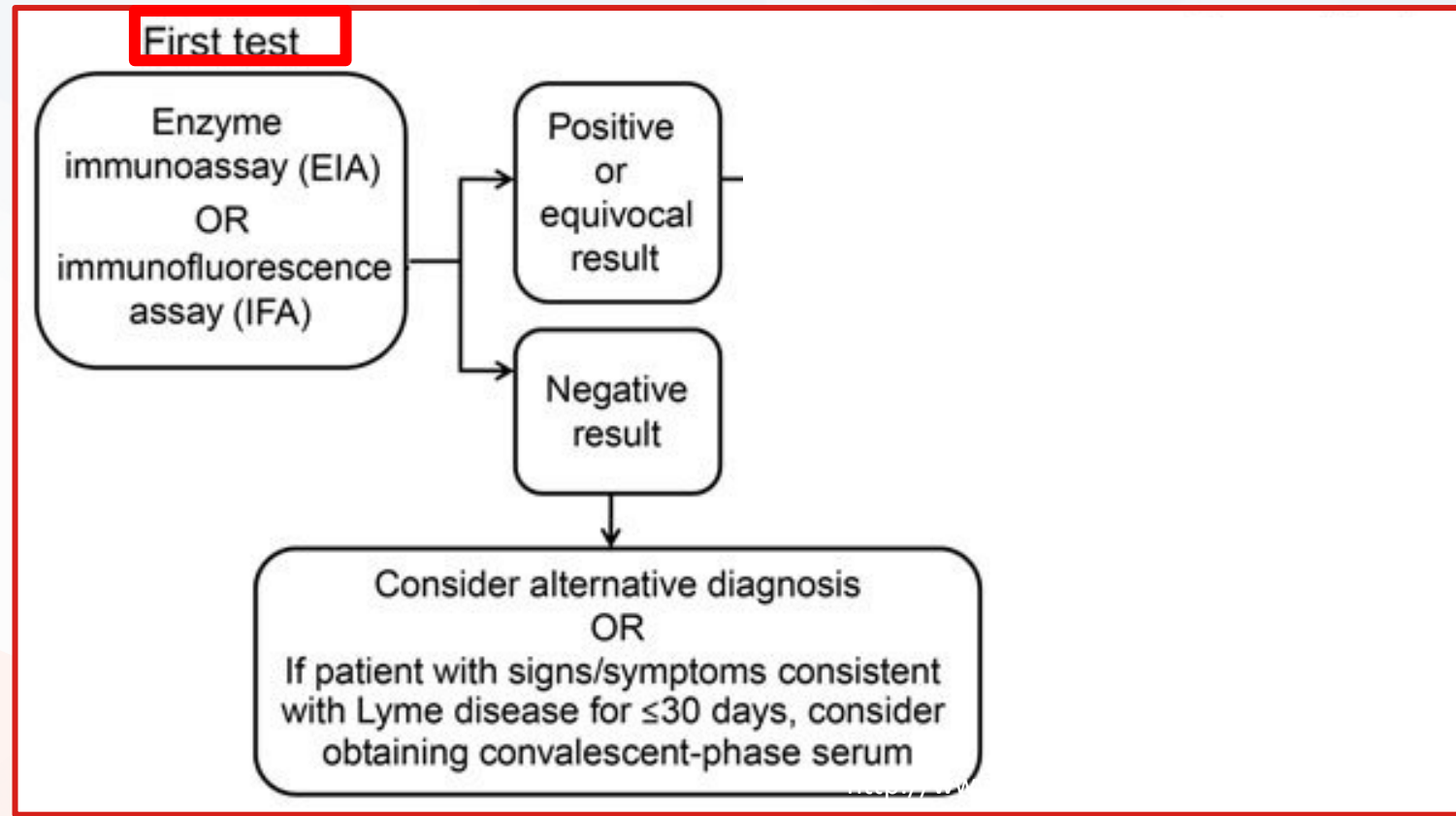
- Plausible exposure to vector tick, and:
 - Meningitis
 - Radiculitis/radiculopathy
 - Mononeuritis multiplex
 - Acute CN palsy (esp VII and VIII)
- **Unlike localized disease, lab confirmation is essential!**



Lab Confirmation of Lyme Disease

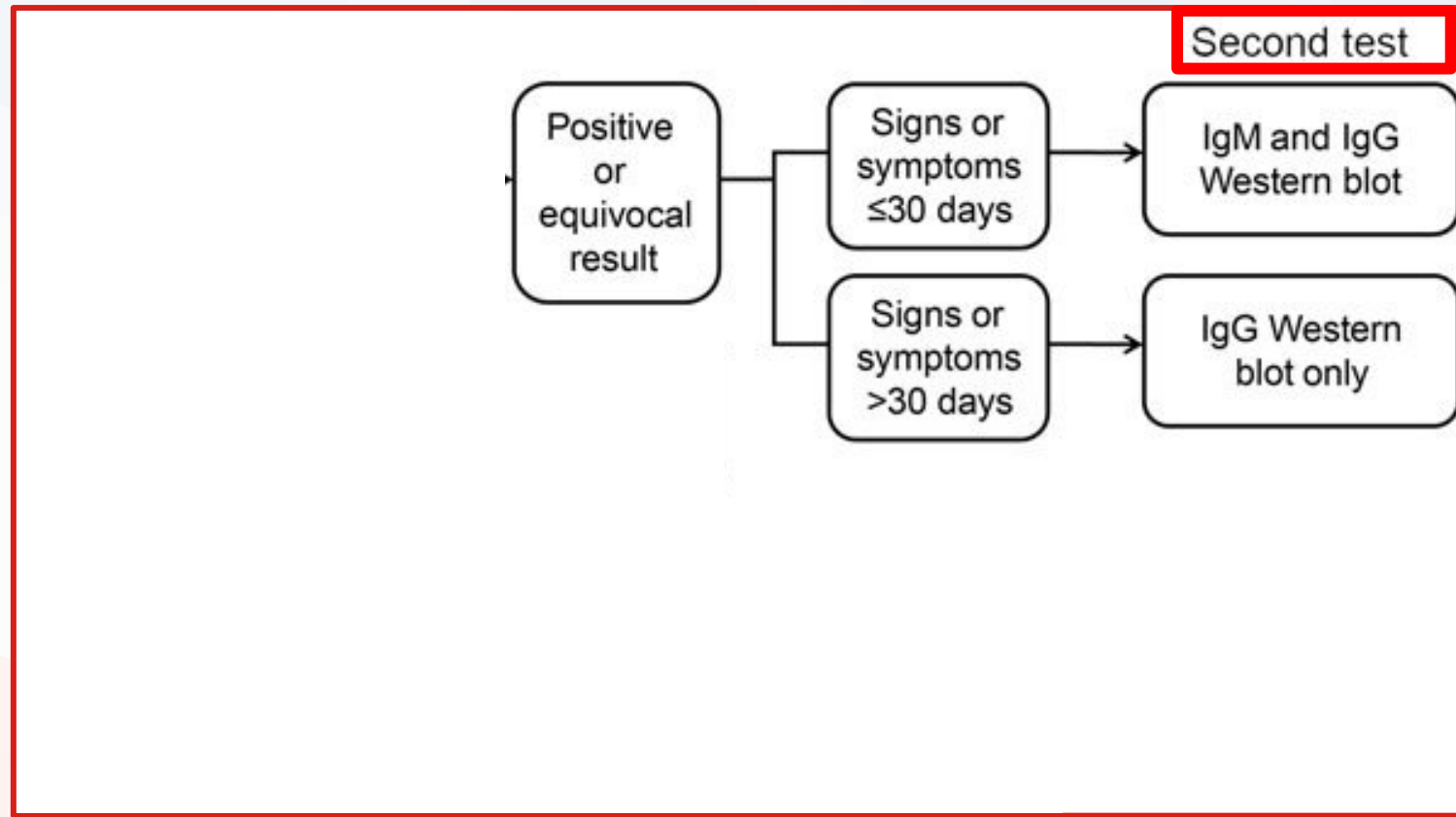


Two-Step Testing for Lyme Disease



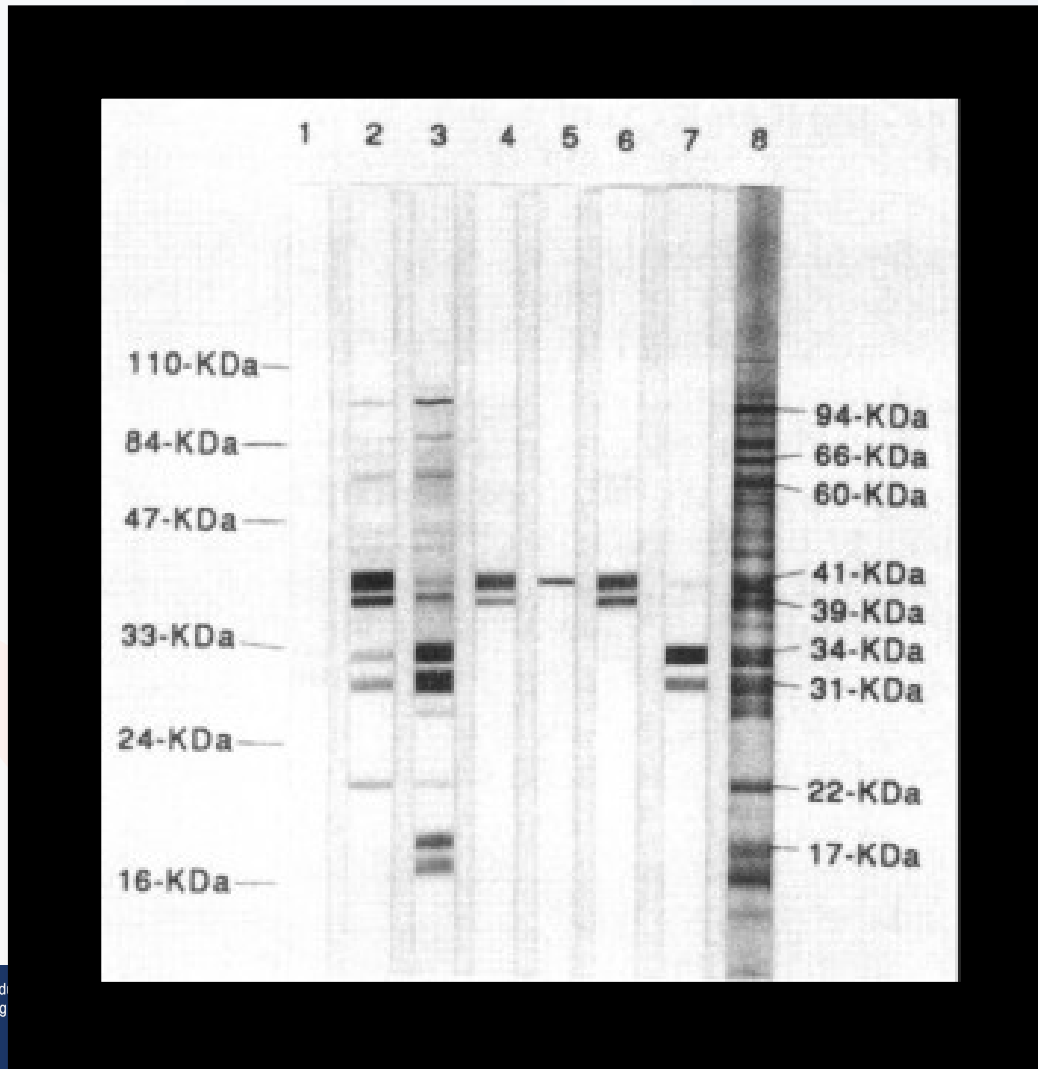
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Two-Step Testing for Lyme Disease



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What is a Positive Western Blot?

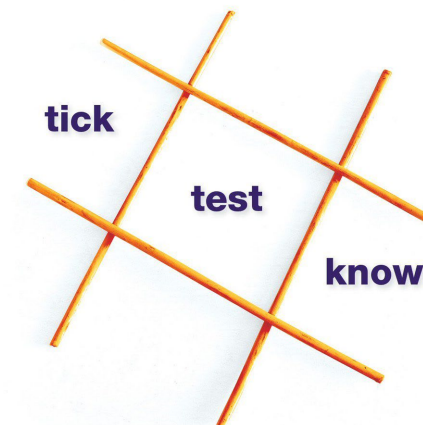


- IgM:
 - $\geq 2/3$ bands or proteins
 - Turns positive EARLY
 - Converts to negative in 1-2 months
 - An isolated IgM after >1 month is almost certainly a **false positive**
- IgG:
 - $\geq 5/10$ bands or proteins present
 - Turns positive after IgM (within first month)
 - Stays positive for prolonged periods
 - **Not useful to trend over time**

Newer diagnostic approaches

- C6 Lyme ELISA
 - FDA approved for initial test in 2-tiered approach
 - Highly conserved protein from invariant region of bacterial lipoprotein
 - When to use: Foreign travel, concern for other *Borrelia* species
- Modified 2-tier test
 - FDA approved 2019
 - 2 sequential or concurrent EIAs
 - Less work intensive, cheaper, and more objective

The **GAME CHANGER** in early Lyme disease detection



Pitfalls in Laboratory Testing

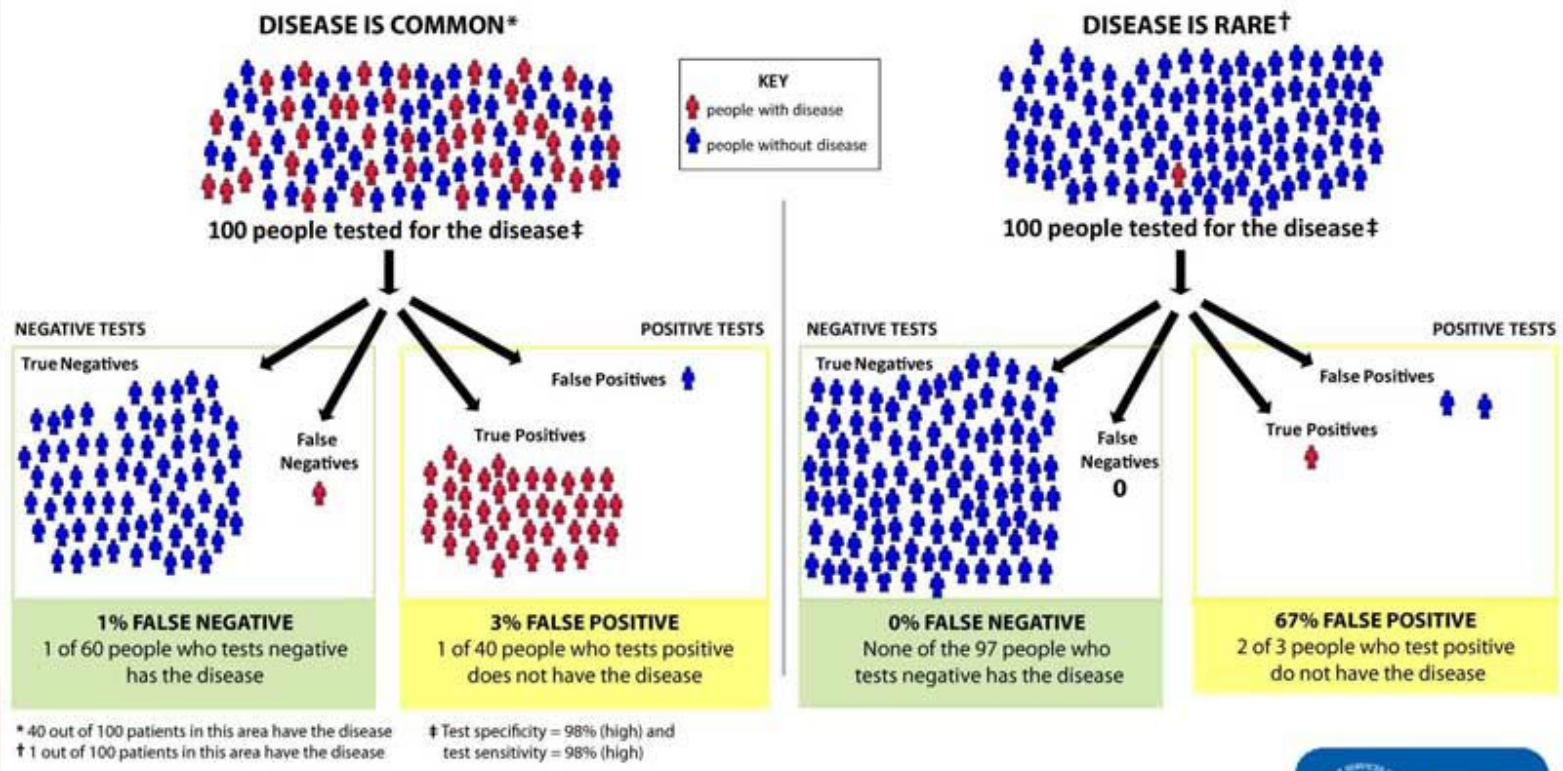
- **Early infection, often seronegative**
- **After >1 month of symptoms, isolated IgM response likely a false positive**
- **Antibodies stay positive for life...don't retest or re-treat based on persistently elevated or rising titers**
- **Likelihood of a false positive goes up in a non-endemic area or with nonspecific symptoms**

Understanding Test Results for Infectious Diseases

Consider the likelihood of disease *before* performing laboratory testing

The likelihood that a patient has a disease depends on many factors:

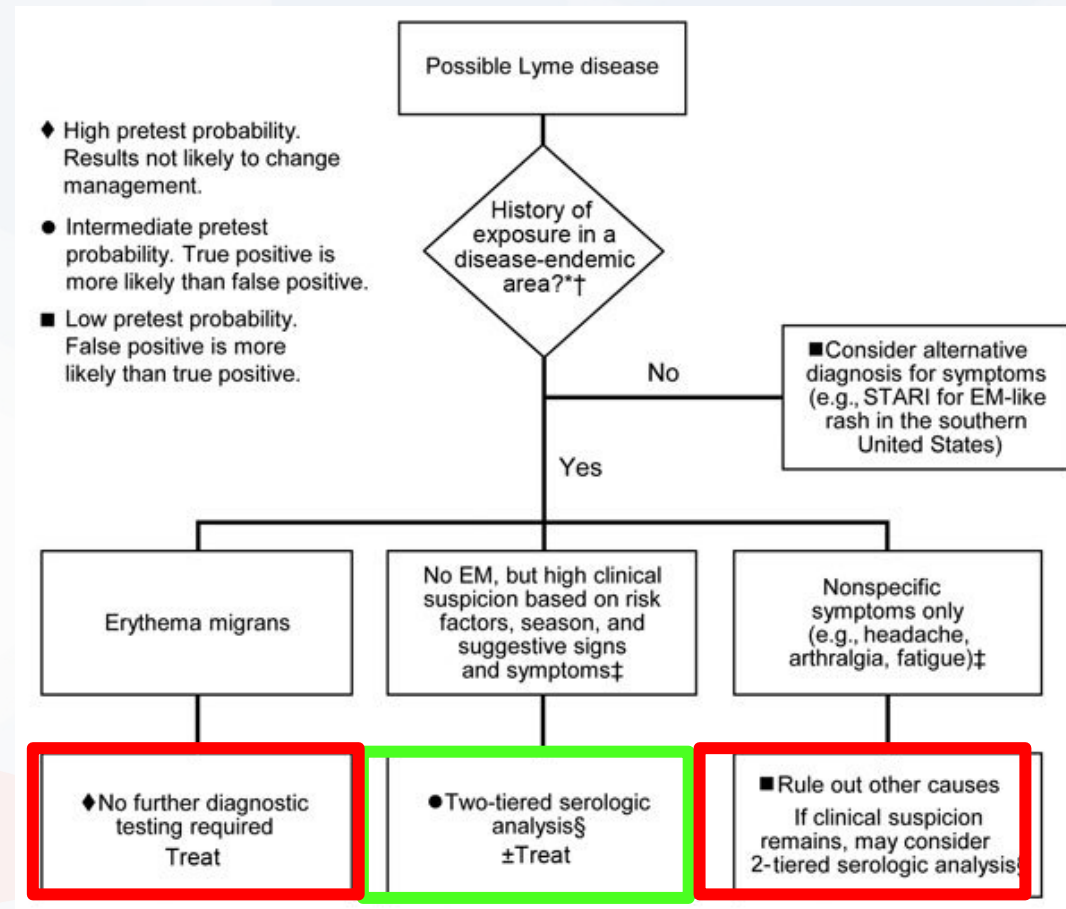
- Has the patient been in an area where the disease is found?
- Does the patient have signs and symptoms typical of the disease?
- Does the patient have risk factors for contracting or developing the disease?



National Center for Emerging and Zoonotic Infectious Diseases
 Division of Vector Borne Diseases | Bacterial Diseases Branch



Testing for Lyme Disease: SUMMARY



IGENEX WESTERN BLOT

PROTOCOL: Western Blotting refers to the electrophoretic transfer of proteins from sodium gels to a nitrocellulose membrane, followed by immunodetection of proteins using antibodies with fluorescent or chemiluminescent detection.

- Very specific, which means that most of the time it will be positive only if a person has been truly infected.
- A relatively inexpensive method to determine relative amounts and relative size of proteins

PRICE: \$125

TEST NUMBER: 188, 189

CPT CODE: 86617

MOST POPULAR!

IGENEX IMMUNO BLOT

PROTOCOL: Recombinant *B. burgdorferi* species antigens are sprayed at specific positions onto a nitrocellulose membrane and cut into strips. These strips are used to detect *B. burgdorferi* specific antibodies in patient serum.

- Easier to interpret than a Western Blot
- Improved specificity because pure proteins are sprayed at specific positions on the blot. Epitope testing for band 31 is not required.
- Improved sensitivity because it includes eight *B. burgdorferi* specific antigens from multiple strains and species of *B. burgdorferi*

PRICE: \$225

TEST NUMBER: 325, 335

CPT CODE: 86617

IGENEX IGXSPOT

PROTOCOL: The IgXSpot is used for detecting and monitoring cellular immune responses to specific antigens. The assay allows visualization of the secretory product(s) of individual activated or responding cells to *Borrelia*-specific antigens. Each spot that develops in the assay represents a single reactive cell.

- Detects specific T-cell responses soon after infection when antibodies to the organisms are not detectable or late in the disease when the levels of antibodies are very low
- Especially useful for seronegative patients (those that do not produce antibodies)
- Allows patients to start treatment earlier. Especially patients with no EM rash, or young people who are at greater risk if symptoms appear.

PRICE: \$295

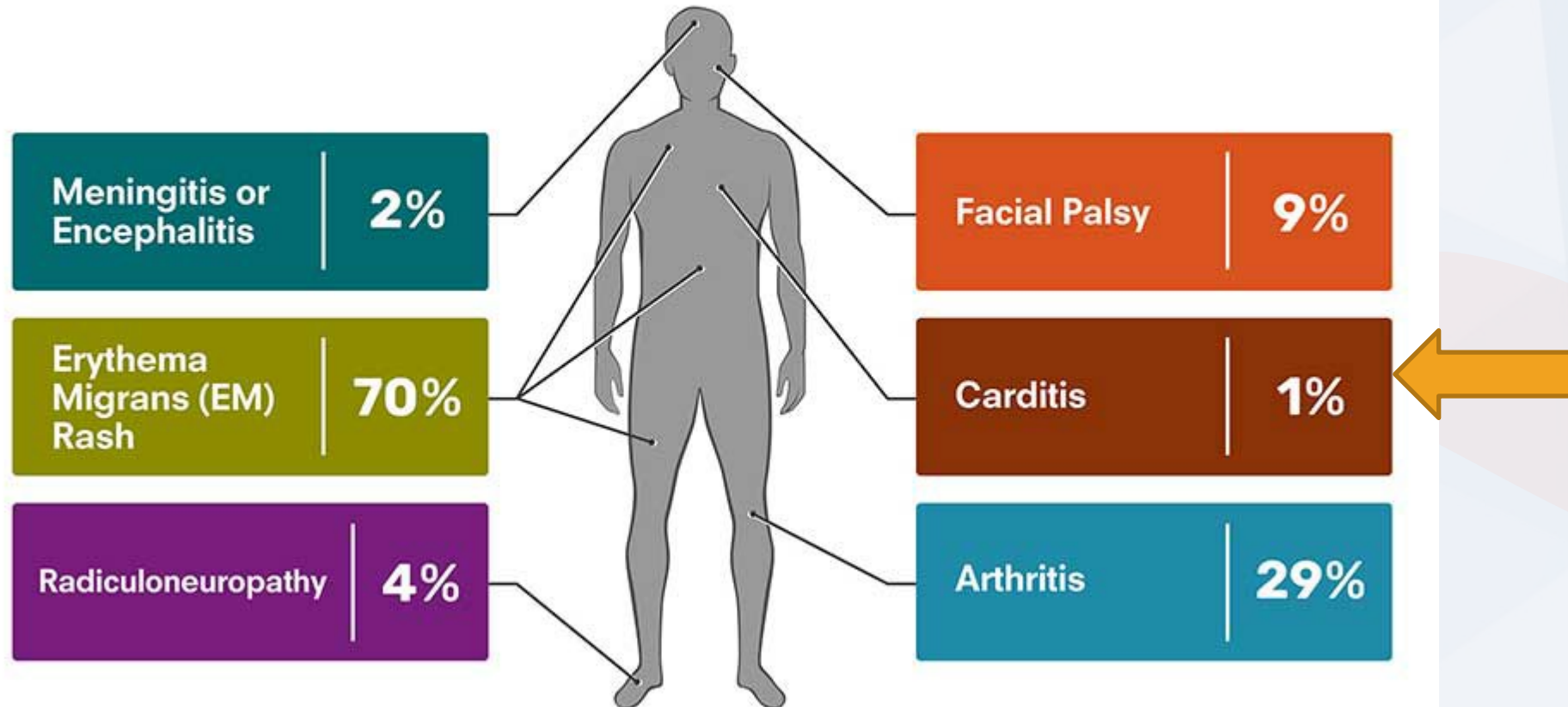
TEST NUMBER: 300

BEWARE THE UNVALIDATED TEST

Clinical Manifestation of Lyme Disease at Diagnosis

LYME DISEASE

Relative frequency of clinical features among confirmed cases - United States, 2008-2018



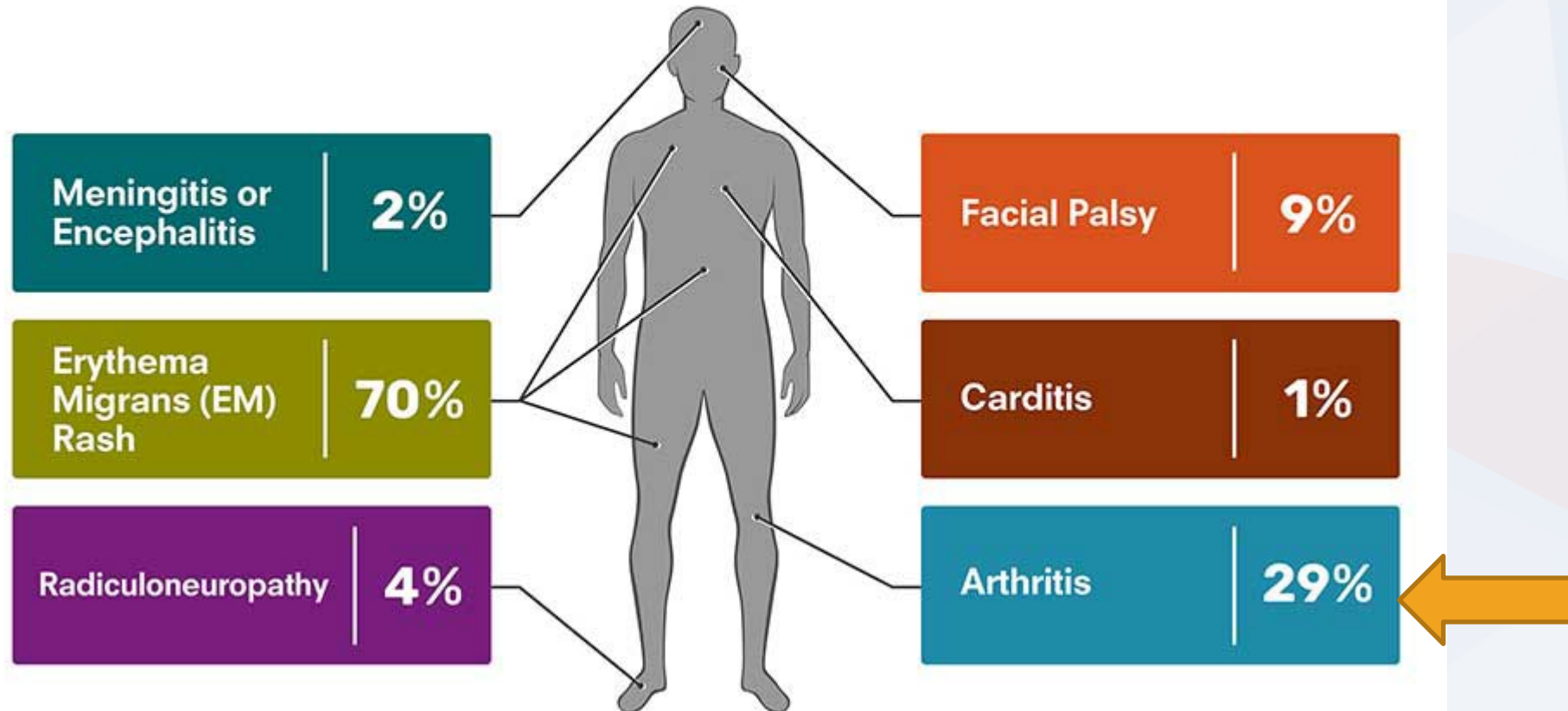
Lyme Carditis

- Conduction abnormalities
 - Rarely myocarditis, pericarditis
 - Reports of sudden death
- Despite this, **routine EKG not recommended**
- **Hospitalization** indicated for:
 - 2nd or 3rd degree HB
 - 1st degree HB with PR >300 milliseconds or symptomatic
- IV treatment until resolution of heart block
- Permanent pacemaker **not** indicated as reversible

Clinical Manifestation of Lyme Disease at Diagnosis

LYME DISEASE

Relative frequency of clinical features among confirmed cases - United States, 2008-2018



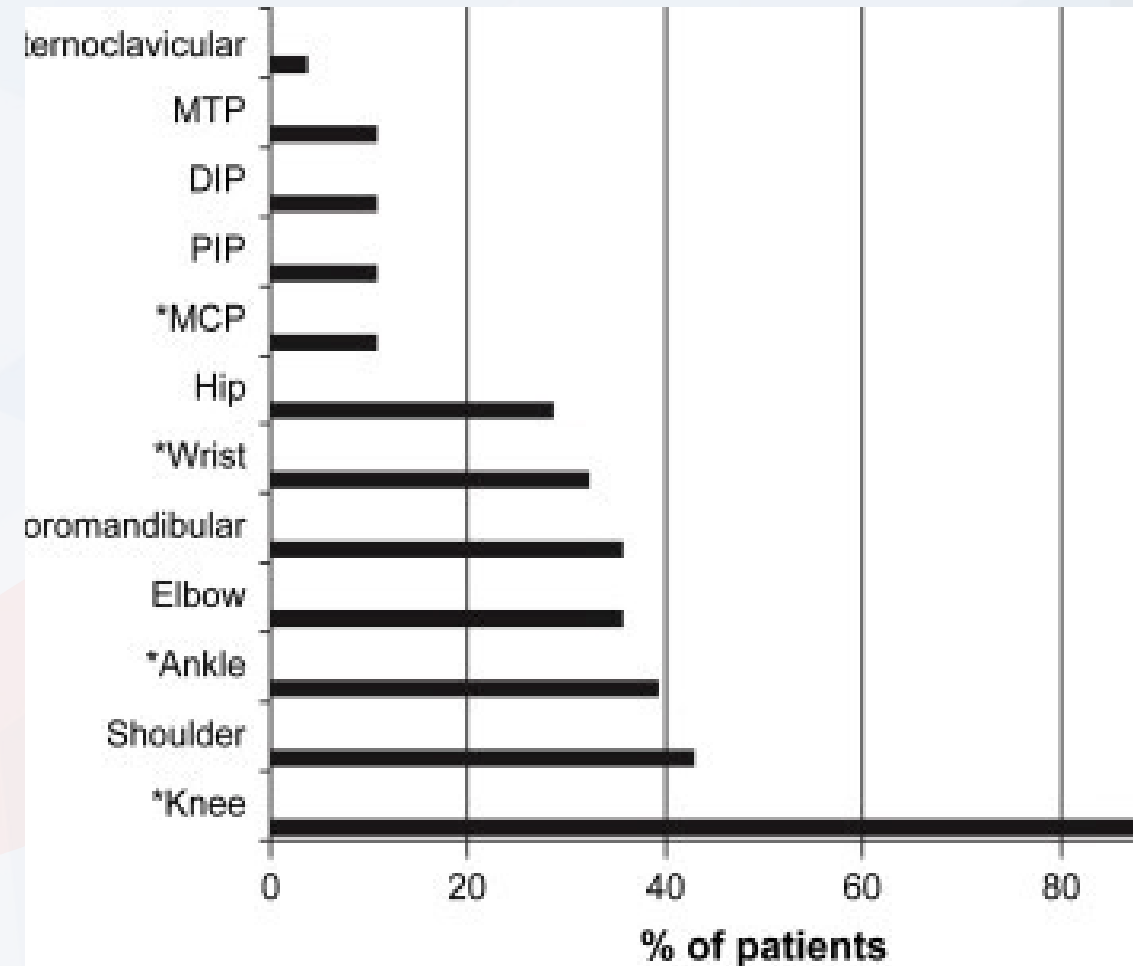
Clinical Presentations of Lyme Arthritis

Occurs **months to years** after infection

Mono or oligoarticular arthritis

60% of *untreated* patients

Migratory (10% persistent)



Therapy for Patients with Disseminated Lyme disease

Indication	2006 Guidelines		2020 Guidelines	
	Route	Duration	Route	Duration
Meningitis	IV	14 (10-28)	Oral or IV	14-21
CN palsy	Oral	14 (14-21)	Oral	14-21
Cardiac	Oral/IV	14 (14-21)	Oral/IV	14-21
Arthritis	Oral	28	Oral	28

YOUR HEALTH

A vaccine for Lyme disease is in its final clinical trial

August 9, 2022 · 12:25 PM ET



“Chronic” Lyme Disease

Chronic Lyme Disease



Post-Lyme Disease Syndrome



Post-Lyme Disease Syndrome

- Persistent symptoms **>2 months** after appropriate treatment
- Occurs in 10-15% of cases
- Constellation of **real but nonspecific symptoms**
 - Arthralgias, myalgias, fatigue, headaches, dizziness, paresthesia
 - Sound familiar????
- Frequency decreases over time
 - 6 months-6%
 - 12 months-4%
- Etiology--? Immunologic; NOT due to latent infection
- No improvement with prolonged antibiotic therapy

Borrelia and HIV Co-Infection

CASE REPORT

Open Access

Severe course of Lyme neuroborreliosis in an HIV-1 positive patient; case report and review of the literature

Nathalie D van Burgel^{1*}, Mayke Oosterloo², Frank P Kroon³, Alje P van Dam⁴

Background

Lyme Neuroborreliosis (LNB) in a human immunodeficiency virus (HIV) positive patient is a rare co-infection and has only been reported four times [1-4]. All published cases are early presentations of Lyme disease and no report of a meningoencephalitis due to *B. burgdorferi* in an HIV patient has been made to date. We present a case of an HIV positive patient that presented with a severe LNB, without any previous sign of Lyme disease.

Lyme Co-infections

CASE REPORT

Babesiosis as a cause of false-positive HIV serology

Mariola Smotrys,¹ Tara Magge,¹ Samer Alkhuja,² Susheer Dilbagh Gandotra¹

- Anaplasmosis
- Babesiosis
- Powassan virus

MAJOR ARTICLE

Persistent and Relapsing Babesiosis in Immunocompromised Patients

Peter J. Krause,^{1,3} Benjamin E. Gewurz,^{6,7} David Hill,^{19,20} Francisco M. Marty,⁶ Edouard Vannier,⁸ Ivo M. Foppa,¹² Richard R. Furman,¹³ Ellen Neuhaus,⁴ Gail Skowron,¹⁵ Shaili Gupta,⁵ Carlo McCalla,¹⁴ Edward L. Pesanti,² Mary Young,¹⁶ Donald Heiman,¹⁷ Gunther Hsue,¹⁸ Jeffrey A. Gelfand,⁷ Gary P. Wormser,¹⁴ John Dickason,¹⁰ Frank J. Bia,⁵ Barry Hartman,¹³ Sam R. Telford III,¹¹ Diane Christianson,^{1,3} Kenneth Dardick,² Morton Coleman,¹³ Jennifer E. Giroto,^{1,3} and Andrew Spielman,^{9,a}



An Illustrative Case

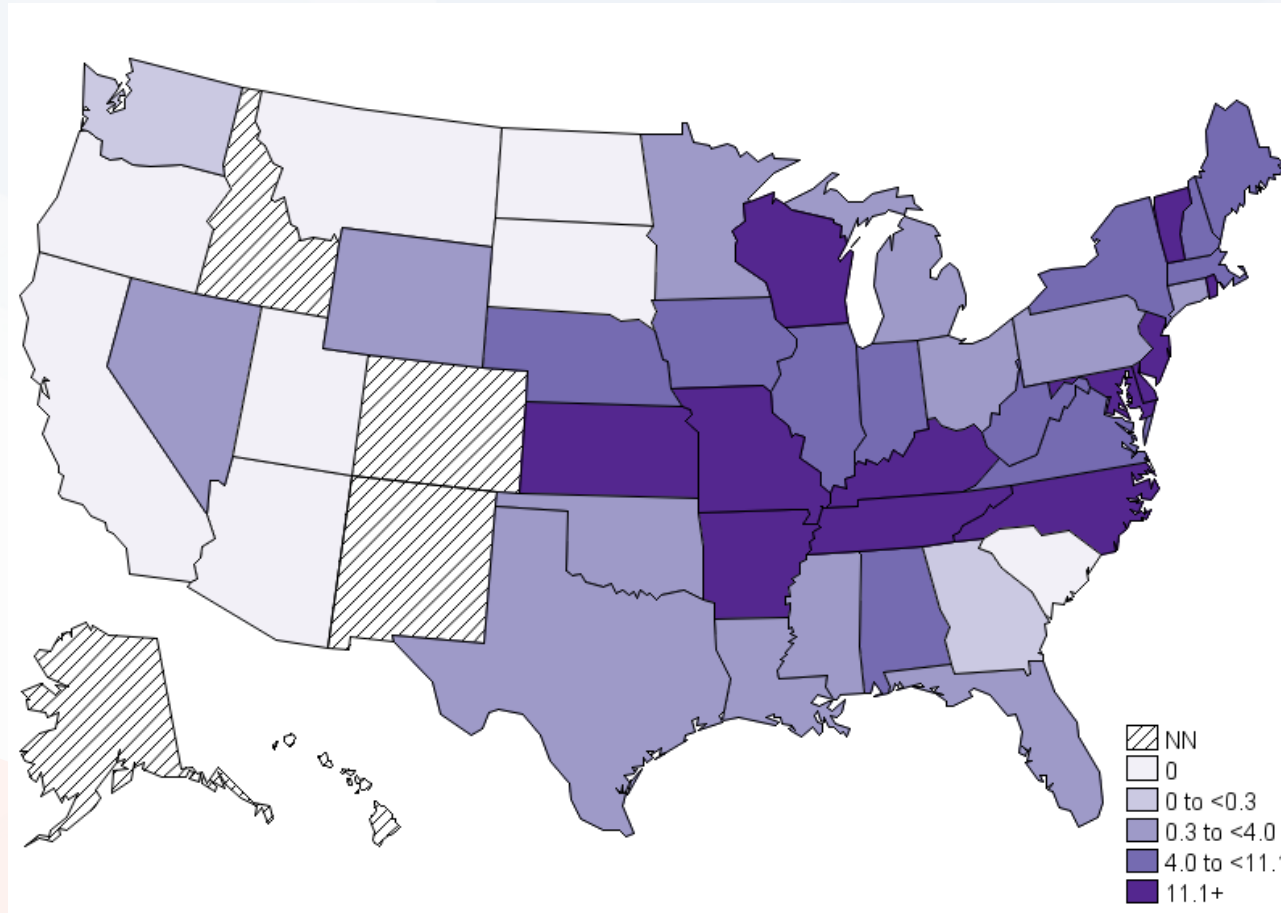


An Illustrative Case

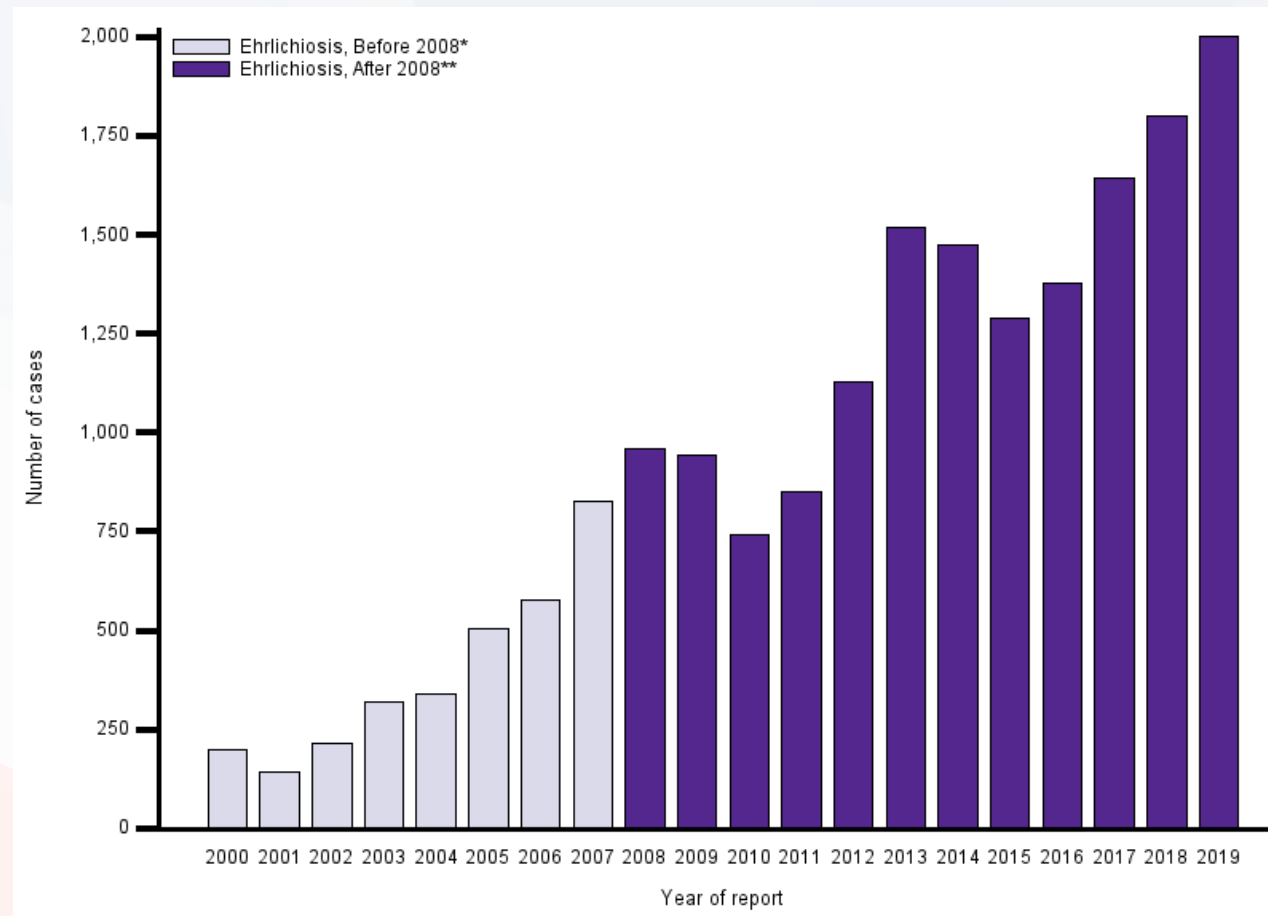
44 yo man with HIV (CD4 220/19%, VL <40) on ART

- Admitted to ICU June 24th with 4 days of fever and HA
- Noted recent tick bites
- Labs: WBC=1.2, plt=26, AST/ALT=424/222
- Ferritin=21,116, LDH=1296, sol IL-2R 8978
- Ehrlichia PCR positive
- Diagnosis: Severe Ehrlichia complicated by HLH

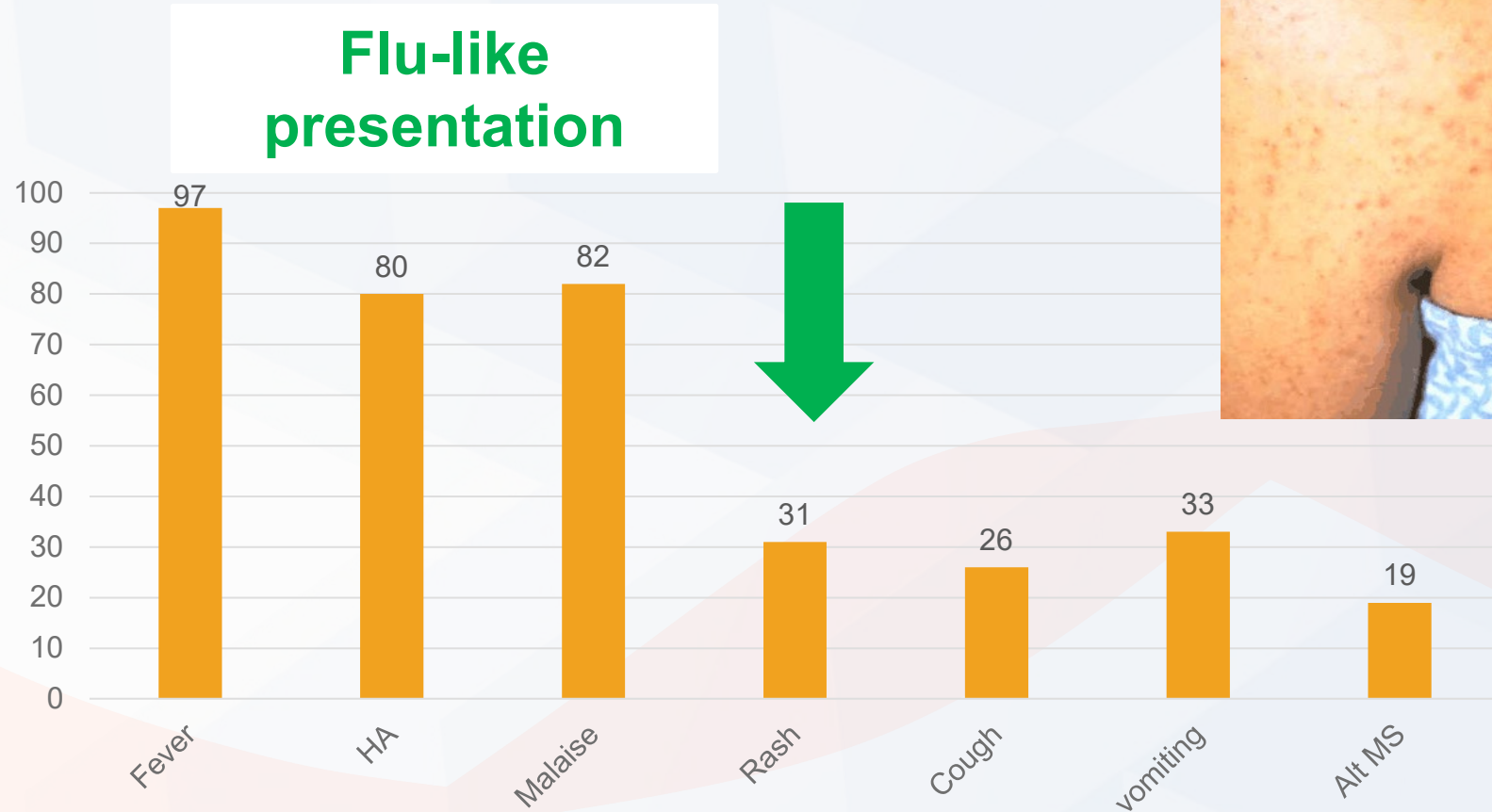
Ehrlichiosis Incidence per million, 2019



Ehrlichiosis, 2000-2019

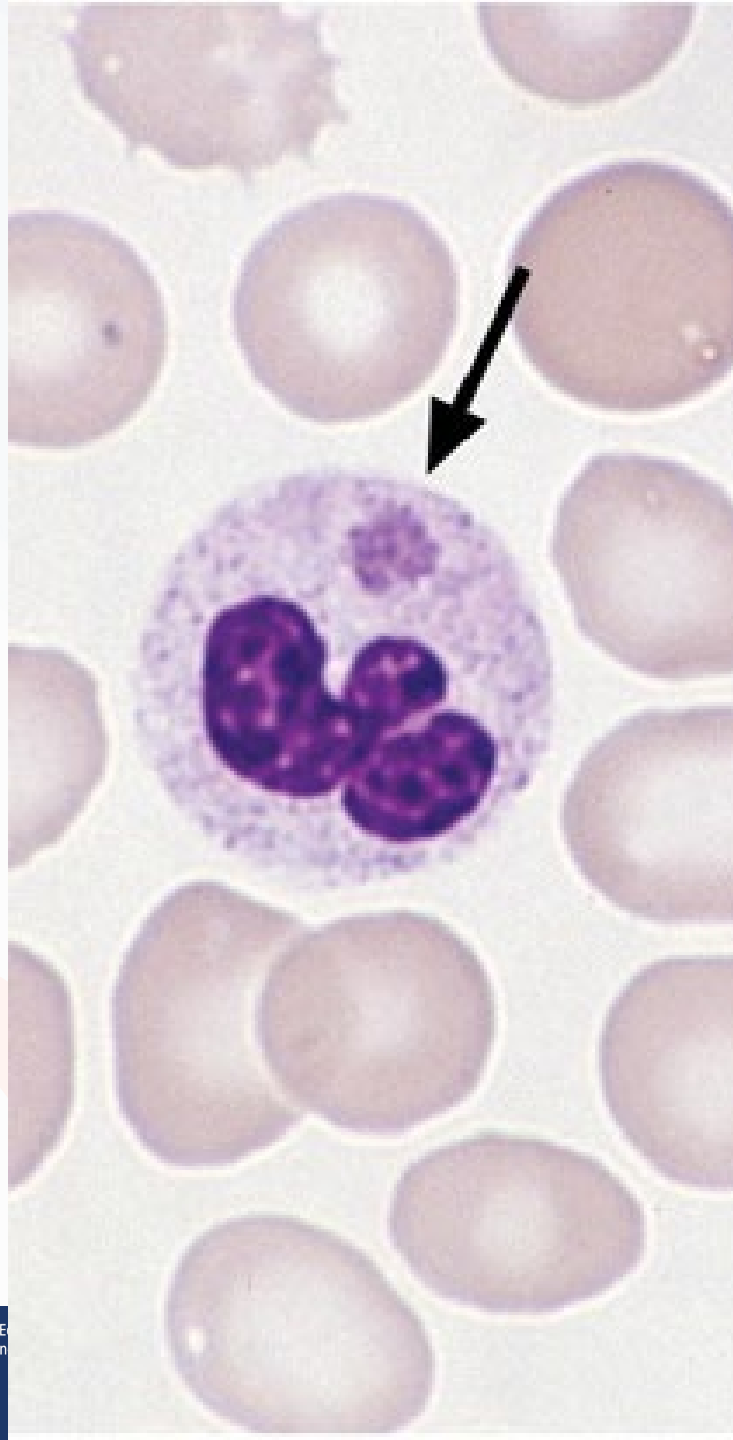


Signs & Symptoms of HME



© Richard Jacobs, MD

Laboratory Findings Suggestive of Ehrlichiosis

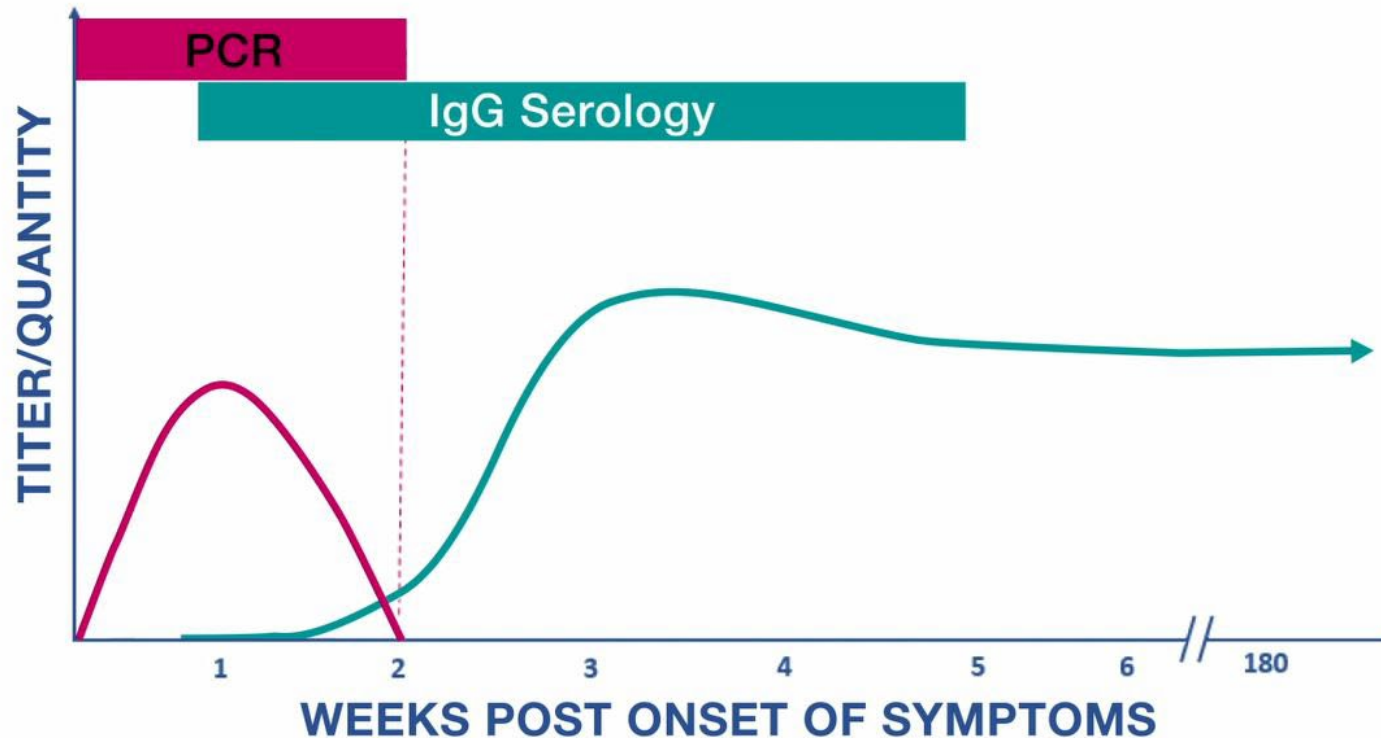


- **Laboratory clues:**
 - Leukopenia
 - Thrombocytopenia
 - Elevated Transaminases

- **Buffy coat smear ~20%**

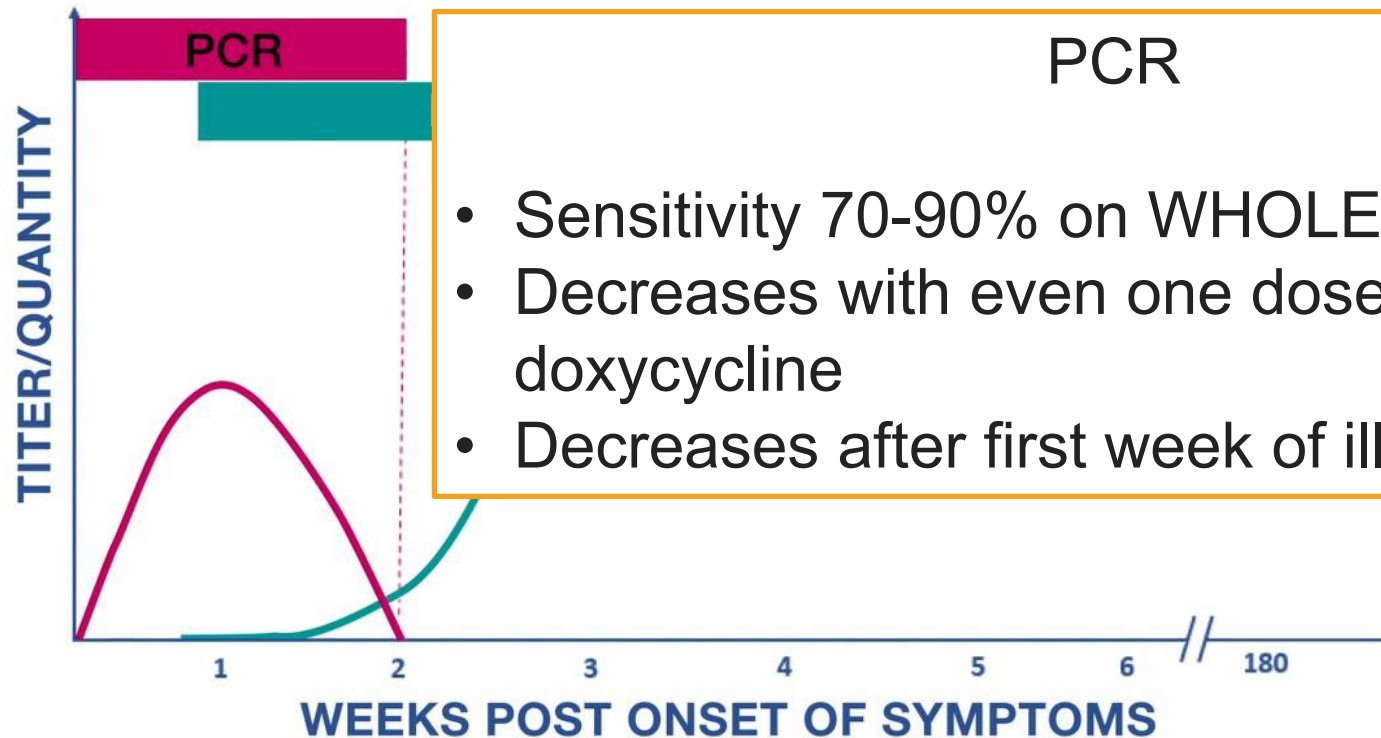
Diagnosis: Time is of the Essence!

Timing of diagnostic assays



Diagnosis: Time is of the Essence!

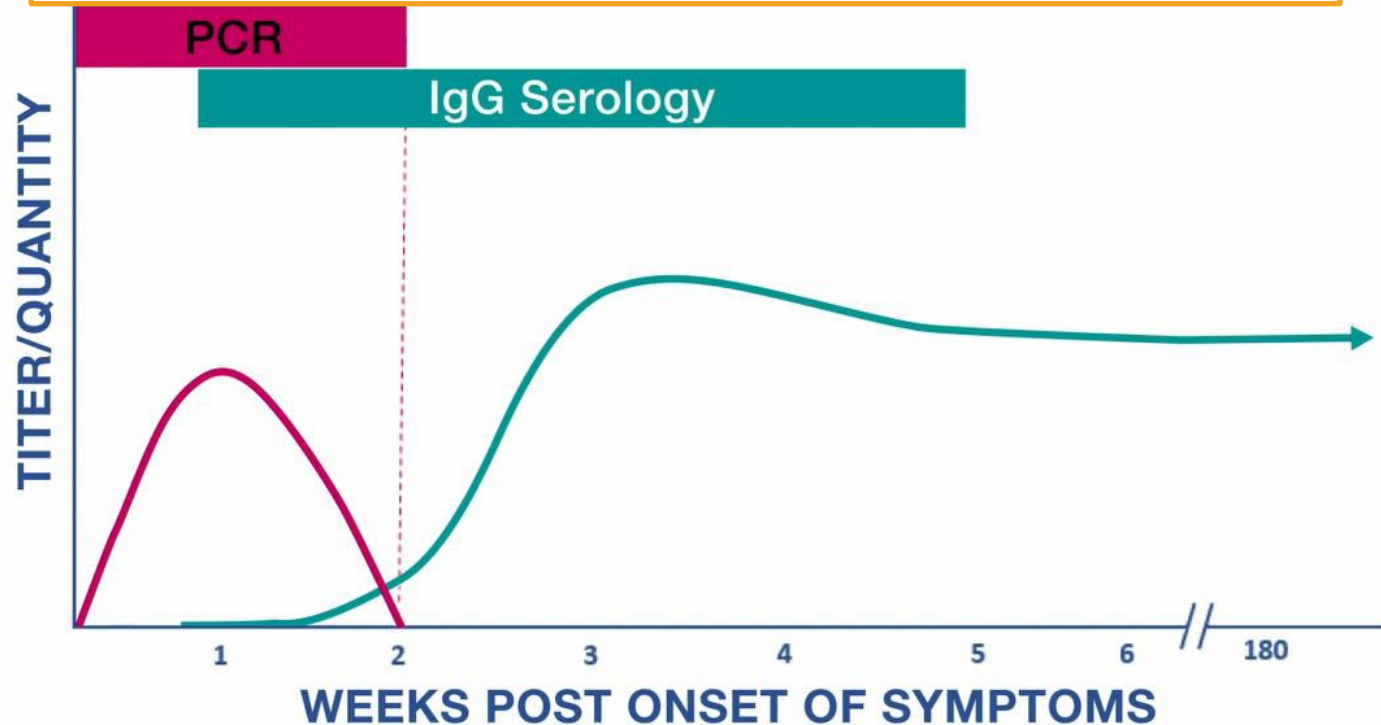
Timing of diagnostic assays



Diagnosis: Time is of the Essence!

Preferred Assay is IFA IgG

- Acute sensitivity: ~30%
- Convalescent sensitivity: >90%



Diagnosis of Ehrlichiosis

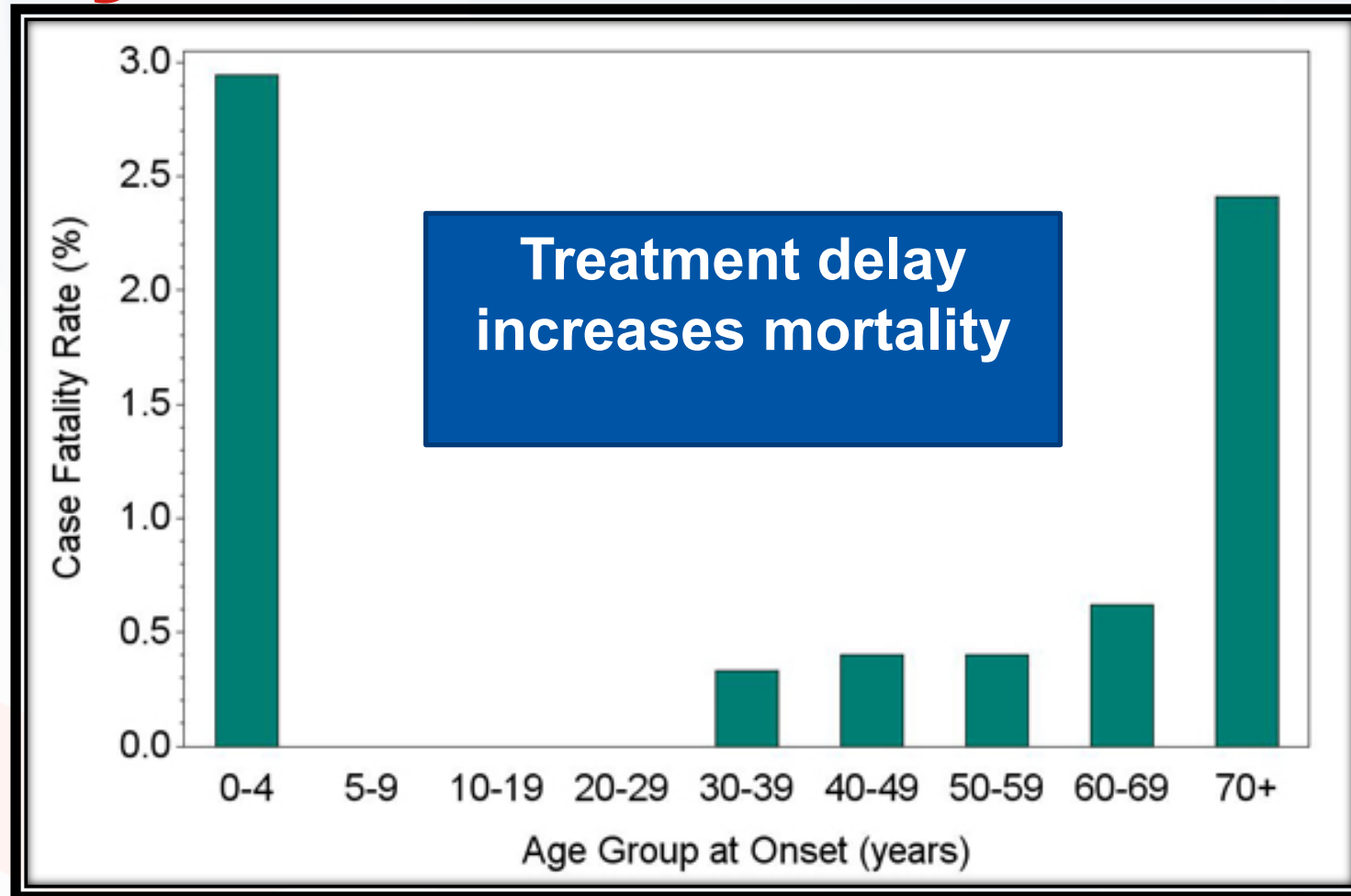
PCR is imperfect

Serology confirmatory late

Treat *regardless* of test results if clinically consistent

Treatment: Doxycycline x 7-14 days

Mortality of Ehrlichiosis



ORIGINAL ARTICLES

www.jpeds.com • THE JOURNAL OF PEDIATRICS

No Visible Dental Staining in Children Treated with Doxycycline for Suspected Rocky Mountain Spotted Fever

Suzanne R. Todd, DVM¹, F. Scott Dahlgren, MSPH¹, Marc S. Traeger, MD², Eugenio D. Beltrán-Aguilar, DMD, DrPH¹, Donald W. Marnette, DDS³, Charlene Hamilton, MPH⁴, Jennifer H. McQuiston, DVM¹, and Joanna J. Regan, MD¹

Objective To evaluate whether cosmetically relevant dental effects occurred among children who had received doxycycline for treatment of suspected Rocky Mountain spotted fever (RMSF).

Study design Children who lived on an American Indian reservation with high incidence of RMSF were classified as exposed or unexposed to doxycycline, based on medical and pharmacy record abstraction. Licensed, trained dentists examined each child's teeth and evaluated visible staining patterns and enamel hypoplasia. Objective tooth color was evaluated with a spectrophotometer.

Results Fifty-eight children who received an average of 1.8 courses of doxycycline before 8 years of age and who now had exposed permanent teeth erupted were compared with 213 children who had never received doxycycline. No tetracycline-like staining was observed in any of the exposed children's teeth (0/58, 95% CI 0%-5%), and no significant difference in tooth shade ($P = .20$) or hypoplasia ($P = 1.0$) was found between the 2 groups.

Conclusions This study failed to demonstrate dental staining, enamel hypoplasia, or tooth color differences among children who received short-term courses of doxycycline at <8 years of age. Healthcare provider confidence in use of doxycycline for suspected RMSF in children may be improved by modifying the drug's label. (*J Pediatr* 2015;166:1246-51).

Tetracycline-class antibiotics (tetracyclines) once were used widely to treat a variety of infections in children, but studies beginning in the 1950s showed a link between their use in young children and staining and enamel hypoplasia of developing teeth.^{1,2} Tetracyclines bind to calcium, which can lead to yellow, gray, and brown staining of developing teeth if administered during tooth crown calcification, which most commonly occurs between birth and the age of 8 years for most permanent teeth except third molars.² Previous studies of children who received tetracyclines during odontogenesis showed visible staining in 23%-92% (Table 1).³⁻⁷ Because of these findings, the Food and Drug Administration requires that all tetracyclines, including doxycycline, carry a label warning that the medication should not be used in children under the age of 8 years because of concerns about dental staining, unless no other effective antibiotics exist.⁸

Doxycycline, a newer medication in the tetracycline class, has been available since 1967 and binds to calcium less readily than other tetracyclines.⁹ There are no published studies linking doxycycline to dental staining when used at the dose and duration recommended for treating rickettsial diseases. A study in 1969 reported possible faint staining of a single deciduous tooth in 1 of 25 pre-term infants treated with doxycycline; however, dose and duration were not provided, and the authors concluded staining was negligible compared to other tetracyclines.¹⁰ Several past studies have looked for evidence of visible dental staining in



Doxycycline saves lives!

A good reason to smile: New research shows NO evidence of tooth staining from short courses of doxycycline.

Doxycycline is the best treatment for suspected rickettsial infections in patients of all ages.



Click to learn more.



Doxycycline Use in Children



HIV and Ehrlichia Co-Infection



Original Investigation | Infectious Diseases

Assessment of Risk Factors and Outcomes of Severe Ehrlichiosis Infection

Kevin Kuriakose, MD; April C. Pettit, MD, MPH; Jonathan Schmitz, MD, PhD; Abelardo Moncayo, PhD; Karen C. Bloch, MD, MPH

Table 1. Demographic and Clinical Characteristics of 155 Patients With Ehrlichiosis

Characteristic	ICU care, No. (%)		P value
	Yes (n = 43 [27.7%])	No (n = 112 [72.3%])	
Demographic characteristics			
Age, median (IQR), y	45 (15-60)	51 (27-65)	.23
Sex			
Women	19 (44.2)	37 (33.0)	.19
Men	24 (55.8)	75 (67.0)	.19
Race			
Non-Hispanic			
White	39 (90.7)	106 (94.6)	
Black	2 (4.7)	3 (2.7)	.59
Hispanic	1 (2.3)	2 (1.8)	
Asian	1 (2.3)	1 (0.9)	
Clinical characteristics			
Immunosuppression*	9 (20.9)	47 (42.0)	.02
HIV with CD4 ⁺ cell count, / μ L			
≤200	3 (7.0)	3 (2.7)	
>200	0	10 (8.9)	
Received prednisone, ≥20 mg/d, or equivalent	0	5 (4.5)	
Organ transplant	3 (7.0)	24 (21.4)	
Baseline neutropenia	1 (2.3)	3 (2.7)	
Systemic chemotherapy	0	7 (6.3)	
Splenectomy	1 (2.3)	1 (0.9)	
Azathioprine	1 (2.3)	1 (0.9)	
Methotrexate	1 (2.3)	3 (2.7)	
Charlson Comorbidity Index level ≥4	16 (37.2)	31 (27.7)	.25
Trimethoprim plus sulfamethoxazole within the previous 2 wk	17 (39.5)	38 (33.9)	.51
Self-reported tick exposure	26 (60.5)	88 (80.7) ^b	.009

A patient with fever, low WBC, low platelets, high LFTs but *Ehrlichia* PCR is negative and no response to doxycycline at day 3?



The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

A New Phlebovirus Associated with Severe Febrile Illness in Missouri

Laura K. McMullan, Ph.D., Scott M. Folk, M.D., Aubree J. Kelly, M.S., Adam MacNeil, Ph.D., Cynthia S. Goldsmith, M.G.S., Maureen G. Metcalfe, B.S., Brigid C. Batten, M.P.H., César G. Albariño, Ph.D., Sherif R. Zaki, M.D., Ph.D., Pierre E. Rollin, M.D., William L. Nicholson, Ph.D., and Stuart T. Nichol, Ph.D.

HRTV → Lone Star Tick

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First Detection of Heartland Virus (Bunyaviridae: *Phlebovirus*) from Field Collected Arthropods

Harry M. Savage,* Marvin S. Godsey Jr., Amy Lambert, Nicholas A. Panella, Kristen L. Burkhalter,
Jessica R. Harmon, R. Ryan Lash, David C. Ashley, and William L. Nicholson

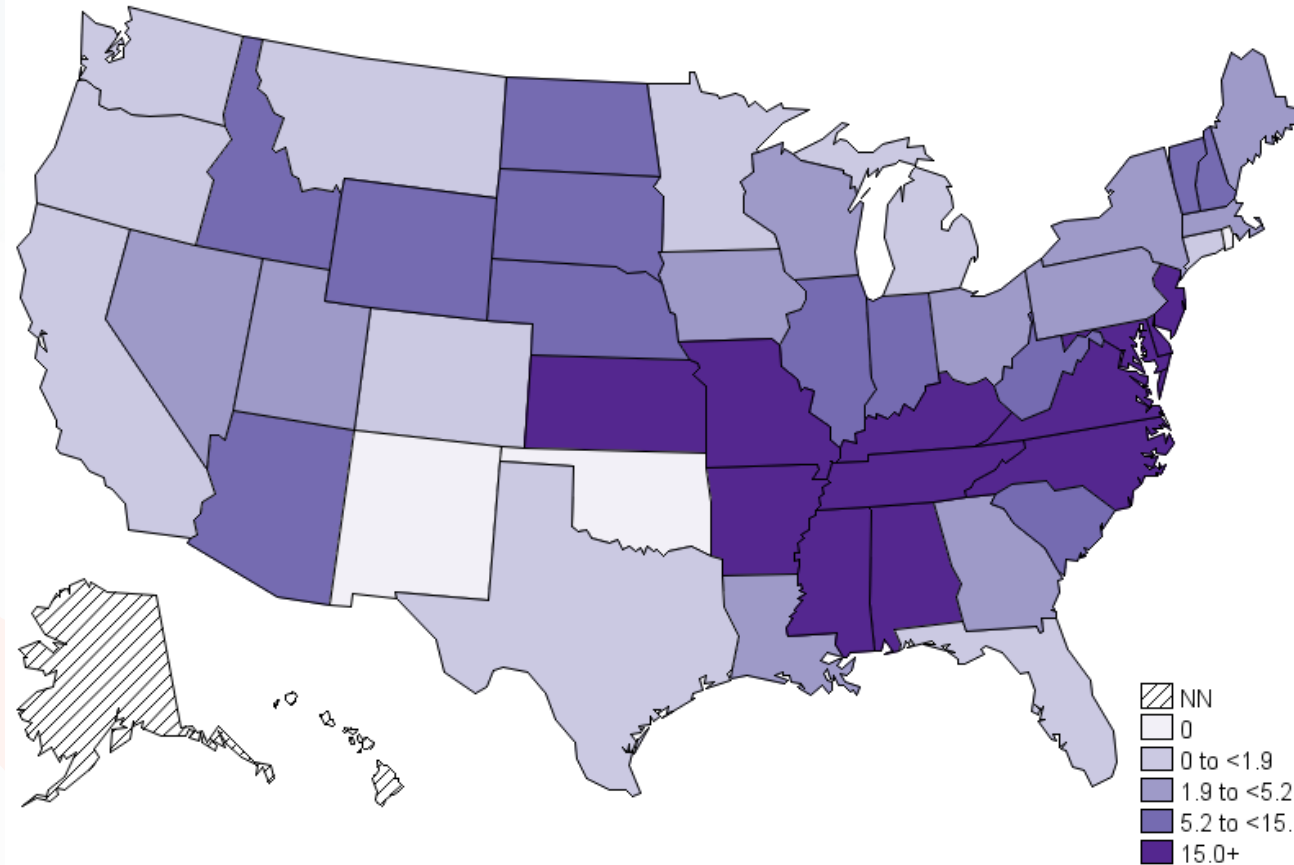
*Centers for Disease Control and Prevention, Fort Collins, Colorado; Centers for Disease Control and Prevention, Atlanta, Georgia;
Department of Biology, Missouri Western State University, St. Joseph, Missouri*

FIGURE. Heartland virus has been found in the Lone Star tick (*Amblyomma americanum*)



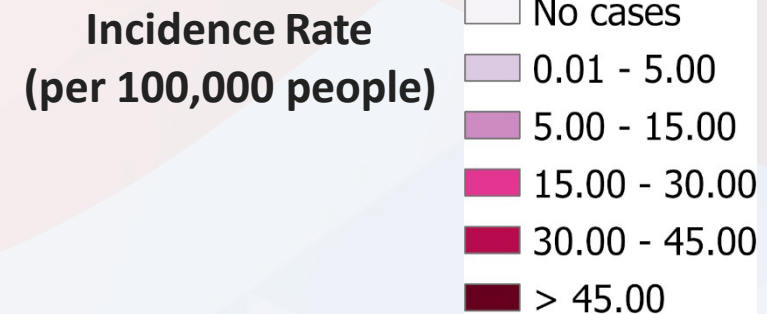
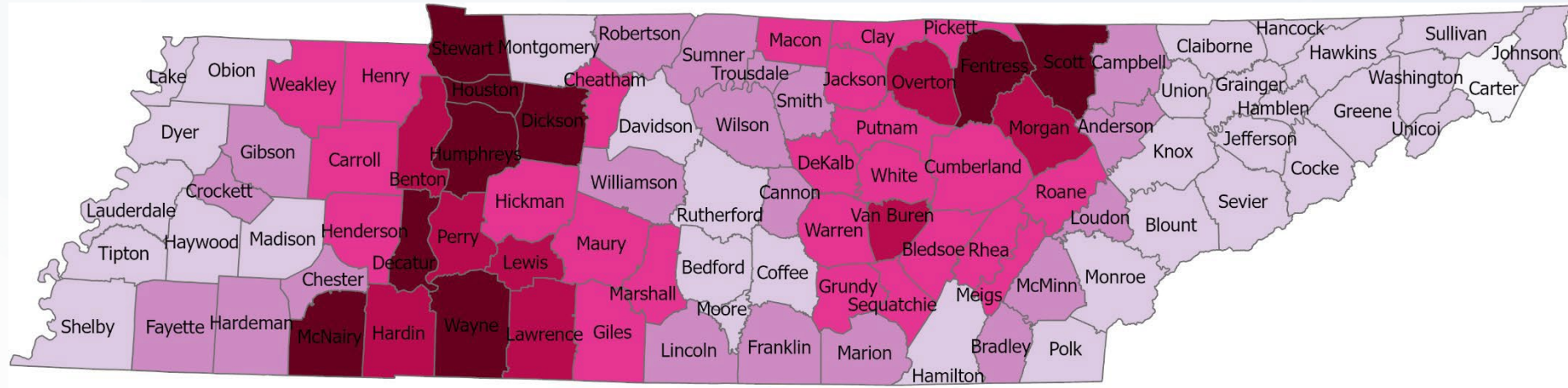
...tick...tick...tick...

Annual Incidence Spotted Fever Rickettsiosis, 2019

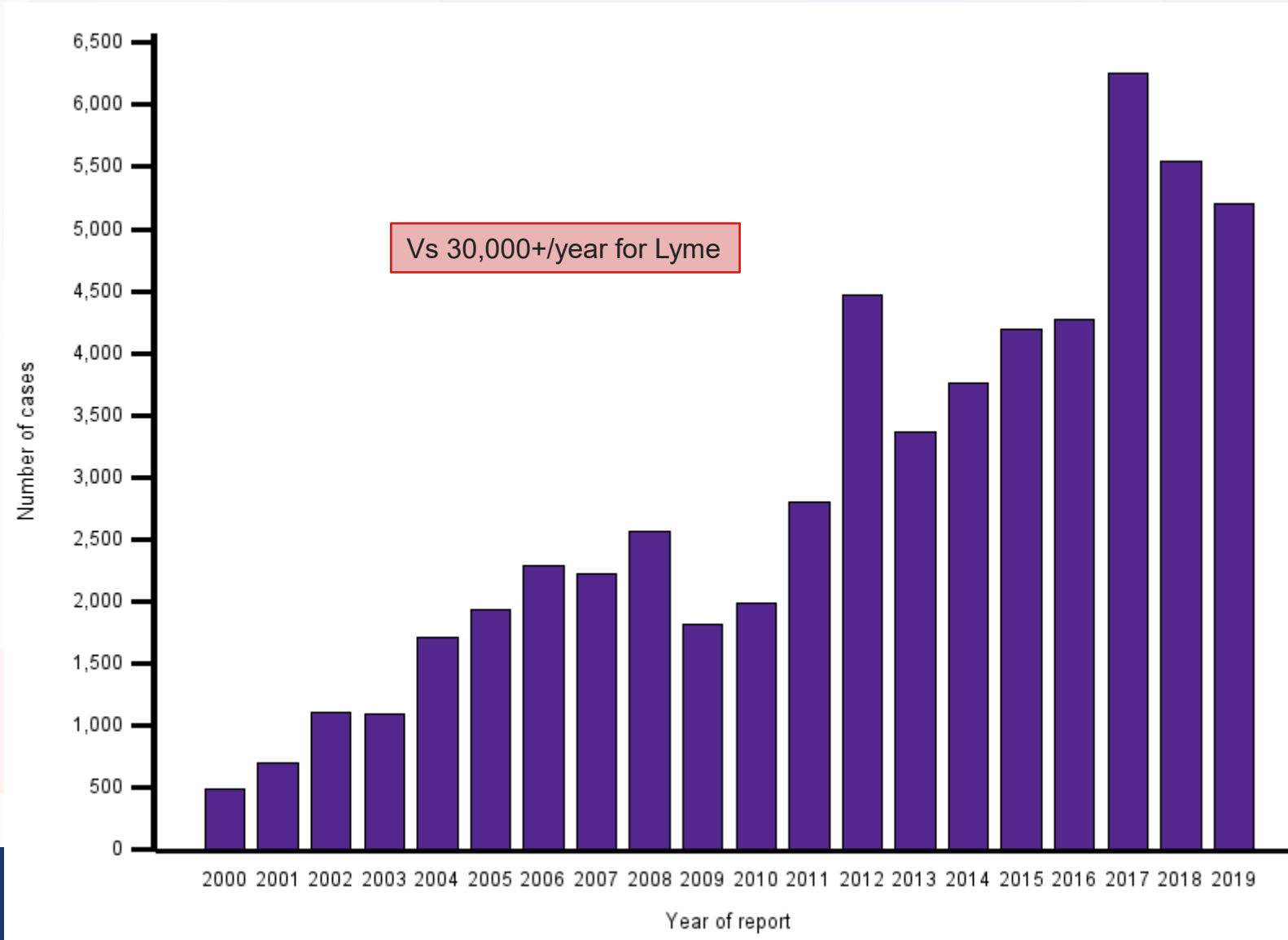


- **RMSF**
- *R. parkeri*
- Pacific Coast tick fever
- Rickettsial pox

SFR Incidence Rate (per 100k) in TN (2011–2021)



Cases of SFR, 2000-2019



RMSF: The Vector

- American dog tick
- Tick attachment ≥ 6 hours required for transmission
- Symptom onset 7 days (range, 2-14 days) after tick bite



RMSF: A Diagnostic Challenge

Classic triad

- Fever-98-100%
- Headache 60-90%
- Rash-80-95%



Days from onset	Signs and symptoms (untreated)
1-2	<ul style="list-style-type: none"> • Fever • Headache, myalgias, malaise (flu-like)
2-4	<ul style="list-style-type: none"> • Rash • Abdominal pain, n/v • Cough • Edema
5-7	<ul style="list-style-type: none"> • High grade fever • Rash becomes petechial
7-9	<ul style="list-style-type: none"> • Purpura fulminans • Sepsis, AKI, ARDS • Meningoencephalitis, coma

Early Macular Rash of RMSF (d2-4)



Petechial Rash of RMSF (day 5-6)

Palms & soles involved in ~50%

Gangrene in ~5% of cases

Absence of rash: Elderly and dark-skinned patients

Atypical or absent rash associated with treatment delay and increased mortality



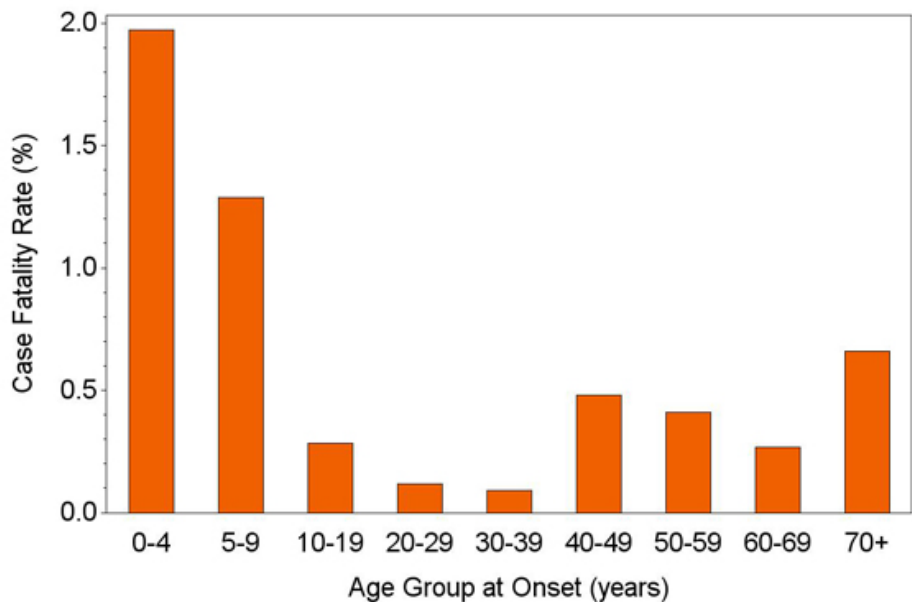
Diagnostic Testing for SFR

Test	SFGR
Acute Serology	15%
Convalescent serology	>90%
Skin biopsy IHC/PCR	70-90%

- **Serologic diagnosis pitfalls**
 - Serology may be negative early
 - IgM less specific and less sensitive (Isolated IgM >1 month false positive)
 - Titers can remain elevated for months or longer (no role for trending)
 - Paired serum samples, 2–4 weeks apart are the most sensitive confirmatory test

Empiric Treatment for SFR

Case Fatality Rate of Spotted Fever Rickettsiosis by Age Group, 2008-13



Age <10 years: 6% cases, 22% deaths

National tx survey of RMSF, 2012

80% rx doxycycline to patients ≥ 8 years vs 35% patients <8 years due to concern for dental toxicity

Time to death of untreated RMSF is 8 days

EMPIRIC treatment with doxycycline can be life-saving at any age!!!

Not all Tick-borne Disease is Infectious....



Tick-Associated Red Meat Allergy

- Galactose-alpha 1,3-galactose (alpha gal) present in tick saliva and red meat
- Human IgE production stimulated by meat consumption
- Symptoms:
 - Hives or skin rash
 - GI: nausea, stomach cramps, indigestion, vomiting, diarrhea
 - Stuffy/runny nose, sneezing
 - Bronchospasm/anaphylaxis



Diagnosis of Alpha-Gal Allergy

**IgE Alpha Gal
immunoassay,
or.....**



Treatment Alpha-Gal Allergy



Summary of Tickborne Disease in SE

- **Lyme:**
 - Emerging infection
 - EM rash: No test needed (just treat)
 - Neuro/cardiac/rheum findings: 2-stage test (EIA +/-equiv→WB or 2nd EIA)
 - WHO to test (and not test) is as important as HOW to test
 - No "test of cure" with repeat titers
- **Ehrlichiosis**
 - Nonspecific presentation, low WBC/plt, high LFTs
 - Early: Whole blood PCR (ideally pre-antibiotics)
 - >1 week: Serology by IgG (ideally paired—4-fold increase diagnostic)
 - IgM insensitive and nonspecific
 - No "test of cure" with repeat titers
 - If on differential, treat empirically (don't wait for lab confirmation)
 - Doxycycline for all ages!

Summary of Tickborne Disease in SE

■ SPR/RMSF

- Nonspecific presentation—RASH 3-5 days after onset of fever
- Rash may be absent in dark skinned/elderly
- Suggestive labs: Low plts, high LFTs
- >1 week: Serology by IgG (ideally paired—4-fold increase diagnostic)
- IgM insensitive and nonspecific
- No “test of cure” with repeat titers
- If on differential, treat empirically (don’t wait for lab confirmation)
- **Doxycycline for all ages!**



Questions?