

Epidemiology and Clinical Features of Lyme Disease

Clinician Outreach and Communication Activity (COCA) Conference Call March 6, 2012

Objectives

At the conclusion of this session, the participant will be able to accomplish the following:

- ❑ **Describe populations at risk of contracting Lyme disease in the United States**
- ❑ **Describe the early signs and symptoms of Lyme disease**
- ❑ **Understand the appropriate use of serologic tests**
- ❑ **Advise patients on personal protective measures against tick bites**

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Today's Presenter



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Centers for disease Control and Prevention

Lyme Disease: Epidemiology and Clinical Features



Alison Hinckley, PhD
Division of Vector-Borne Diseases
National Center for Emerging and Zoonotic Infectious Diseases
March 6, 2012

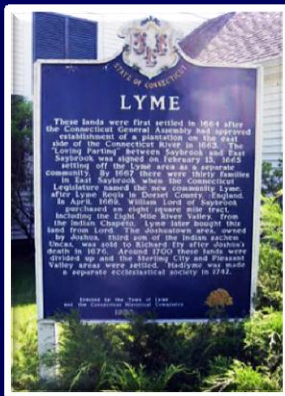
Overview

- Lyme disease background
- Epidemiology
- Clinical features
- Laboratory diagnosis
- Treatment
- Prevention
- Resources for clinicians and health departments

BACKGROUND

Lyme borreliosis in the United States

- ❑ 1976 Steere *et al.* investigated a cluster of juvenile and adult arthritis cases in Connecticut
- ❑ Soon recognized as late manifestation of multi-system disease associated with tick bite in US and Europe
- ❑ 1981 Burgdorfer *et al.* isolated spirochete from *Ixodes* ticks, then patients with erythema migrans



Borrelia burgdorferi sensu lato

| | North America | Europe | Continental Asia | Japan |
|-----------------------|---------------|--------|------------------|-------|
| <i>B. andersonii</i> | X | | | |
| <i>B. bissettii</i> | X | X? | | |
| <i>B. burgdorferi</i> | X | X | | |
| <i>B. afzelii</i> | | X | | |
| <i>B. garinii</i> | | X | | |
| <i>B. spielmanii</i> | | X | | |
| <i>B. lusitaniae</i> | | X | | |
| <i>B. valaisiana</i> | | X | X | |
| <i>B. sinica</i> | | | X | |
| <i>B. japonica</i> | | | | X |
| <i>B. tanukii</i> | | | | X |
| <i>B. turdae</i> | | | | X |

X—Known cause of human illness

Biology of *B. burgdorferi*

- ❑ Motile, spiral shaped bacterium
- ❑ Numerous outer-surface proteins (OSPs)
 - Roles in transmission and pathogenesis
 - Some differentially expressed
 - VlsE, undergoes antigenic variation



Blacklegged Tick Life Stages

Blacklegged Tick (*Ixodes scapularis*)



adult
female



adult
male



nymph



larva



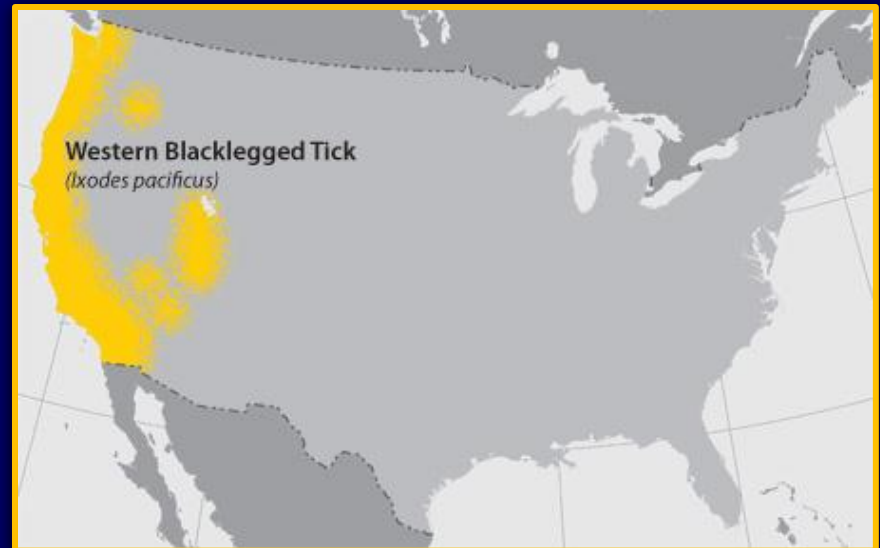
Blacklegged tick nymph and adult

Distribution of Lyme Disease Vectors in U.S.



Ixodes scapularis

Ixodes pacificus



Enzootic Cycles in North America

WEST

EAST

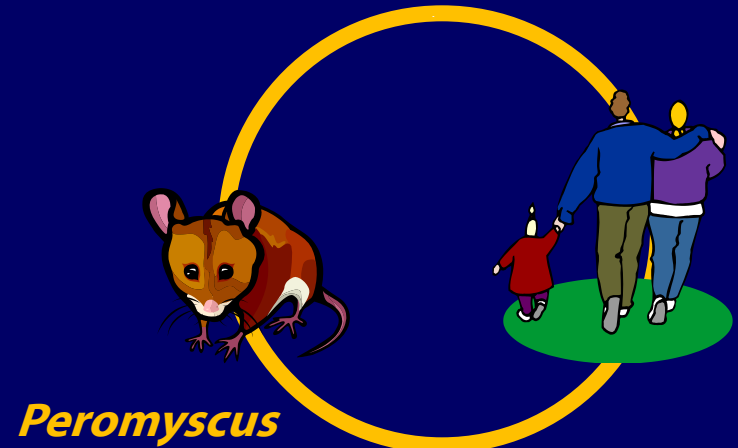
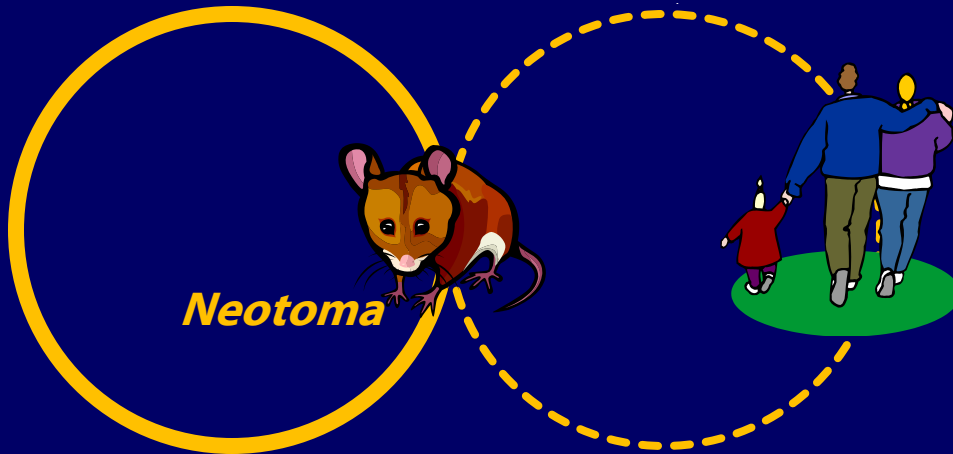
I. neotomae



I. pacificus

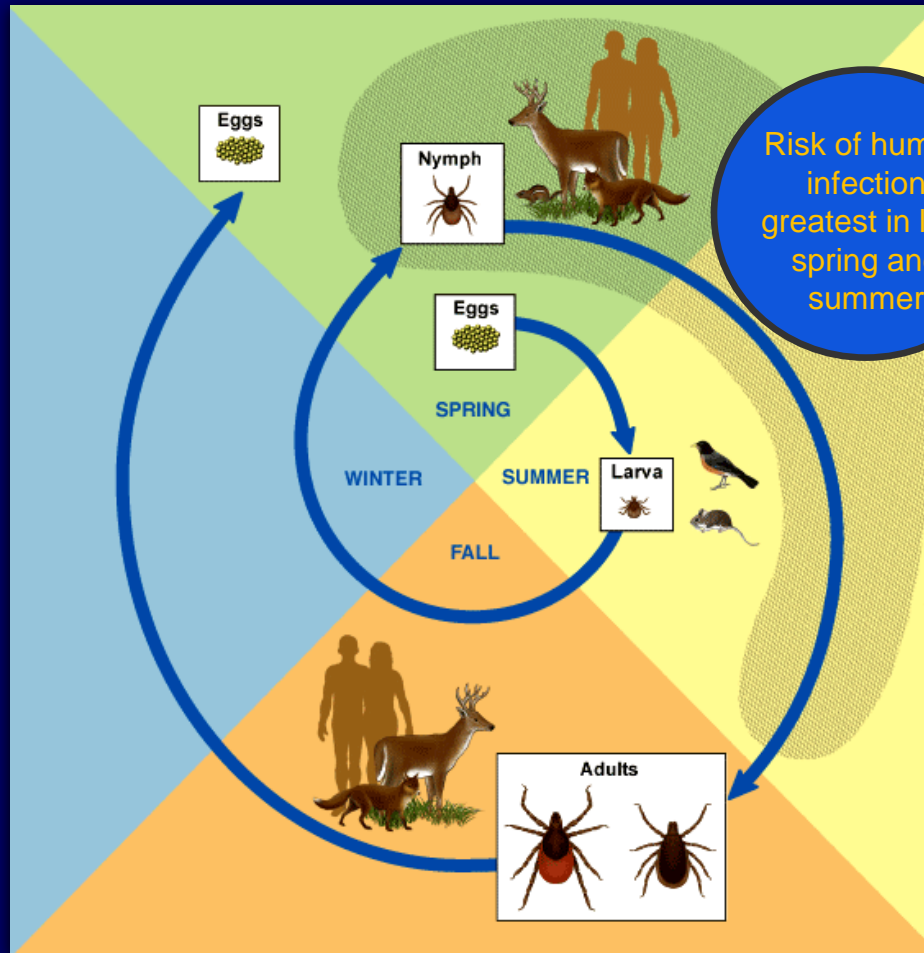


I. scapularis

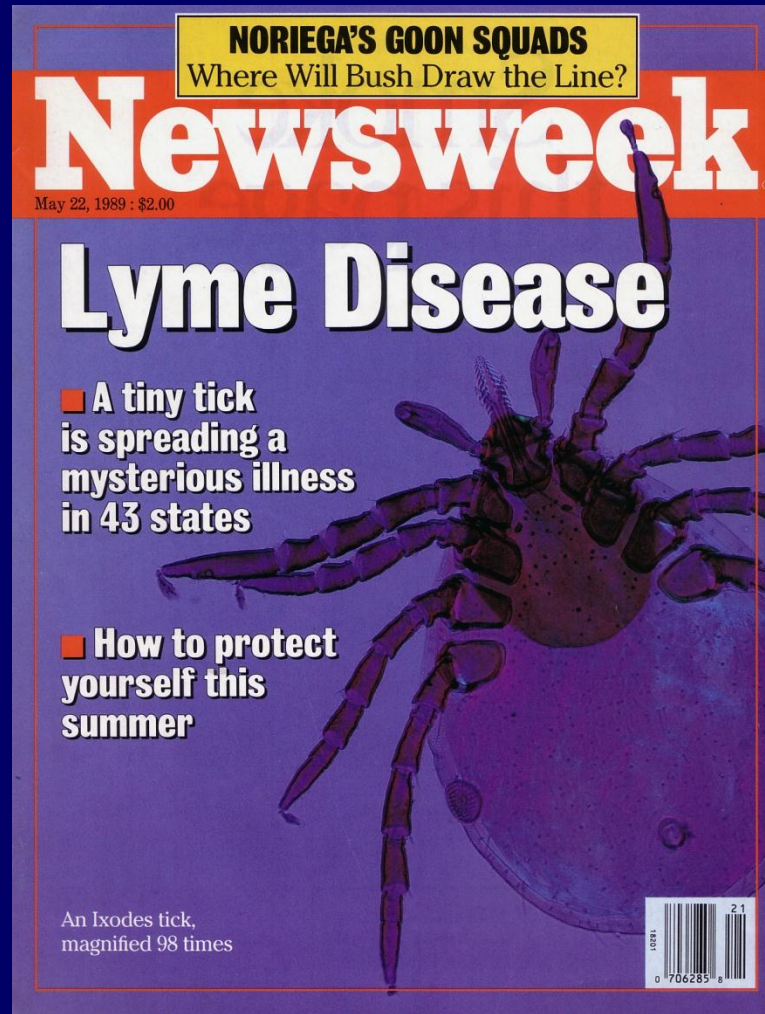


Adapted from Science 1992;256:1385

Lyme Disease Transmission Cycle



Lyme Disease in Popular Media



Tickborne Disease—Emergence in the U.S.



**From: Kirby Stafford, Tick Control Handbook, Connecticut
Agricultural Experiment Station**

Lyme Disease Emergence and Changing Land Use Patterns (1860s – 1980s)



**Chipman Hill,
Middlebury, VT, 1860s**



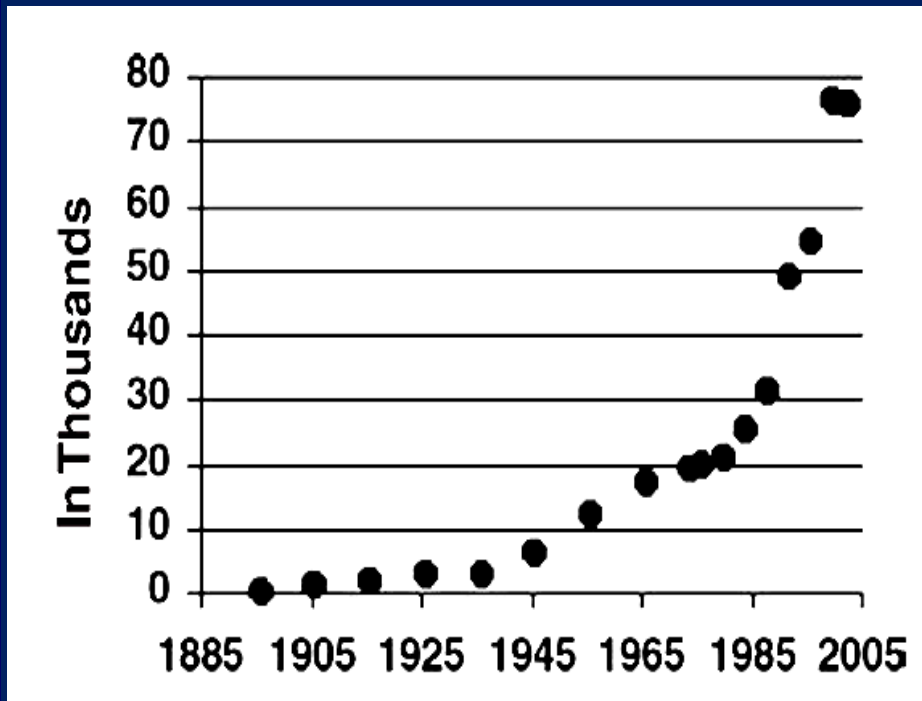
Chipman Hill, 1900s



Chipman Hill, 1980s

Source: Henry Sheldon Museum - <http://henrysheldonmuseum.org>

Deer Populations in Connecticut , 1885-2005

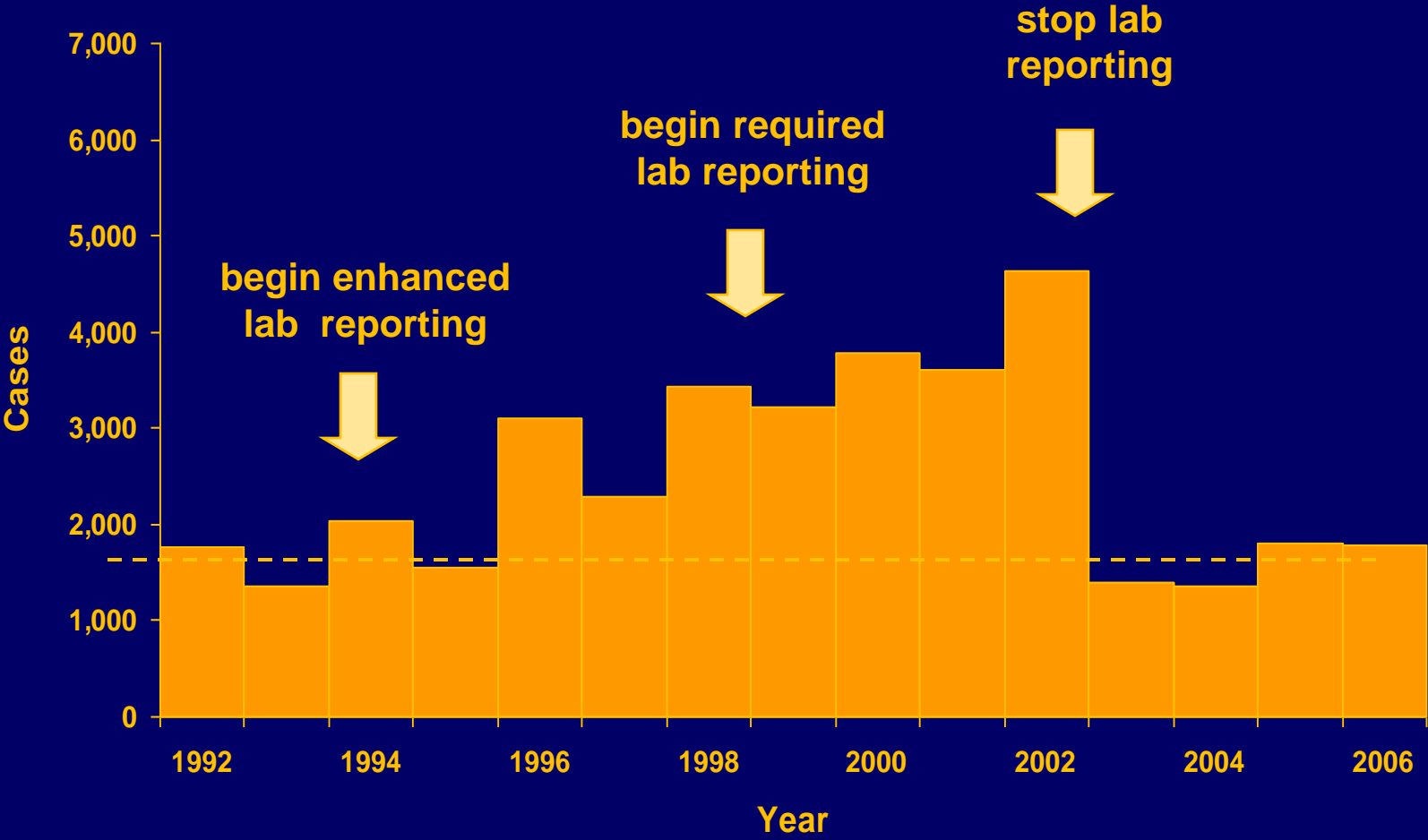


From: Kirby Stafford, Tick Control Handbook,
Connecticut Agricultural Experiment Station

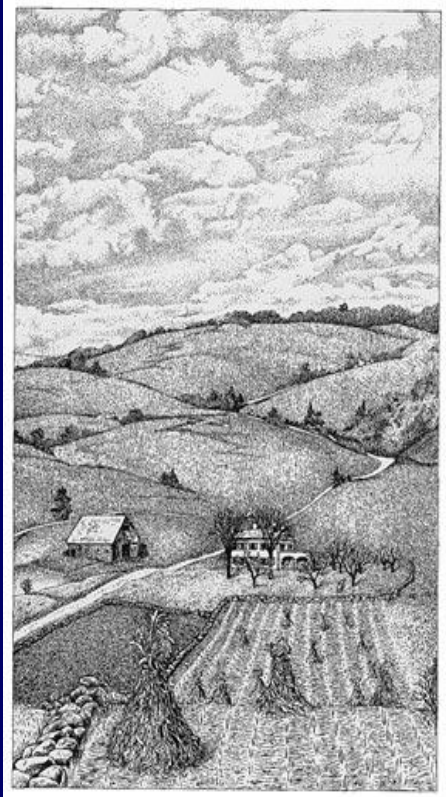
Suburbanization of Reforested Areas



Reported Lyme Disease Cases, Connecticut 1992-2006



Tickborne Disease Emergence – Re-emergence in the U.S.



Source:

Bald hills: New England before the trees returned. From *Thoreau's Country*.

American Scientist Online

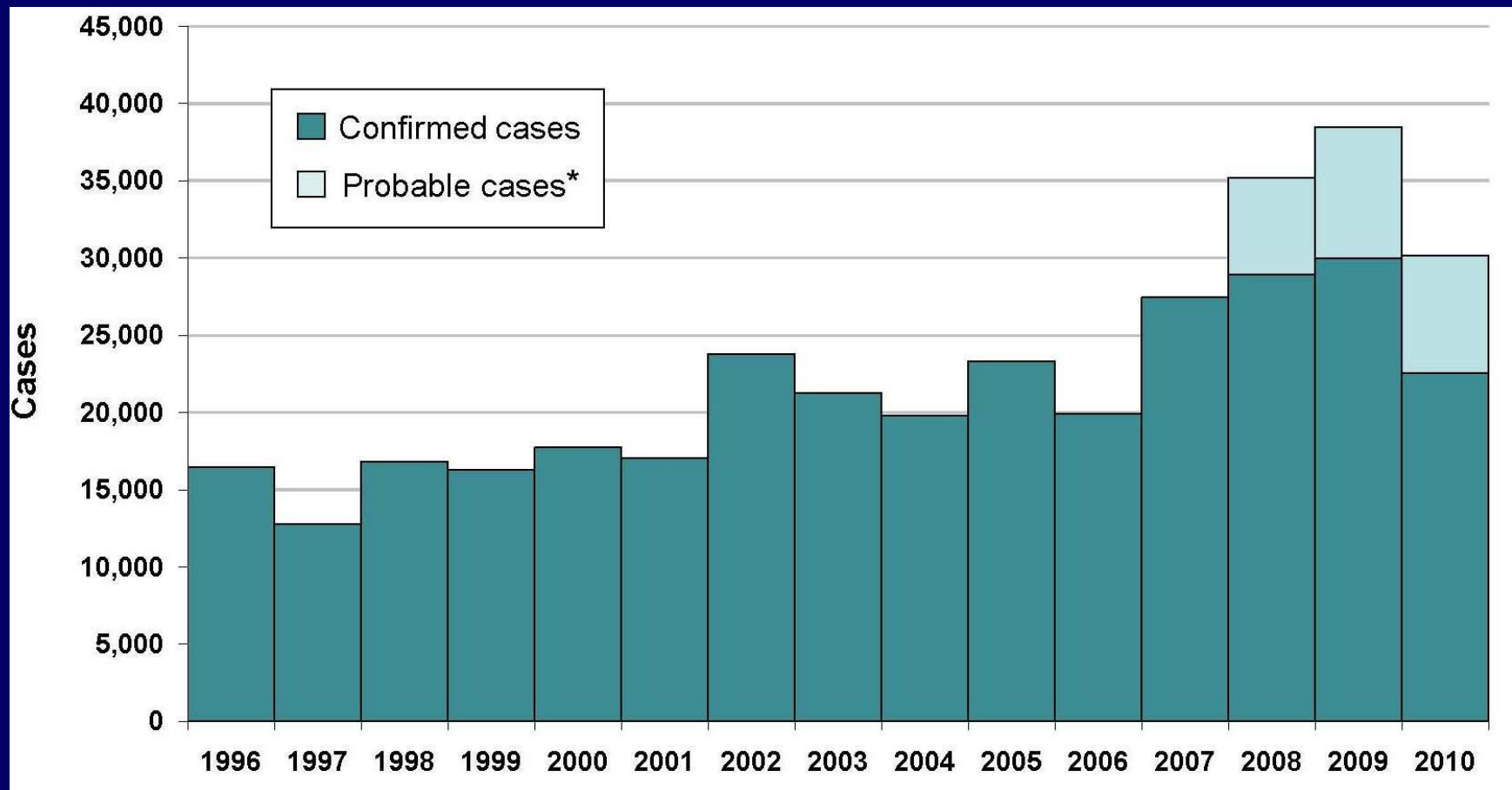
[Http://www.americanscientist.org](http://www.americanscientist.org)

- Reforestation
- Overabundant deer
- Increased numbers of ticks
- Expansion of suburbia into wooded areas
- Increased exposure opportunities
- Changes in diagnostic, surveillance, and reporting practices



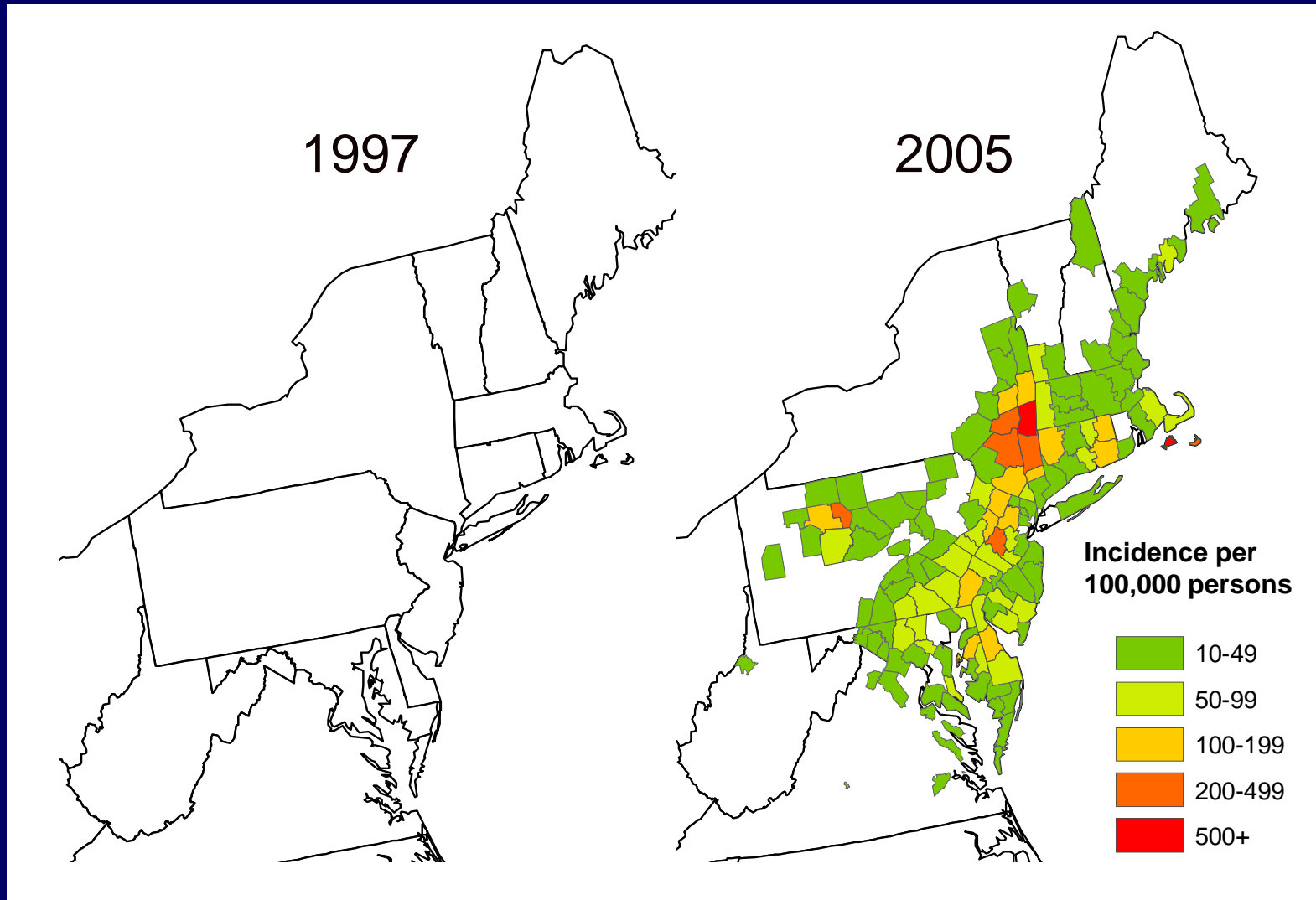
EPIDEMIOLOGY

Reported Lyme Disease Cases, U.S., 1996-2010

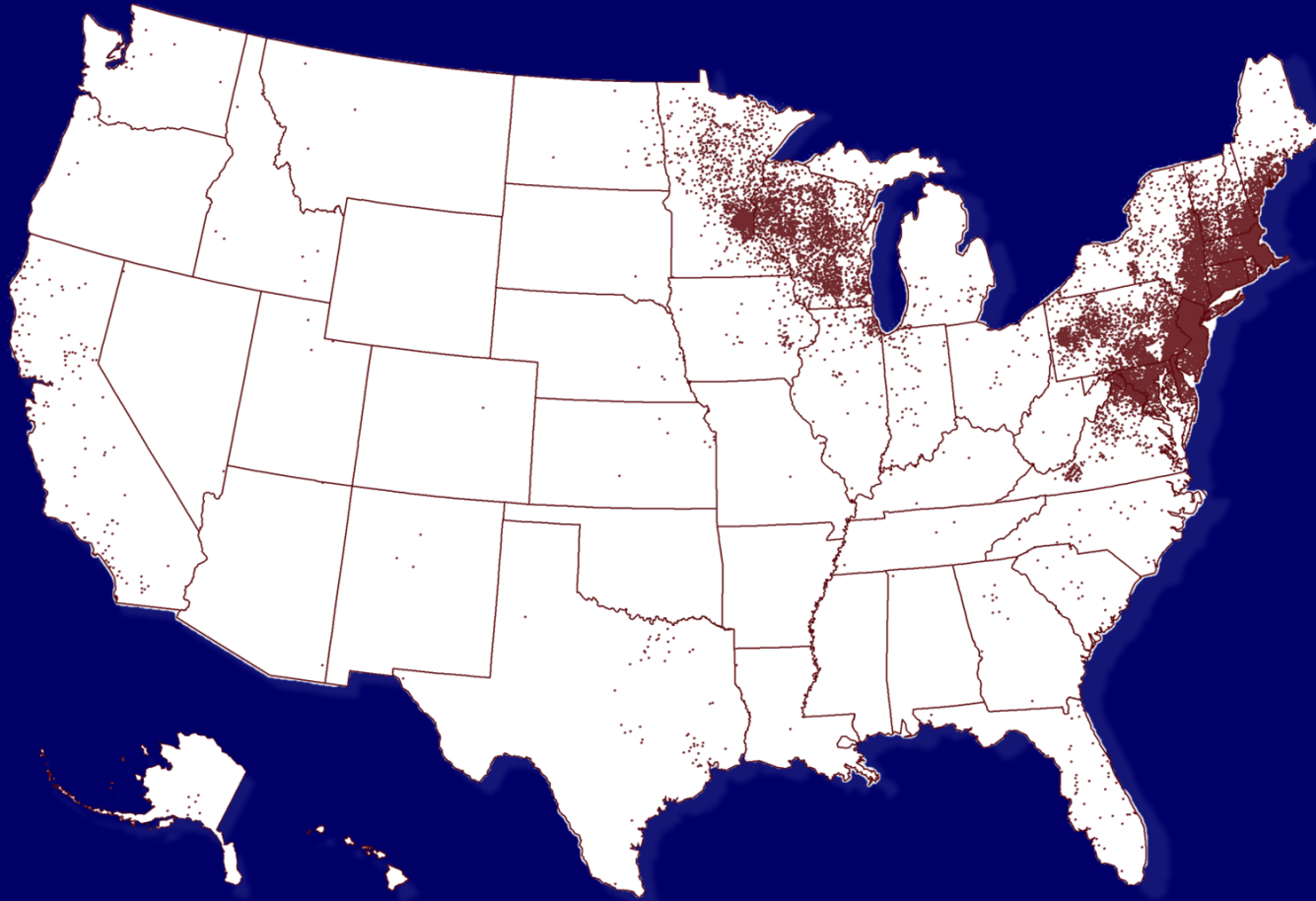


*National Surveillance case definition revised in 2008 to include probable cases; details at http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/lyme_disease_2008.htm

Lyme Disease High Incidence Counties, Northeastern United States

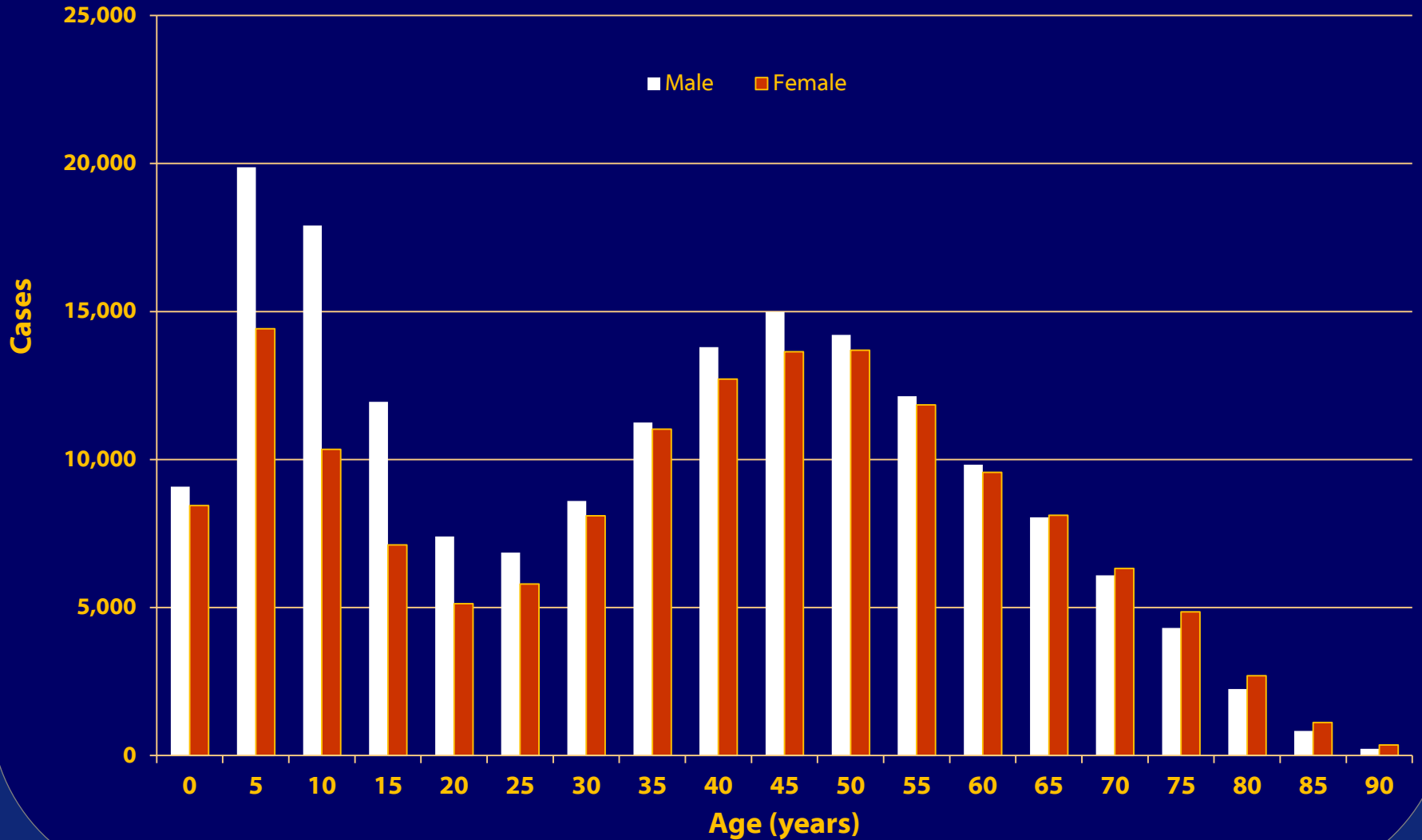


Reported Cases of Lyme Disease, 2010

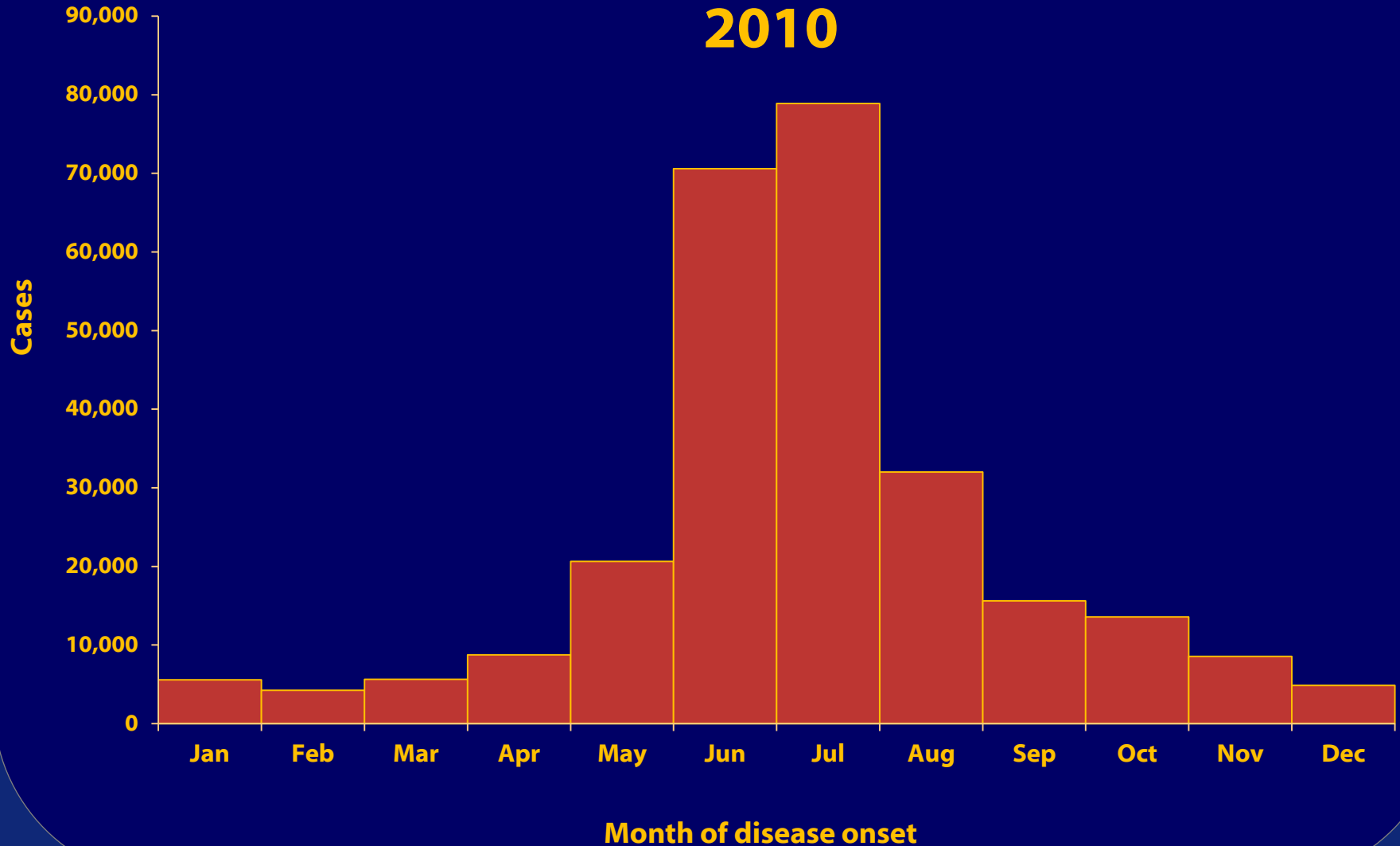


Though Lyme disease cases have been reported in nearly every state, cases are reported from the infected person's county of residence, not the place where they were infected.

Confirmed Lyme Disease Cases by Age and Sex--United States, 2001-2010

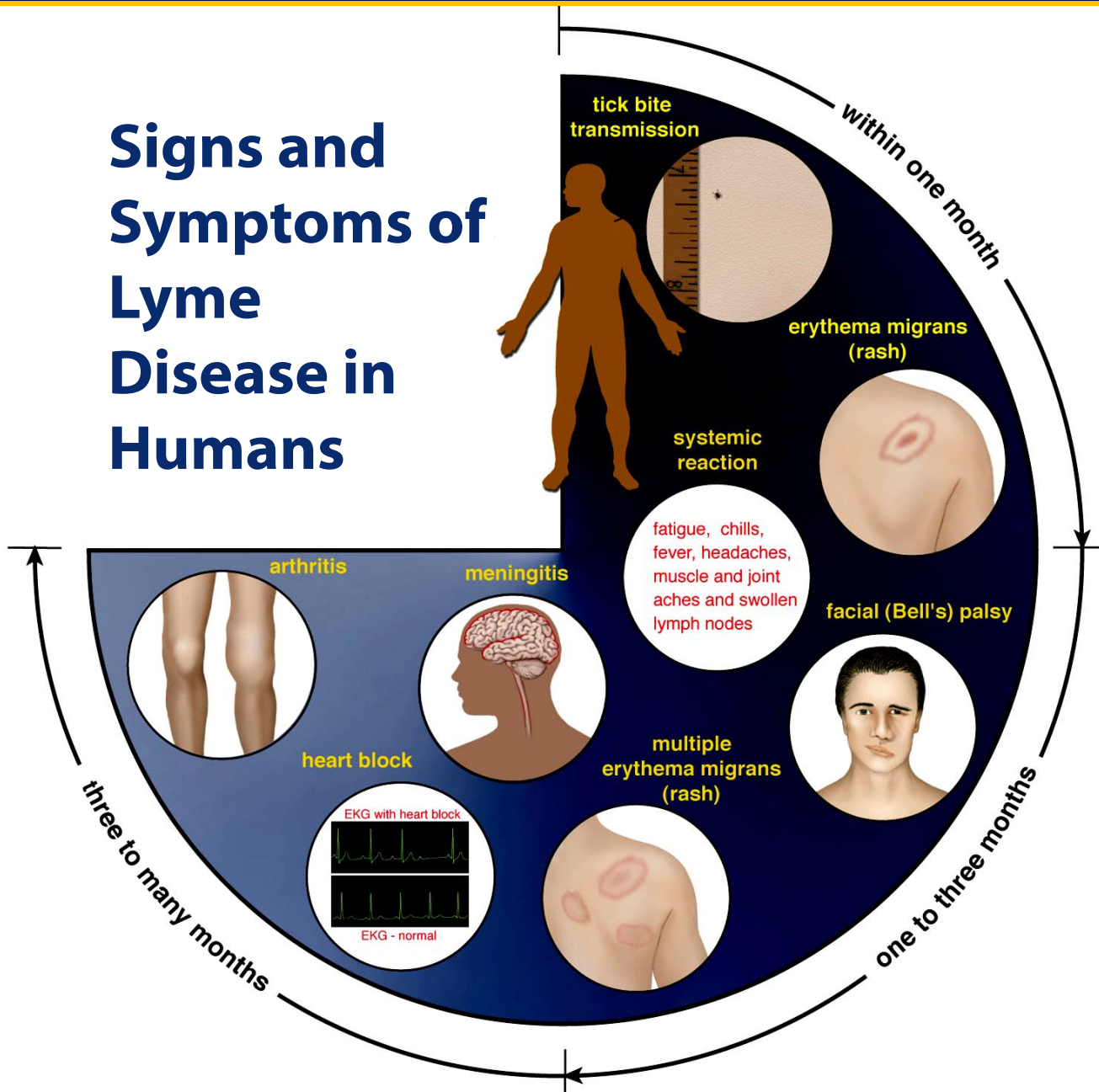


Confirmed Lyme Disease Cases by Month of Disease Onset--United States, 2001-2010

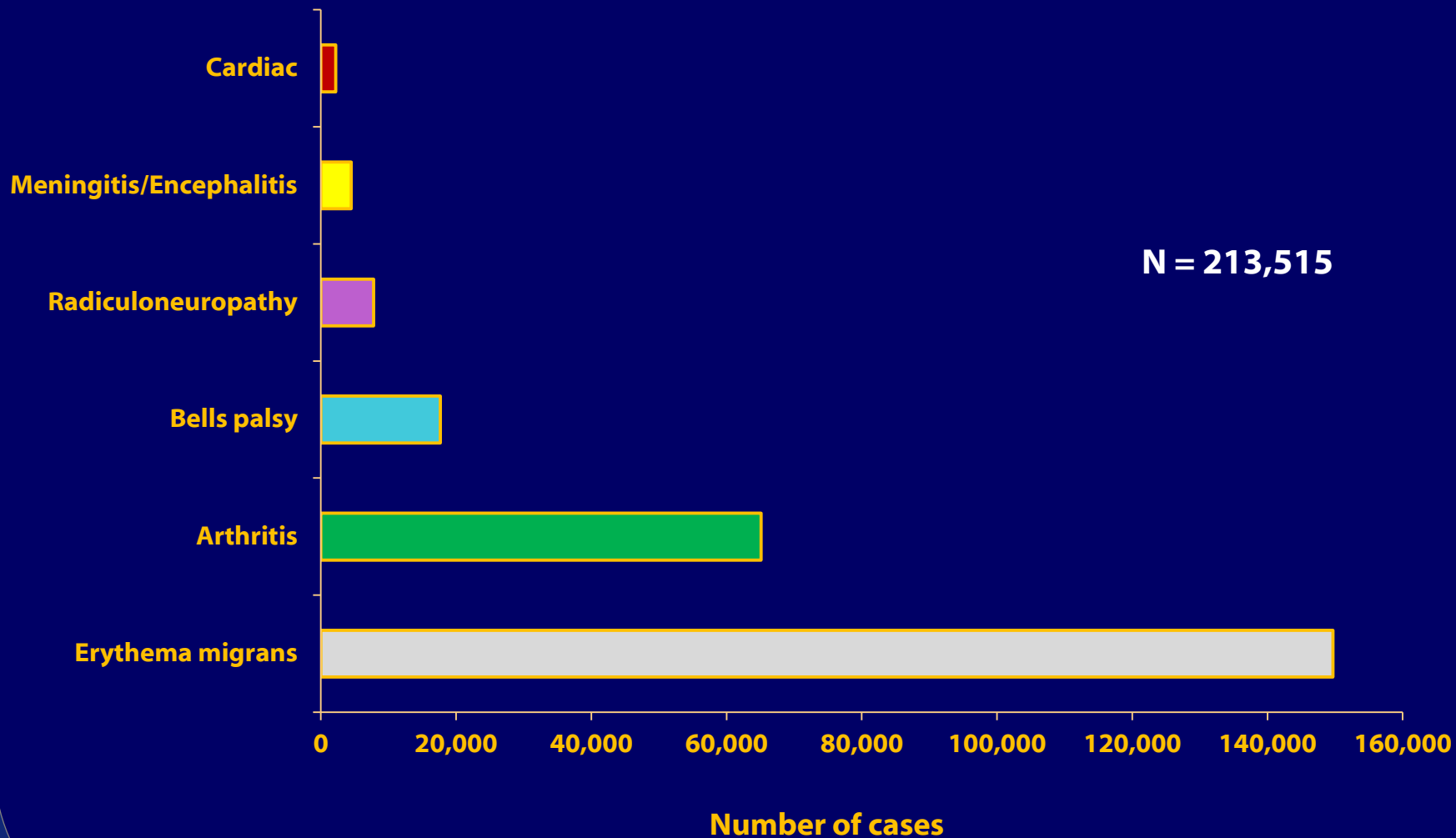


CLINICAL FEATURES

Signs and Symptoms of Lyme Disease in Humans



Clinical Symptoms of Confirmed Lyme Disease Cases--United States, 2001-2010



Erythema Migrans (EM)

- ❑ 60-80% of cases
- ❑ ~7-14 days after tick bite
- ❑ Expands over days
- ❑ Rarely painful
- ❑ Distinguish from allergic reaction



Other EM Presentations



From: Nadelman RB, Wormser GP. Management of tick bites and early Lyme disease. Rahn DW, Evans J eds. *Lyme disease*. 1998; Philadelphia: American College of Physicians. 49-75

Disseminated and Late Lyme Disease

□ Facial palsy

- Summer months
- May be bilateral
- \pm CSF pleocytosis

□ Arthritis

- Intermittent
- Oligoarticular

□ Late-stage neurologic

- Encephalopathy
- Peripheral neuropathy



STARI or Lyme Disease?

- ❑ Southern Tick-Associated Rash Illness (STARI)
 - Rash indistinguishable from Lyme disease EM
 - May be accompanied by fatigue, fever, headache, muscle and joint pains
 - Follows bite of lone star tick, *Amblyomma americanum*
- ❑ Also known as Master's disease
- ❑ The cause of STARI is not known

Southern Tick-associated Rash Illness (STARI)



Life stages of
lone star tick
(*Amblyomma
americanum*)

Selected Features of Patients with EM or EM-like lesions in NY or MO

| | Missouri (n=21) | New York (n=101) |
|----------------------------------|-----------------|------------------|
| Age of adults - mean | 48 years | 48 years |
| Males | 62% | 71% |
| ‡ Known tick bite at lesion site | 86% | 20% |
| † Mean days to EM | 6.1 ± 4.2 | 10.4 ± 6.1 |
| Multiple EMs | 5% | 27% |
| ‡ Symptomatic | 19% | 76% |
| ‡ Mean number of symptoms | 0.8 ± 1.8 | 3.4 ± 3.1 |
| † Lymphadenopathy | 5% | 27% |

‡ p<.001

† p<.05

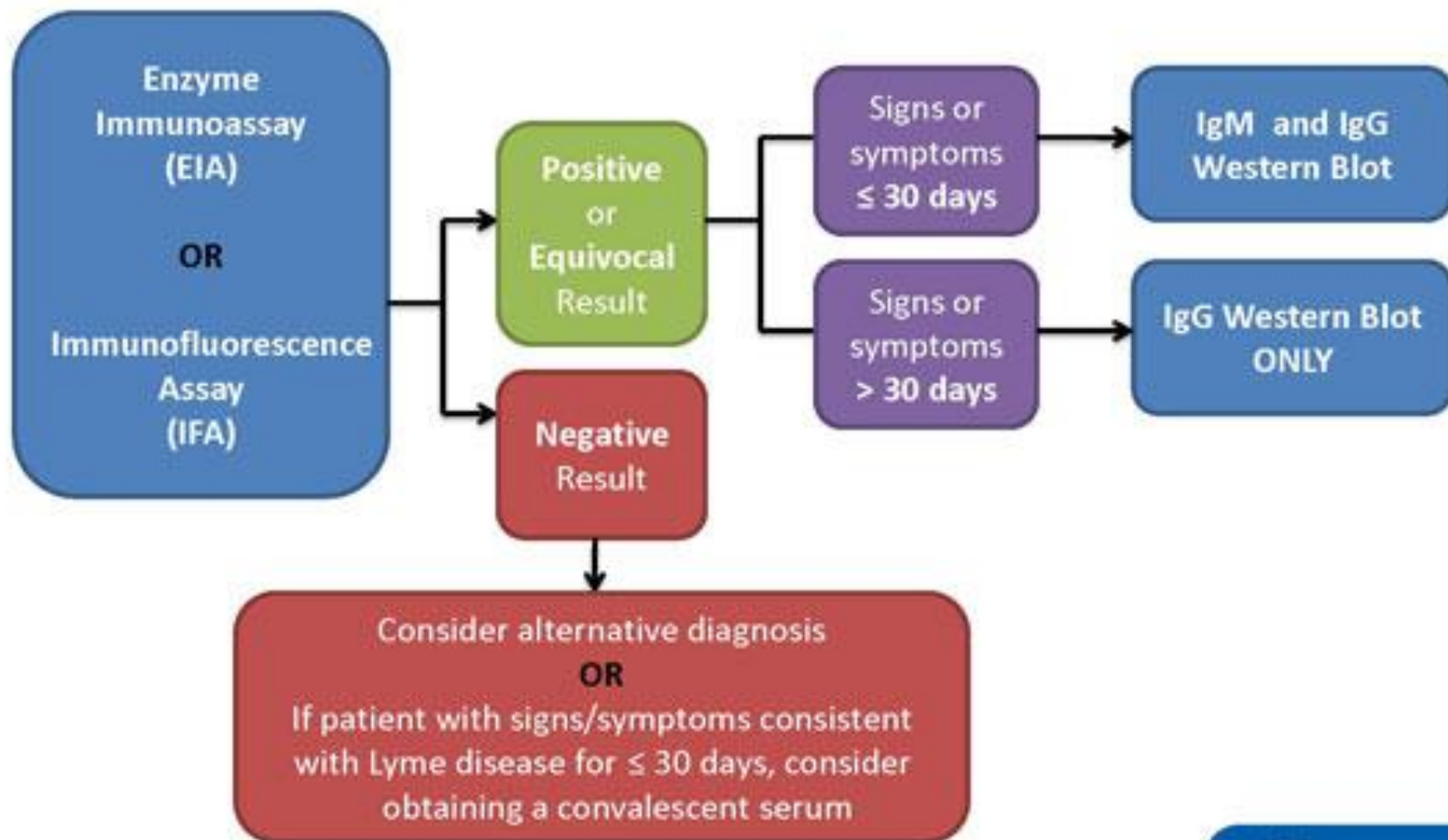
Wormser G *et al.* 2005 Clin Infect Dis

LABORATORY DIAGNOSIS

Two-Tiered Testing for Lyme Disease

First Test

Second Test



Sensitivity of Two-Tiered Serologic Testing

| Lyme Disease Stage | Sensitivity (%)* |
|------------------------|------------------|
| EM rash (acute) | 38 |
| EM rash (convalescent) | 67 |
| Early neurologic | 87 |
| Late neurologic | 100 |
| Arthritis | 97 |

*Specificity of two-tiered testing is generally $\geq 95\%$

- Good in later stages of disease
- Testing of EM patients not generally necessary

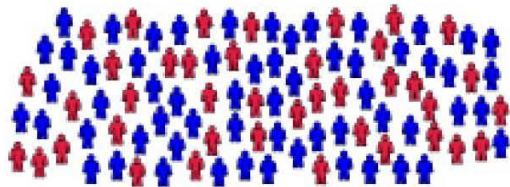
Understanding Test Results for Infectious Diseases

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?

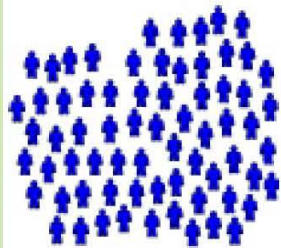
DISEASE IS COMMON*



100 people tested for the disease ‡

NEGATIVE TESTS

True Negatives



1% FALSE NEGATIVE

1 of 60 people who tests negative has the disease

False Negatives



POSITIVE TESTS

False Positives



True Positives



3% FALSE POSITIVE

1 of 40 people who tests positive does not have the disease

KEY

people with disease

people without disease

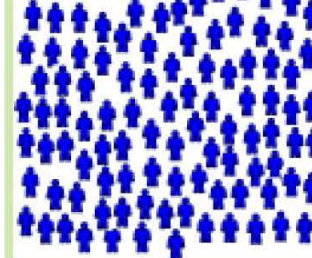
DISEASE IS RARE†



100 people tested for the disease ‡

NEGATIVE TESTS

True Negatives



0% FALSE NEGATIVE

None of the 97 people who tests negative has the disease

False Negatives

0

POSITIVE TESTS

False Positives



True Positives



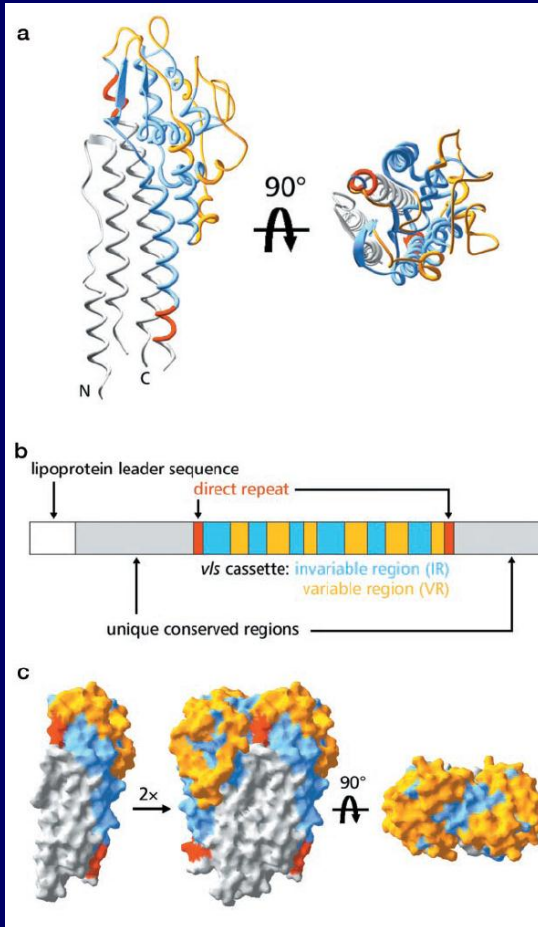
67% FALSE POSITIVE

2 of 3 people who test positive do not have the disease

* 40 out of 100 patients in this area have the disease.
† 1 out of 100 patients in this area have the disease.

‡ Test specificity = 98% (high) and test sensitivity = 98% (high)

VlsE and C6 Assays



Eicken et al. JBC 2002;277:21691

- Based on antibody to
 - VlsE surface antigen
 - C6 peptide (sub-component)
- FDA-approved as 1st tier assays
- C6 under evaluation as “stand alone” alternative to two-tiered testing
- Advantages
 - Greater sensitivity for early disease (EM)
 - Can detect non-U.S. strains
 - Objective, less labor intensive
 - Titer may wane faster

Direct Detection Diagnostics: Culture

- ❑ Moderate to high sensitivity
 - Skin biopsies (best for atypical rash or no history of exposure)
 - Blood (first 2-3 weeks of infection)

- ❑ Very low sensitivity
 - CSF
 - Synovial fluid

- ❑ Overall, culture is labor intensive, slow, and expensive

Direct Detection Diagnostics: PCR

- ❑ Moderate to high sensitivity
 - Skin biopsies
 - Synovial fluid
- ❑ Low sensitivity or not validated:
 - CSF, blood (low sensitivity)
 - Urine, breast milk, semen, other (not validated)
- ❑ Regardless of specimen, PCR has a high potential for false positives

Additional Tests: Questionable Utility

- Single-tier IgM or IgG immunoblot tests without a previous EIA/IFA
- Capture assays for antigens in urine
- Culture, immunofluorescence staining, or cell sorting of cell wall-deficient or cystic forms of *B. burgdorferi*
- Lymphocyte transformation tests
- Quantitative CD57 lymphocyte assays
- “Reverse Western blots”
- In-house criteria for interpretation of immunoblots
- Measurements of antibodies in joint fluid (synovial fluid)

More info on www.cdc.gov/Lyme

TREATMENT

Recommended Therapy for Patients with Lyme Disease

| Indication | Treatment | Duration, days (range) |
|--|--|-------------------------|
| Tick bite in the United States | Doxycycline, 200 mg in a single dose ^{a,b} ; (4 mg/kg in children ≥8 years of age) and/or observation | ... |
| Erythema migrans | Oral regimen ^{c,d} | 14 (14–21) ^e |
| Early neurologic disease | | |
| Meningitis or radiculopathy | Parenteral regimen ^{c,f} | 14 (10–28) |
| Cranial nerve palsy ^{a,g} | Oral regimen ^c | 14 (14–21) |
| Cardiac disease | Oral regimen ^{a,c,h} or parenteral regimen ^{a,c,h} | 14 (14–21) |
| Borrelial lymphocytoma | Oral regimen ^{c,d} | 14 (14–21) |
| Late disease | | |
| Arthritis without neurologic disease | Oral regimen ^c | 28 |
| Recurrent arthritis after oral regimen | Oral regimen ^{a,c} or parenteral regimen ^{a,c} | 28 14 (14–28) |
| Antibiotic-refractory arthritis ⁱ | Symptomatic therapy ^j | ... |
| Central or peripheral nervous system disease | Parenteral regimen ^c | 14 (14–28) |
| Acrodermatitis chronica atrophicans | Oral regimen ^c | 21 (14–28) |
| Post-Lyme disease syndrome | Consider and evaluate other potential causes of symptoms; if none is found, then administer symptomatic therapy ^a | ... |

NOTE. Regardless of the clinical manifestation of Lyme disease, complete response to treatment may be delayed beyond the treatment duration. Relapse may occur with any of these regimens; patients with objective signs of relapse may need a second course of treatment.

Recommended Antimicrobial Regimens for Treatment of Patients with Lyme Disease

| Drug | Dosage for adults | Dosage for children |
|----------------------------------|---|---|
| Preferred oral regimens | | |
| Amoxicillin | 500 mg 3 times per day ^a | 50 mg/kg per day in 3 divided doses (maximum, 500 mg per dose) ^a |
| Doxycycline | 100 mg twice per day ^b | Not recommended for children aged <8 years For children aged ≥8 years, 4 mg/kg per day in 2 divided doses (maximum, 100 mg per dose) |
| Cefuroxime axetil | 500 mg twice per day | 30 mg/kg per day in 2 divided doses (maximum, 500 mg per dose) |
| Alternative oral regimens | | |
| Selected macrolides ^c | For recommended dosing regimens, see footnote <i>d</i> in table 3 | For recommended dosing regimens, see footnote in table 3 |
| Preferred parenteral regimen | | |
| Ceftriaxone | 2 g intravenously once per day | 50–75 mg/kg intravenously per day in a single dose (maximum, 2 g) |
| Alternative parenteral regimens | | |
| Cefotaxime | 2 g intravenously every 8 h ^d | 150–200 mg/kg per day intravenously in 3–4 divided doses (maximum, 6 g per day) ^d |
| Penicillin G | 18–24 million U per day intravenously, divided every 4 h ^d | 200,000–400,000 U/kg per day divided every 4 h ^d (not to exceed 18–24 million U per day) |

^a Although a higher dosage given twice per day might be equally as effective, in view of the absence of data on efficacy, twice-daily administration is not recommended.

^b Tetracyclines are relatively contraindicated in pregnant or lactating women and in children <8 years of age.

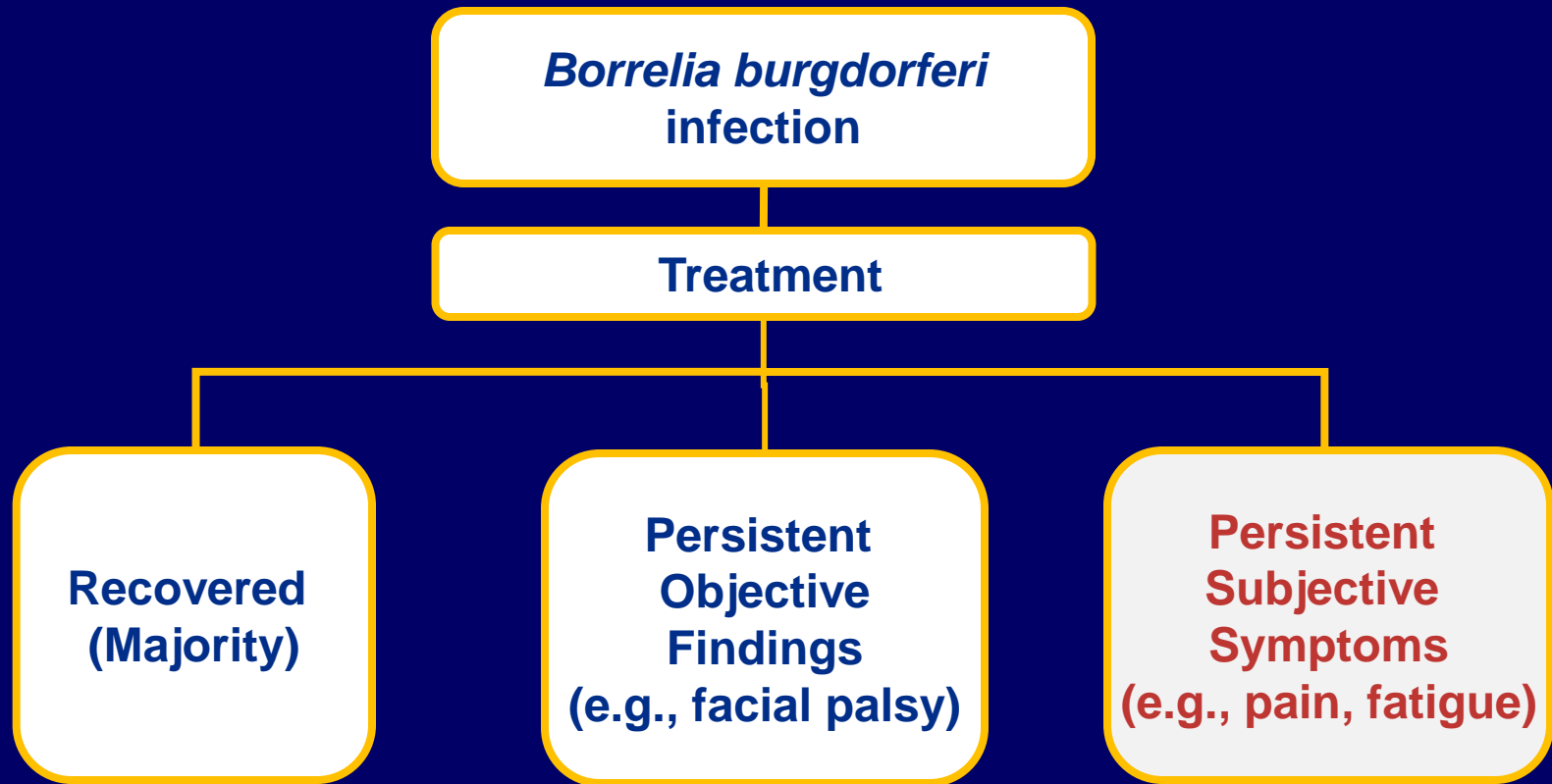
^c Because of their lower efficacy, macrolides are reserved for patients who are unable to take or who are intolerant of tetracyclines, penicillins, and cephalosporins.

^d Dosage should be reduced for patients with impaired renal function.

Treatment

- ❑ Lyme disease is treated with antibiotics
- ❑ Recommended regimens range from 2-4 weeks, orally or intravenously, depending on stage of illness
- ❑ In patients with persistent or recurrent joint swelling, re-treatment with a second 4-week course may be needed
- ❑ Most patients treated with antibiotics recover completely
- ❑ Some patients, particularly those diagnosed with later stages of disease may have persistent symptoms
 - Objective (e.g., facial paralysis, arthritis)
 - Subjective (e.g., fatigue, muscle aches, reduced concentration)

Post-Treatment Lyme Disease Syndrome



Key Challenges...

Polarization, mistrust, and differing views on what the disease is and how to manage it clinically



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VANITY FAIR
<http://www.vanityfair.com/online/oscars/2009/06/qa-the-lyme-disease-controversy.html>

Q&A: The Lyme Disease Controversy

by Frank DiGiacomo June 26, 2009, 2:24 pm



THE NEW ENGLAND JOURNAL OF MEDICINE

REVIEW ARTICLE

CURRENT CONCEPTS

A Critical Appraisal of "Chronic Lyme Disease"



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Health
Lyme Inc.
David Whelan 03.12.07

Forbes Ticks aren't the only parasites living off patients in borreliosis-prone areas.

ANALYSIS

'What we've got here is failure to communicate.'

The Ongoing 30-Year Lyme Disease War: Case Study of a Failure to Communicate

By Leslie P. King, MD, MPH | November 25, 2008

“Post Lyme disease syndrome” and “Chronic Lyme disease”

- ❑ Terms used to describe patients with persistent subjective symptoms after recommended treatment
- ❑ Question *is not* whether these symptoms are real
- ❑ Questions are:
 - What is the cause of the symptoms?
 - Are additional antibiotics the best treatment?
- ❑ Placebo-controlled studies have found no sustained benefit to prolonged antibiotic treatment
 - Prolonged antibiotic treatment not recommended

Death from Inappropriate Therapy for Lyme Disease

- ❑ 30-year-old woman received 27 months i.v. ceftriaxone through Groshong catheter
- ❑ Death due to embolization of large *Candida* septic thrombus from tip of catheter
- ❑ Review of medical record provided no substantive evidence for diagnosis of Lyme disease

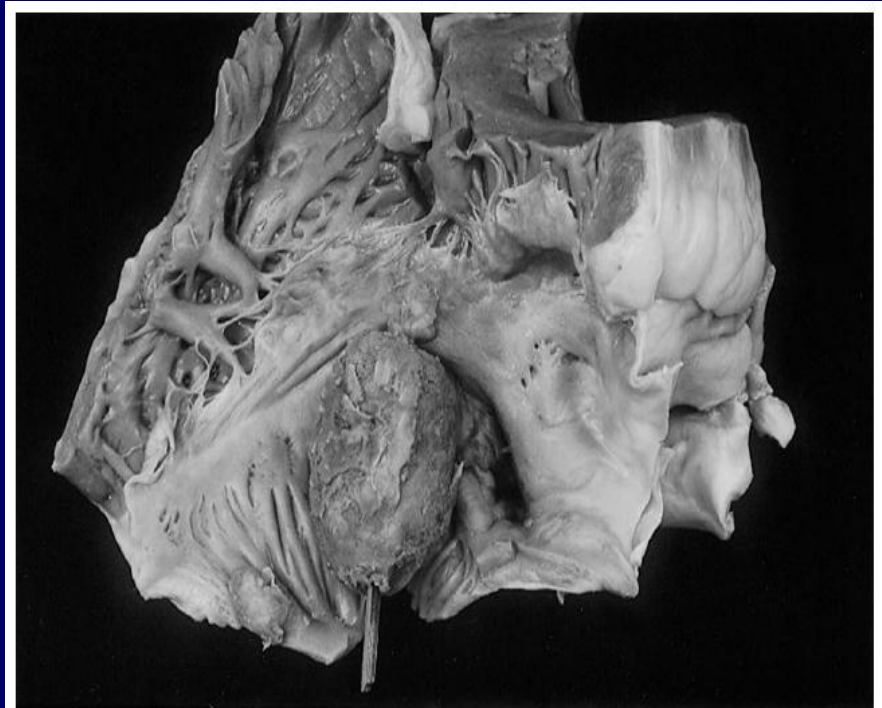
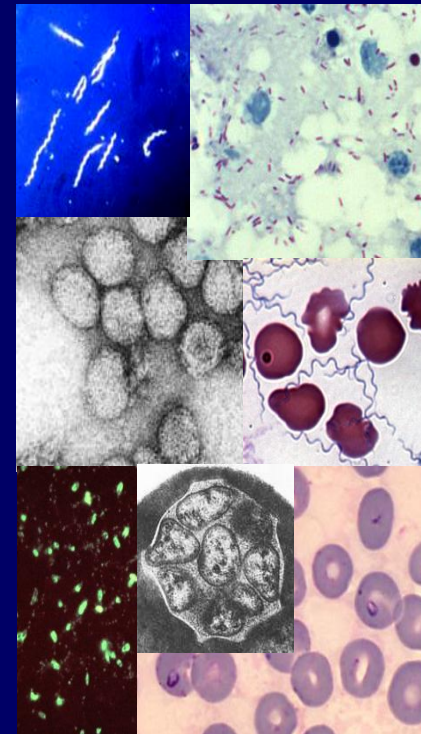


Figure 1. Opened right atrium from a patient who died because of inappropriate therapy for Lyme disease. The photo shows a large infected thrombus on the fractured tip of the patient's Groshong catheter.

Other Tickborne Diseases transmitted by the Blacklegged Tick

Coinfection with other tickborne disease agents may be considered, especially in patients with more severe initial symptoms

- Anaplasmosis*
- Babesiosis*
- Deer tick virus (lineage II)
- Ehrlichia muris-like agent (EML)



*reportable to CDC

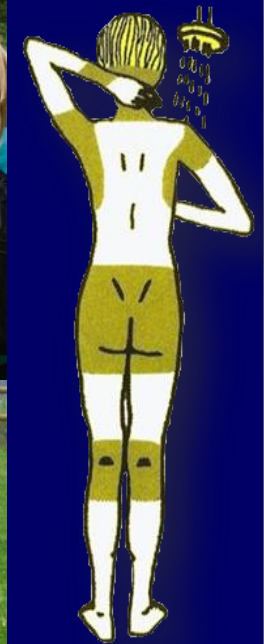
PREVENTION

Tick Bite Prophylaxis?

- A single dose of doxycycline may be offered to patients > 8 years to prevent Lyme disease, provided:
 - Attached tick is an engorged *I. scapularis*
 - Prophylaxis can be started within 72 h of tick removal time
 - Local rate of tick infection with *B. burgdorferi* is high (>20%)

Personal Protection Against Ticks

- Avoid tick habitat
- Wear protective clothing
- Use insect repellents
- Check for ticks daily
- Bathe promptly after exposure



Preventing Ticks in the Yard

- Clear tall grasses and brush
- Create barrier at the wood-lawn interface
- Mow lawn frequently
- Remove leaf litter, wood, trash, debris
- Apply pesticides outdoors





Ongoing Research

- Lyme and Other Tickborne Diseases Prevention Study (LTDPS)
 - A prospective, blinded, placebo-controlled trial to evaluate the efficacy of a single springtime application of commercially available, EPA-registered acaricide (bifenthrin) to prevent Lyme and other tickborne diseases in humans
 - Over 1,500 households enrolled in CT, MD, and NY in 2011
 - Recruitment began in February 2012 for Year 2 of study

For more information www.cdc.gov/ticknet/ltdps

**RESOURCES FOR CLINICIANS AND
HEALTH DEPARTMENTS**

Online Resources

- ❑ Continuing medical education (CMEs)
- ❑ Clarified diagnosis, treatment and testing info
- ❑ Maps and statistics
- ❑ FAQs
- ❑ A physician's guide to tickborne diseases in the U.S.
- ❑ Resources for talking to or caring for patients with ongoing symptoms
- ❑ CDC-info

Lyme Disease Communication Toolkit

❑ Brochure

- Lyme Disease: A Public Information Guide

❑ Fact Sheets

- Lyme disease prevention fact sheet for outdoor workers
- Lyme disease prevention fact sheet for hikers
- Lyme disease prevention fact sheet for golfers
- Lyme disease fact sheet for pregnant women
- Lyme disease fact sheet for parents

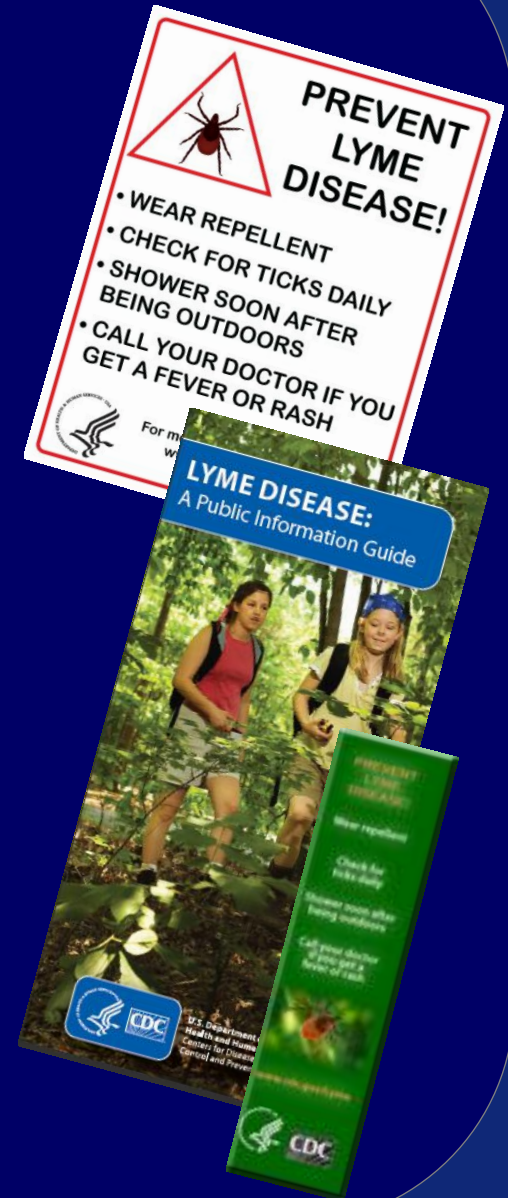
❑ Radio PSAs

- Lyme disease prevention (3 versions)
- Talking to Patients about Preventing Tick Bites

❑ Trail Sign

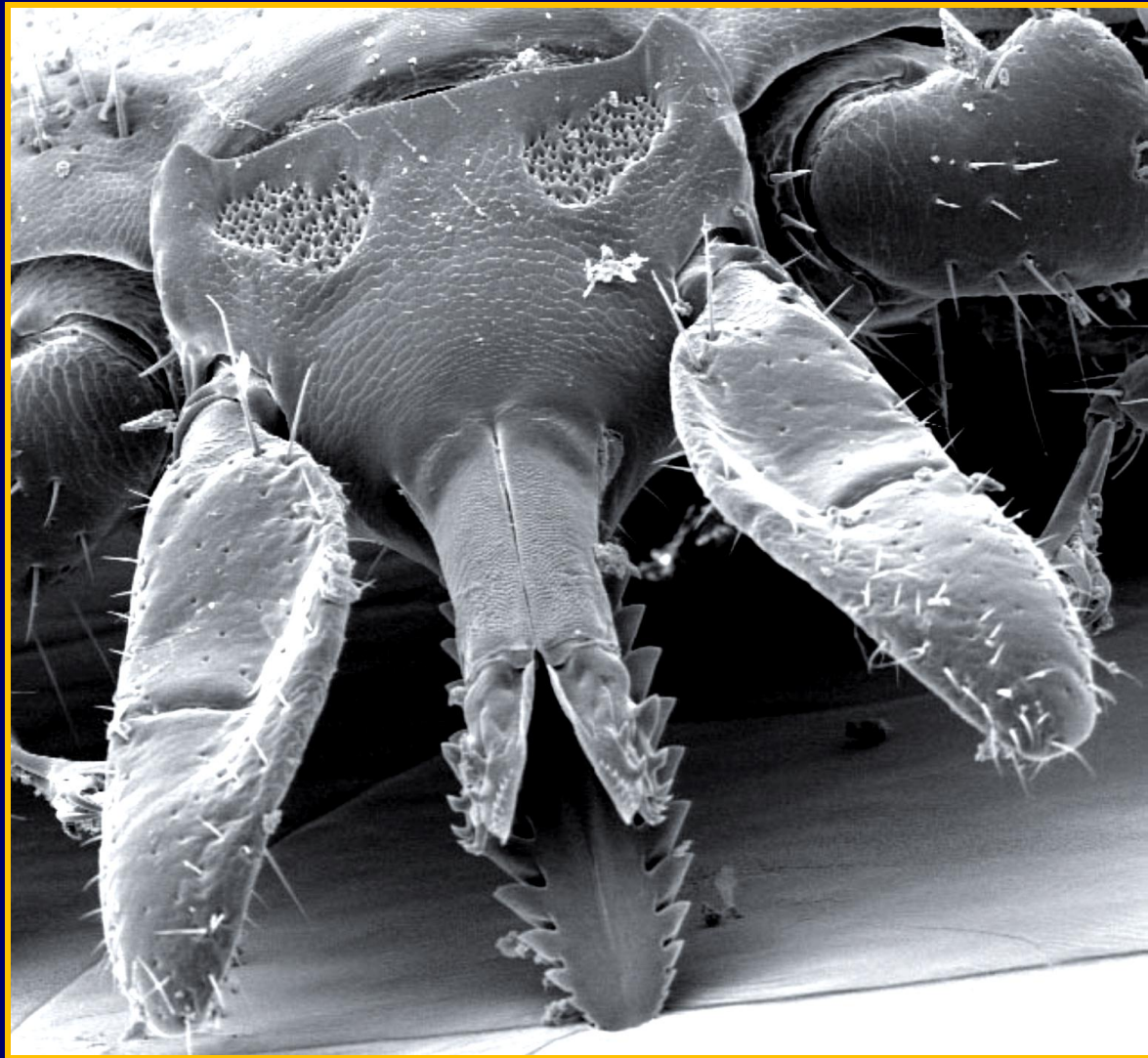
❑ Lyme Disease Prevention for Kids

- Crossword puzzle and information sheet for kids
- Prevention bookmarks



THANK YOU!

A Face that Only a Mother Could Love





Centers for Disease Control and Prevention Atlanta, Georgia

Continuing Education Credit/Contact Hours for COCA Conference Calls

Continuing Education guidelines require that the attendance of all who participate in COCA Conference Calls be properly documented. All Continuing Education credits/contact hours (CME, CNE, CEU, CECH, and ACPE) for COCA Conference Calls are issued online through the CDC Training & Continuing Education Online system <http://www2a.cdc.gov/TCEOnline/>

Those who participate in the COCA Conference Calls and who wish to receive CE credit/contact hours and will complete the online evaluation by **Apr 5, 2012** will use the course code **EC1648**. Those who wish to receive CE credits/contact hours and will complete the online evaluation between **Apr 6, 2012** and **Mar 5, 2013** will use course code **WD1648**. CE certificates can be printed immediately upon completion of your online evaluation. A cumulative transcript of all CDC/ATSDR CE's obtained through the CDC Training & Continuing Education Online System will be maintained for each user.

Thank you for joining!
Please email us questions at
coca@cdc.gov

Emergency Preparedness and Response

Emergency Preparedness & Response

Specific Hazards

Preparedness for All
Hazards

What CDC Is Doing


What You Can Do

Blog: Public Health
Matters

What's New

A - Z Index

Epidemiology and Clinical Features of Lyme Disease

 = Continuing Education Credits

Date: Tuesday, March 6, 2012

Time: 2:00 - 3:00 pm (Eastern Time)

Participate by Phone:

Dial: 888-790-6180

Passcode: 1281914

Participate by Webinar:

[https://www.mymeetings.com/nc/join.php?
i=PW7035569&p=1281914&t=c](https://www.mymeetings.com/nc/join.php?i=PW7035569&p=1281914&t=c)

Presenter(s):



Alison Hinckley, PhD

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Atlanta, GA 30333

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(800-232-4636)
TTY: (888) 232-6348

<http://emergency.cdc.gov/coca>

Join Us on Facebook

CDC Facebook page for Health Partners! “Like” our page today to receive COCA updates, guidance, and situational awareness about preparing for and responding to public health emergencies.



The screenshot shows the Facebook interface for the CDC Health Partners Outreach page. At the top, there is a navigation bar with the Facebook logo, a search bar, and login options for email and password. Below the navigation bar, the page header includes a 'Sign Up' button and the tagline 'Facebook helps you connect and share with the people in your life.' The main content area features the CDC Health Partners Outreach profile, which includes a cover photo, a profile picture, and a 'Like' button. The page is categorized as a 'Government Organization' in 'Atlanta, Georgia'. The 'Wall' section displays several posts, including a post about a webinar on Crisis and Emergency Risk Communication - Radiation, and a post about the CDC Emergency Preparedness and Response team. The page also shows a 'Wall' section with 'Top Posts' and a 'Likes' section with 'See All'.

<http://www.facebook.com/CDCHealthPartnersOutreach>