



Lyme Disease

1st Quarter 2011 DIDE Training

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Objectives

- **Describe the epidemiologic characteristics of Lyme disease**
- **Review the clinical symptoms, diagnosis, and treatment of Lyme disease**
- **Explain how the Lyme disease case definition is used to classify reported cases of Lyme disease**

Epidemiology

- **Bacterial tick-borne infectious disease**
 - **Agent: *Borrelia burgdorferi***
 - **Vector: Blacklegged tick (*Ixodes scapularis*)**
- **Endemic foci in U.S., Europe and Asia**
- **Incubation period: 3–32 days (mean 7–10 days)**
 - **24–48 hours of attachment required for transmission to occur**

Borrelia burgdorferi



Reservoirs and Hosts

- **White-footed mouse**
(*Peromyscus leucopus*)
 - Important in maintaining pathogen in nature

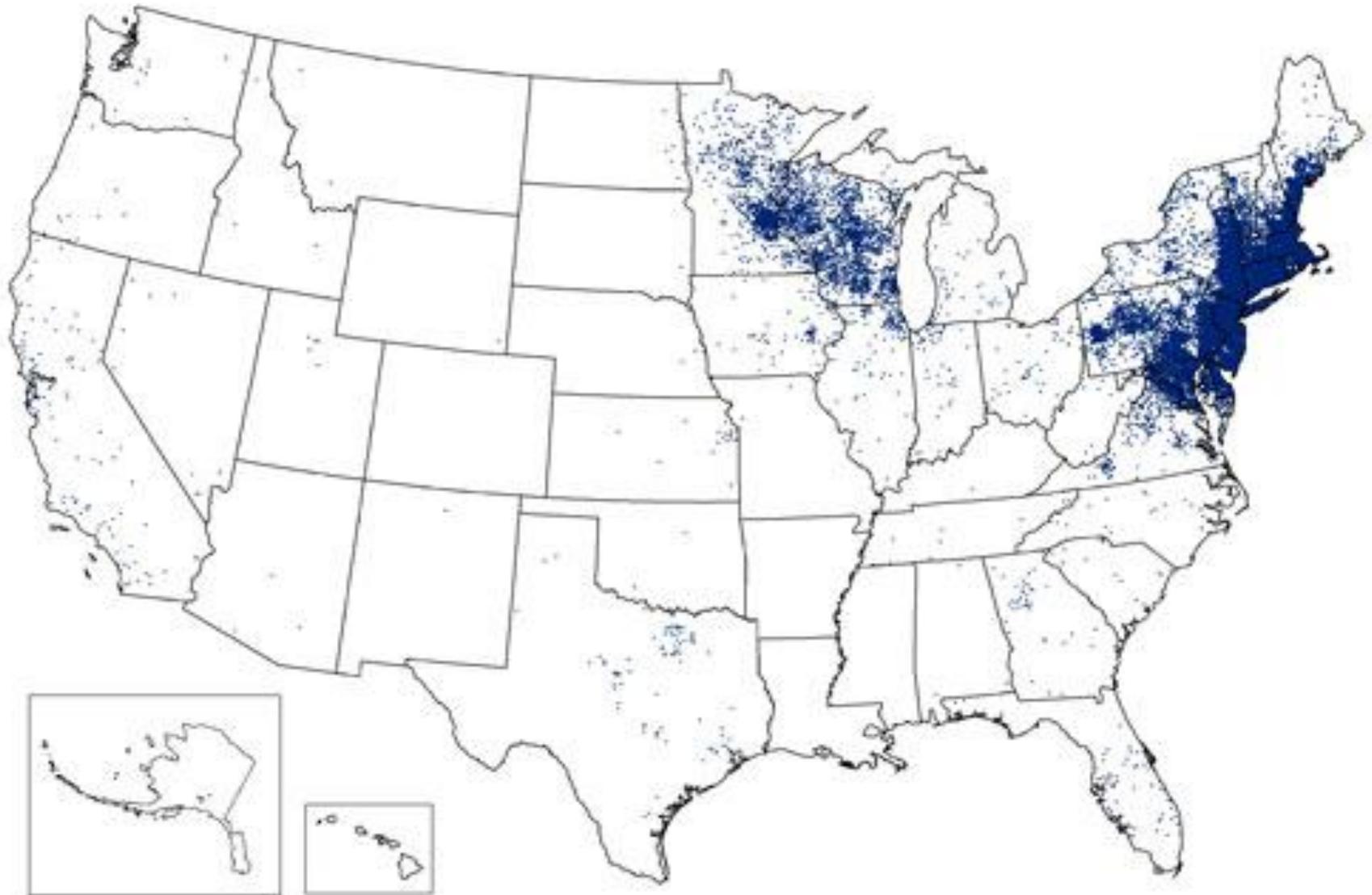
- **White-tail deer**
(*Odocoileus virginianus*)
 - Important in maintaining tick population



Geographic Distribution of Blacklegged Tick



Reported Cases of Lyme Disease -- United States, 2009

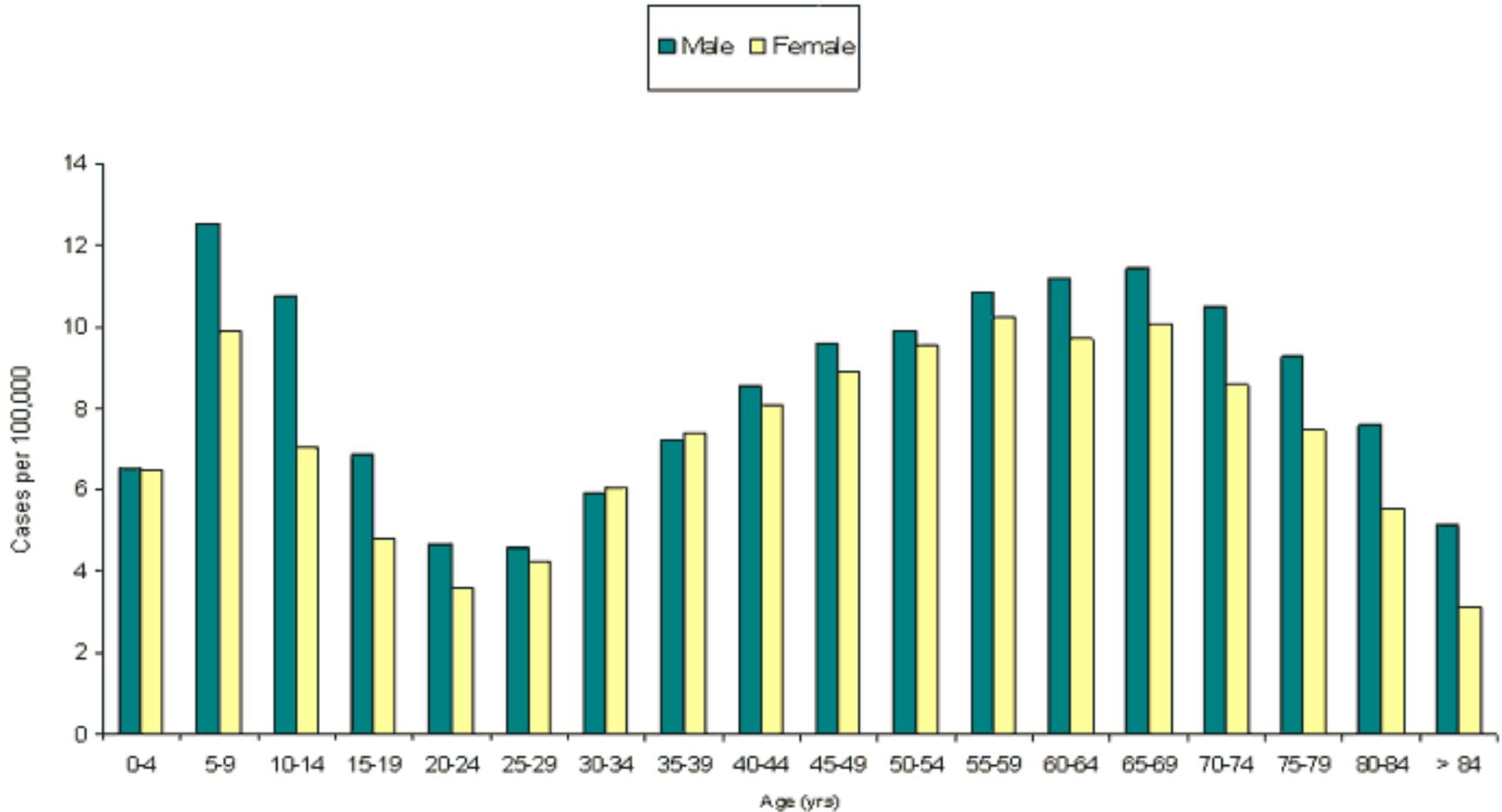


1 dot placed randomly within county of residence for each confirmed case

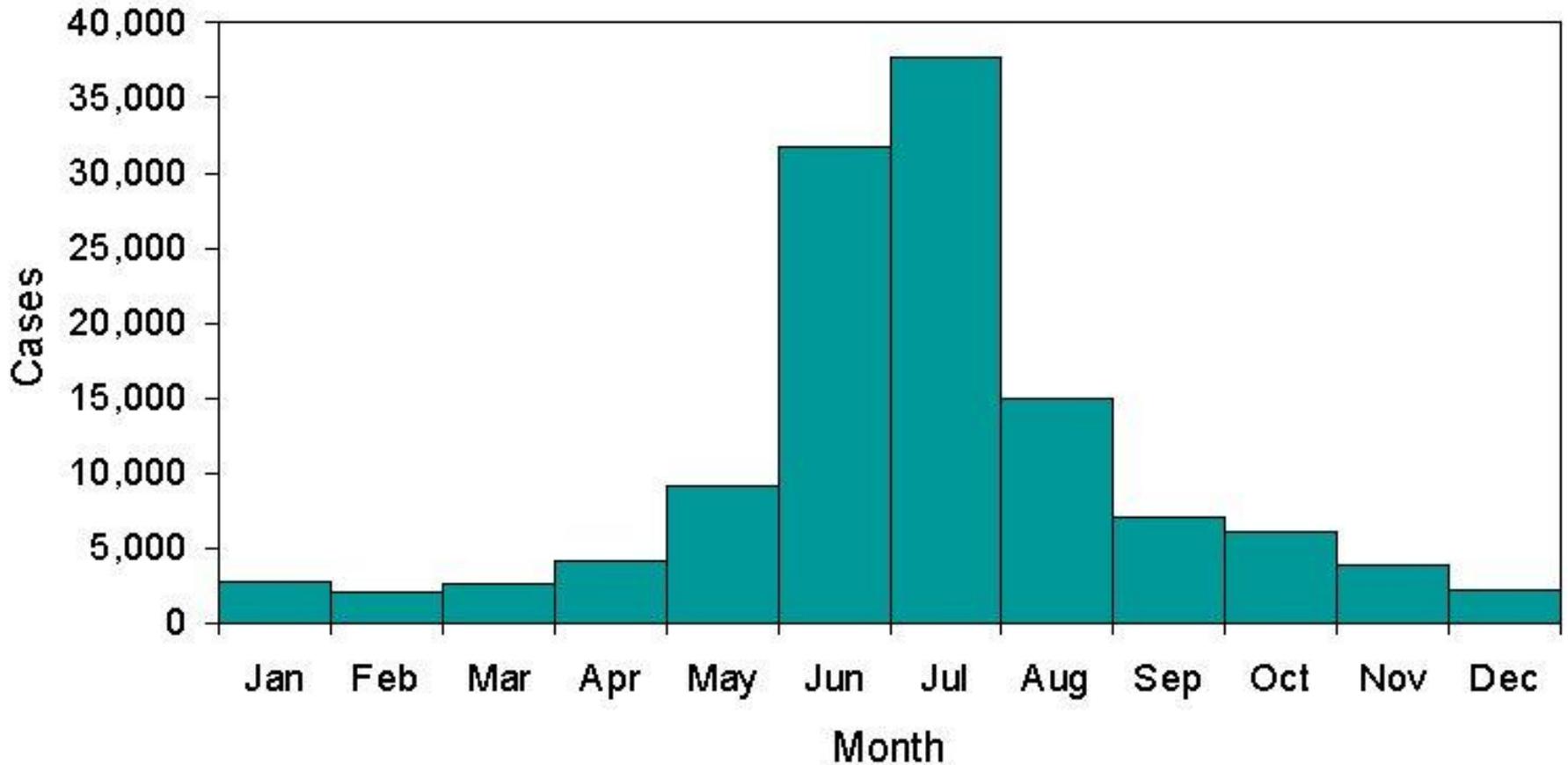
Lyme Disease Incidence in 2009

State	Rate per 100,000 persons
West Virginia	7.9
Virginia	8.9
Maryland	25.7
Pennsylvania	39.3
Ohio	0.4
Kentucky	0.0

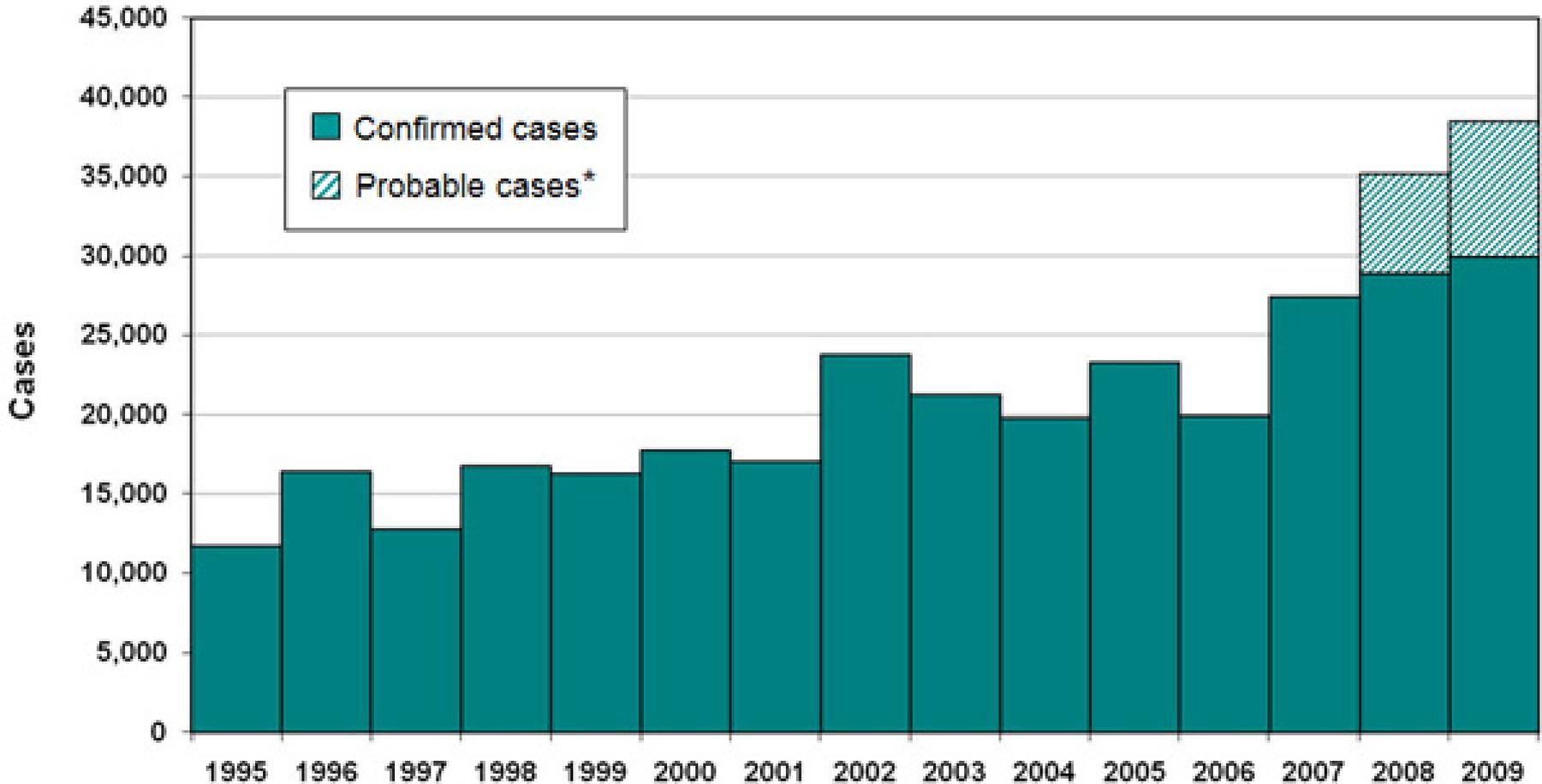
Rates by Age and Sex (U.S., 1994–2004)



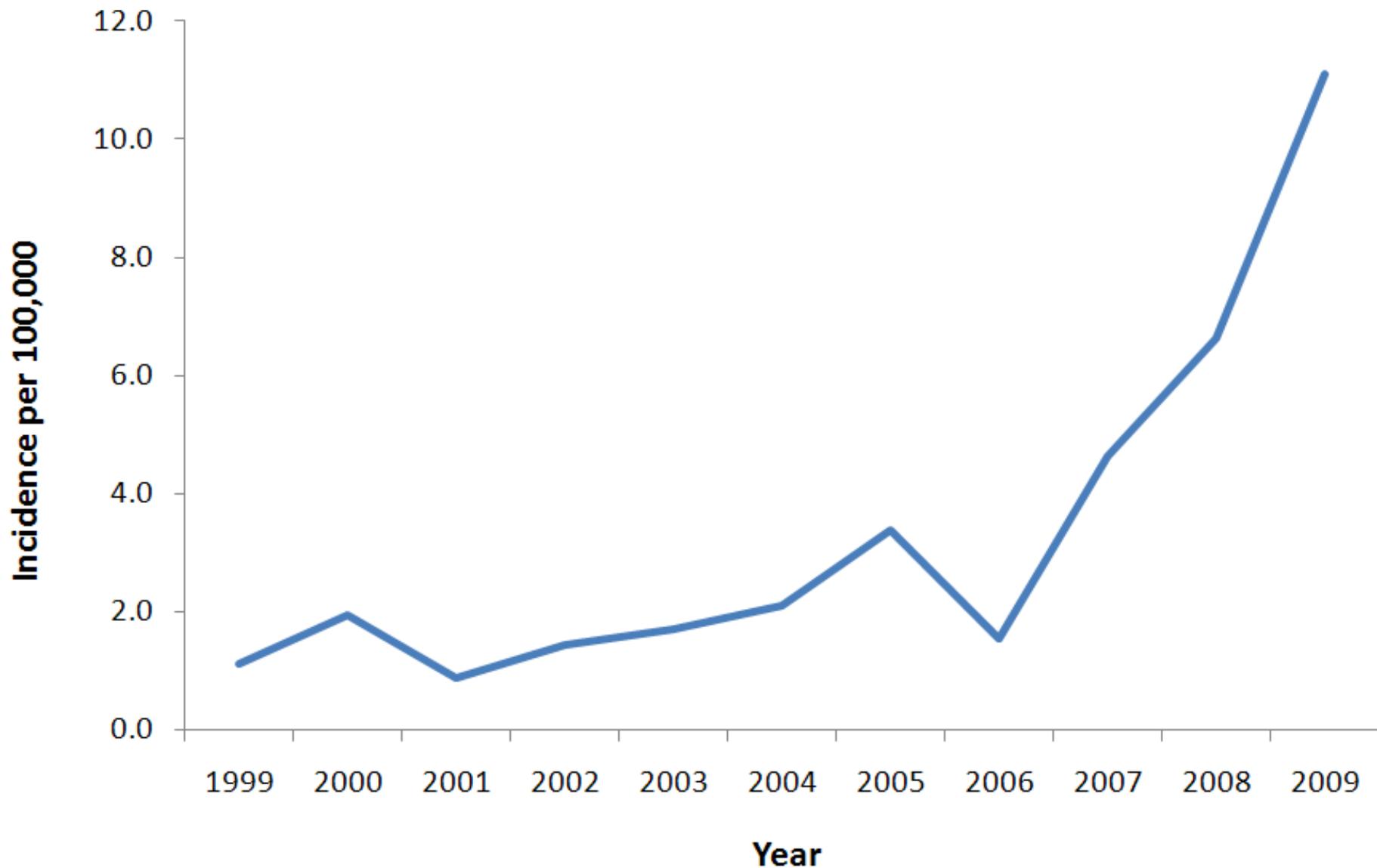
Cases by Month (U.S., 1994–2004)



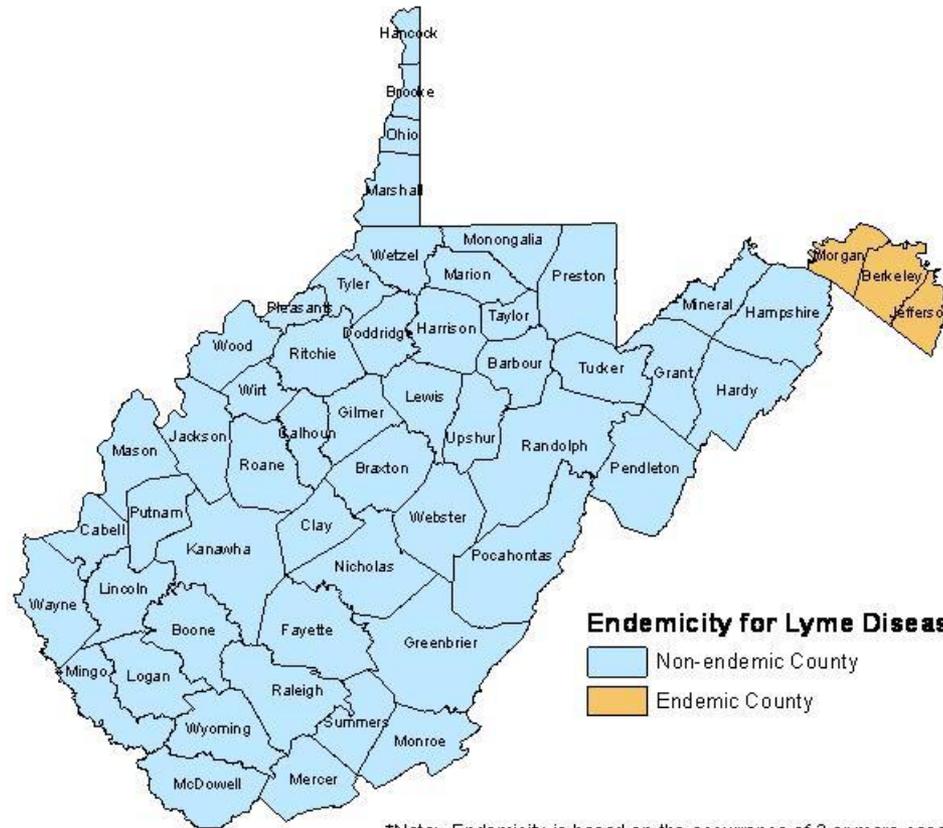
Cases by Year (U.S., 1995–2009)



Lyme Disease Incidence Rate per 100,000 Persons, West Virginia, 1999–2009

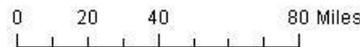


Counties with Endemic Status



*Note: Endemicity is based on the occurrence of 2 or more cases where the county is named as the county of exposure within 30 days of symptom onset.

Endemicity status is considered only on the basis of reported cases where the following criteria are true: 1) case was classified as confirmed; and 2) physician documented erythema migrans (EM) ≥ 5 cm; and 3) county of exposure was known and was within WV; and 4) case was reported from 2007 through 2009; and 5) Appropriate confirmatory laboratory results per CDC case definition. This restriction criteria resulted in 64 cases, with only 3 counties meeting the definition for endemicity.



Date created: 8/24/2010 (jml)

Why the Increase?

- **Changes to surveillance case definition**
 - Addition of “probable” case classification in 2008
- **Human population growth in endemic counties**
 - Berkeley in top 100 fastest growing counties in U.S. (2000–09) per US Census
- **New residential construction**
 - Fragmented hardwood forests border tick habitats
 - Explosive population growth of animal hosts

Clinical Features

- **Multisystem disease with a complex infectious process**
 - **Phase 1: Early/Acute**
 - **Skin**
 - **Phase 2: Disseminated**
 - **Neurologic, cardiovascular**
 - **Phase 3: Persistent**
 - **Neurologic, musculoskeletal (joints)**
- **Significant morbidity but rarely fatal**

Clinical Signs and Symptoms — Early

- **Erythema migrans**
 - **Hallmark of acute infection**
 - **Bulls-eye appearance**
 - **Present in 60 to 80% of patients**
- **Other symptoms: fever, headache, fatigue, muscle/joint aches, etc.**

Erythema Migrans



Clinical Signs and Symptoms — Disseminated

- **Days to weeks following initial infection**
 - **Skin**
 - Secondary EM
 - **Musculoskeletal**
 - Recurrent, brief attacks of large joint pain, swelling
 - **Neurologic**
 - Meningitis, facial palsy, etc.
 - **Cardiovascular**
 - 2nd or 3rd degree heart block
- **Primarily affects those not previously treated**

Bell's Palsy



Clinical Signs and Symptoms — Persistent

- **Months to years later**
 - **Musculoskeletal**
 - Intermittent arthritis (primarily large joints)
 - **Nervous system**
 - Peripheral neuropathy, encephalopathy, etc
- **Primarily affects those not previously treated**

Diagnosis

- **Primarily a clinical diagnosis**
 - **EM and exposure in endemic area**
- **Serology useful if no exposure or late symptoms**
 - **Two-tier test**
 - **EIA or IFA (sensitive)**
 - **Western blot (specific) –IgM and/or IgG**

Western Blot

- **Measures presence of specific proteins (“bands”)**
 - **Based on molecular weight (kDa)**
- **Standardized interpretation**
 - **IgM: Positive if 2 of the 3 bands detected**
 - 24 kDa (OspC), 39 kDa (BmpA), and 41 kDa (Fla)
 - **IgG: Positive if 5 of the 10 bands detected**
 - 18 kDa, 21 kDa (OspC), 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa (Fla), 45 kDa, 58 kDa (not GroEL), 66 kDa, and 93 kDa

Notes about labs

- **EIA/IFA screening synonyms and results**
 - “Lyme screen” or “Lyme assay”
 - Results can be numeric or qualitative

- **Western blot results**
 - IgM positives do not count if:
 - No EIA/IFA screen
 - Specimen date more than 30 days after onset
 - Beware of results from “IGENEX” laboratory

Lab Result Example 1

Lyme Disease

Lyme Disease Assay

INDETERMIN A

NONREACTIV

INTERPRETATION:

NONREACTIV: NO DETECTABLE IgG/IgM ANTIBODY; RESULT DOES NOT EXCLUDE B. BURGDORFERI INFECTION. AN ADDITIONAL SAMPLE SHOULD BE TESTED IN 4-6 WEEKS IF EARLY INFECTION IS SUSPECTED.

INDETERMIN: THE RESULT CANNOT BE INTERPRETED WITHOUT SUPPLEMENTAL WESTERN BLOT TESTING. THE SPECIMEN HAS BEEN REFERRED TO A REFERENCE LAB FOR WESTERN BLOT TESTING.

Lyme IgG Western Blot

Positive A

Band(s) present: 93, 66, 58, 45, 41, 39, 30, 28, 23, 18 kDa
TEST INFORMATION: Borrelia Burgdorferi Ab, IgG Western Blot

IgG Positive: Any 5 of the following 10 bands:

18, 23, 28, 30, 39, 41, 45, 58, 66, or 93 kDa.

IgG Negative: Any pattern that does not meet the IgG positive criteria.

Lyme IgM Western Blot

Positive A

Band(s) present: 41, 39, 23 kDa

TEST INFORMATION: Borrelia Burgdorferi Ab, IgM Western Blot

IgM Positive: Any 2 of the following 3 bands:

23, 39, or 41 kDa.

Lab Result Example 1

Lyme Disease

Lyme Disease Assay

INDETERMIN A

NONREACTIV

INTERPRETATION:

NONREACTIV: NO DETECTABLE IgG/IgM ANTIBODY; RESULT DOES NOT EXCLUDE B. BURGDORFERI INFECTION. AN ADDITIONAL SAMPLE SHOULD BE TESTED IN 4-6 WEEKS IF EARLY INFECTION IS SUSPECTED.

INDETERMIN: THE RESULT CANNOT BE INTERPRETED WITHOUT SUPPLEMENTAL WESTERN BLOT TESTING. THE SPECIMEN HAS BEEN REFERRED TO A REFERENCE LAB FOR WESTERN BLOT TESTING.

Lyme IgG Western Blot

Positive A

Band(s) present: 93, 66, 58, 45, 41, 39, 30, 28, 23, 18 kDa

TEST INFORMATION: Borrelia Burgdorferi Ab, IgG Western Blot

IgG Positive: Any 5 of the following 10 bands:

18, 23, 28, 30, 39, 41, 45, 58, 66, or 93 kDa.

IgG Negative: Any pattern that does not meet the IgG positive criteria.

Lyme IgM Western Blot

Positive A

Band(s) present: 41, 39, 23 kDa

TEST INFORMATION: Borrelia Burgdorferi Ab, IgM Western Blot

IgM Positive: Any 2 of the following 3 bands:

23, 39, or 41 kDa.

OLS Lyme Disease Testing

- **OLS offers EIA screen w/reflex to western blot**
 - <http://www.wvdhhr.org/labservices/labs/serology/index.cfm>
- **Service to be discontinued in 2011 if no increase in demand**
- **Work with providers in area to submit specimens through LHD**

Treatment

- **IDSA Guidelines (Published 2006)**
 - <http://cid.oxfordjournals.org/content/43/9/1089.full>
- **Antibiotics, type and regimen varies with stage of disease**
 - **Early (EM): 14 days of doxycycline, amoxicillin, OR cefuroxime axetil**
 - **Late: varies by clinical manifestation**
- **No “test of cure” available**
- **“Tick bite prophylaxis” not recommended**

Surveillance

- **First reportable in 1980**
 - **Standardized case definition in 1991**
- **Reportable to health department within 1 week**
- **Lyme disease case investigation toolkit**
 - **<http://www.wvidep.org>**
 - **A to Z index of infectious disease**
 - **“Lyme Disease”**

Case Definition — Clinical

1) Erythema migrans (EM)

- **Must be physician-diagnosed; AND**
- **Must be 5cm or greater in diameter**

Case Definition — Clinical

2) Late manifestations (physician-diagnosed)

- **Musculoskeletal (e.g., recurrent, brief attacks of joint swelling); OR**
- **Neurologic (e.g., facial palsy); OR**
- **Cardiovascular (e.g., atrioventricular conduction defects)**

Case Definition — Clinical

3) A physician diagnosis

- No EM
- No late manifestations

Case Definition — Lab

- 1) **Positive Culture for *B. burgdorferi***
- 2) **Two-tier testing interpreted using established criteria, where:**
 - **Positive IgM is sufficient only when ≤ 30 days from symptom onset; OR**
 - **Positive IgG is sufficient at any point during illness**
- 3) **Single-tier IgG immunoblot seropositivity using established criteria**
- 4) **CSF antibody positive for *B. burgdorferi* by Enzyme Immunoassay (EIA) or Immunofluorescence Assay (IFA), when the titer is higher than it was in serum**

Case Definition — Exposure

- **Only relevant if a patient has EM**
- **Defined as having been in tick habitat in endemic county (in past 30 days)**
 - **2 or more confirmed cases acquired in county**
- **In WV only 3 counties are classified as endemic**
 - **Berkeley, Jefferson, and Morgan**
 - **Out-of-state border counties evaluated on a case-by-case basis**

Case Status

- **Confirmed**
 - EM + Exposure
 - EM + Lab
 - Late manifestation + Lab
- **Probable**
 - Any other physician diagnosis + Lab
- **Suspect**
 - EM + No exposure + No Lab
 - Lab only

Summary

- **Lyme disease incidence is increasing in WV**
 - **Most cases seen during summer months**
 - **Highest incidence in children 5-14 years**
- **Review labs carefully**
- **Reach out to providers to offer testing via OLS**
- **Ensure case investigation captures needed data**