Minnesota Tick-Borne Diseases

David Neitzel, MS
Minnesota Department of Health
Acute Disease Investigation & Control

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Mr. Neitzel indicated no potential conflict of interest to this presentation. He does not intend to discuss any unapproved/investigative use of a commercial product/device.

Objectives

- **Identify signs and symptoms of tick-borne diseases (TBDs)**
- **Explain regional endemicity of TBDs, including emerging diseases and incidence**
- **Describe available testing for TBDs and appropriate use of testing**
- **Identify practical approaches for diagnosis and treatment of the patient with a possible TBD**
- **Summarize current guidelines on prevention and treatment of TBDs**

Diseases from Blacklegged Ticks (Deer Ticks) in MN

DISEASE	AGENT	TYPE OF AGENT
Lyme disease	*Borrelia burgdorferi*	Bacterium (spirochete)
Babesiosis	*Babesia microti*, *Babesia* spp.	Protozoan
Human anaplasmosis (HA)	*Anaplasma phagocytophilum*	Bacterium (Rickettsial)
Human ehrlichiosis (HE)	*Ehrlichia muris*-like (EML) agent	Bacterium (Rickettsial)
Powassan	Powassan virus	Virus

Transmission of Disease Agents from Blacklegged Ticks to Humans

- **Bacterial or protozoan**
  - **Must be nymph or an adult female**
  - **Must be attached for a long time**
    - **24-48 hours (Lyme disease)**
    - **12-24 hours (anaplasmosis)**

- **Powassan virus**
  - **Might be transmitted by all tick stages**
  - **Transmission time <15 minutes in mice**

Blacklegged Tick ("Deer Tick")
Ixodes scapularis

Nymph

Adult
(female)

Larva

Tim Leonard and Russell Johnson
University of Minnesota

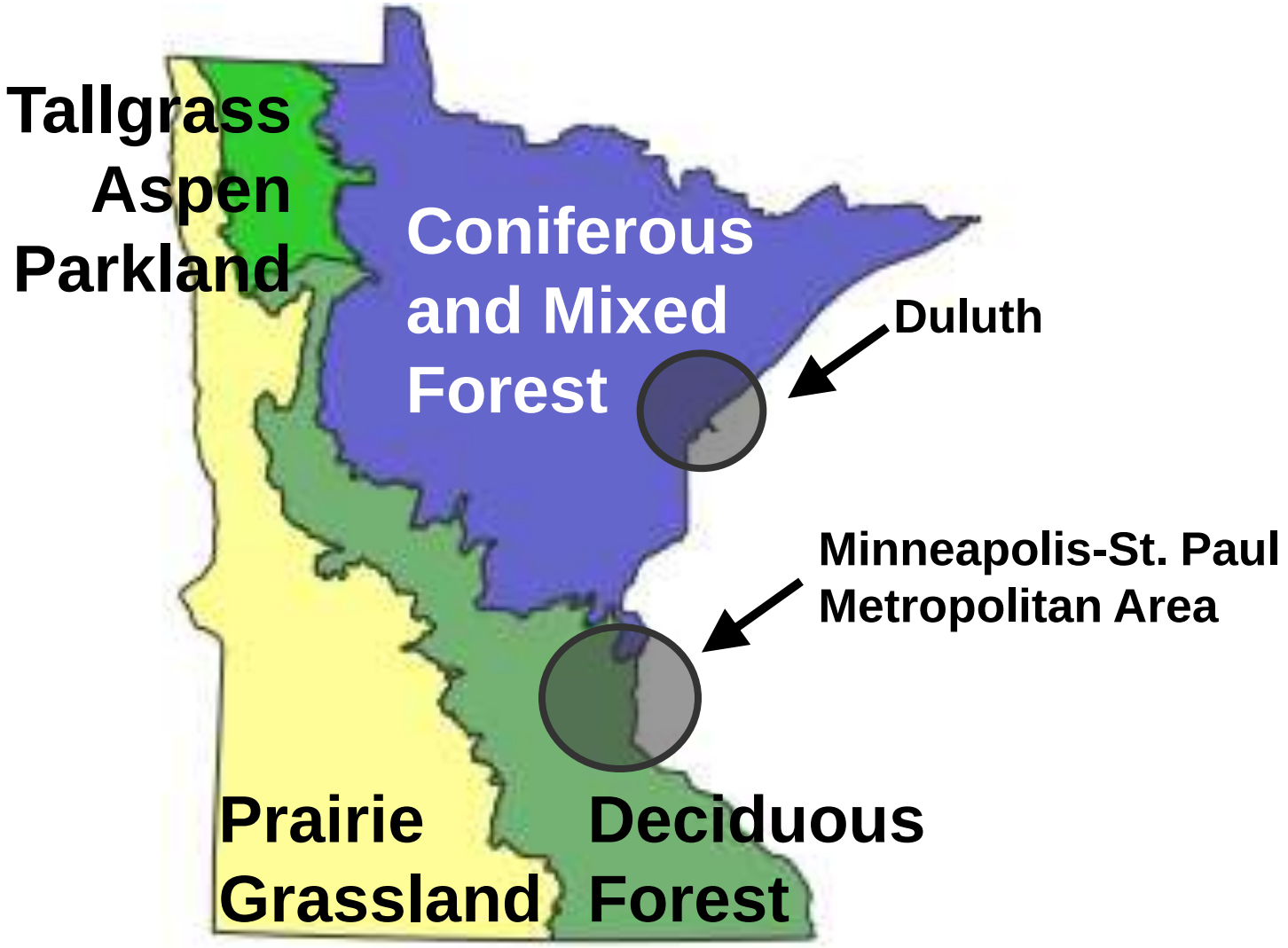

Blacklegged Tick
(Deer Tick)
Nymph

Engorged Blacklegged Tick (Deer Tick)

MDH

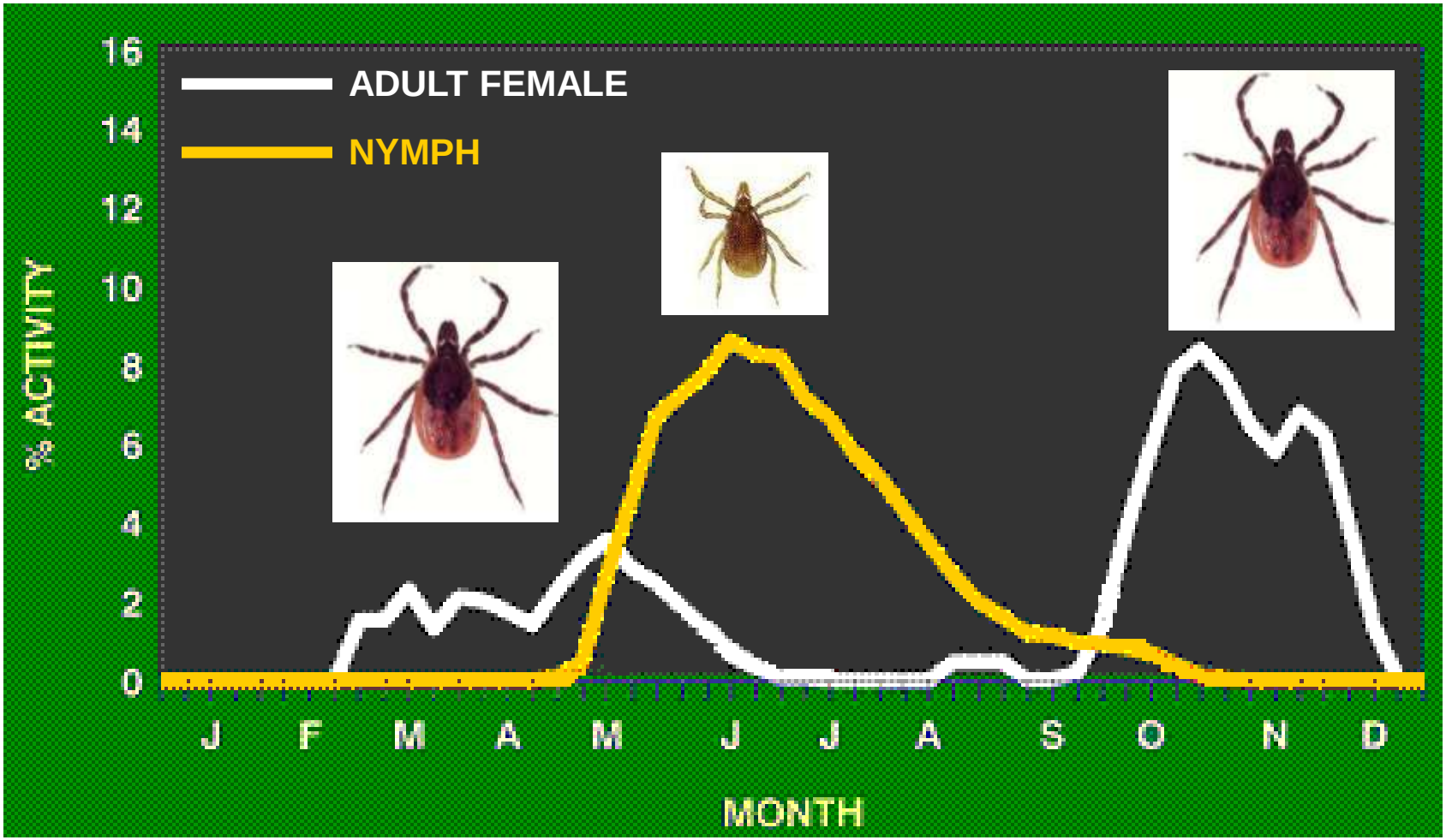
Blacklegged Tick Habitat

Minnesota Biomes



Modified from Minnesota DNR, http://www.dnr.state.mn.us/biomes/index.html

Seasonality of *Ixodes scapularis* Host-Seeking Activity



Images and Graph modified from American Lyme Disease Foundation, http://www.aldf.com/deerTickEcology.shtml

Other Tick Vectors and Potential Tick-Borne Diseases (TBDs) in MN

TICK	DISEASE	AGENT
American dog tick (*Dermacentor variabilis*) **-Very common in MN** 	**Rocky Mountain spotted fever (RMSF)**	***Rickettsia rickettsii***
Lone star tick (*Amblyomma americanum*) **-Not common In MN, but isolated specimens have been found** 	**Human ehrlichiosis (HE)**	***Ehrlichia chaffeensis***

Tick-Borne Diseases (TBDs) to Consider in Minnesota (MN)

Lyme Disease

- **Agent: *Borrelia burgdorferi***

- **Stages**
  - **Early localized (3-30 days after infection)**
    - **Erythema migrans (EM rash)**
  - **Disseminated**
    - **Early (days to weeks after infection)**
    - **Late (months after infection)**

Early and Late Disseminated Lyme Disease

- Multiple EM lesions
- Constitutional signs and symptoms
- Lyme carditis (usually AV block)
- Neuroborreliosis
  - Peripheral nervous system (e.g., Bell's palsy, radiculopathy)
  - Central nervous system (e.g., meningitis)
- Lyme arthritis (large joints; intermittent)
- Severe fatigue

Erythema Migrans (EM)

Lyme Arthritis

- **Large joints, especially the knee**
- **Intermittent**
- **Usually not painful or red (may be hot)**

Lyme Disease Diagnosis

- History of exposure to ticks or woods
- Serology
  - Not needed for early Lyme disease with single EM rash; antibodies may not be detectable for 2-3 weeks
  - Important for diagnosing disseminated Lyme or illness without EM; if ill >30 days, Western blot IgG should be positive
- PCR
  - Usefulness limited to joint fluid, if paired with serology

Lyme Disease Treatment *

- **Oral regimen**
  - **Doxycycline (not for children < 8 yrs), amoxicillin, cefuroxime axetil**
- **Parenteral regimen**
  - **Ceftriaxone (preferred), cefotaxime, penicillin G**
- **Duration: 2-4 weeks**
  - **Long-term treatment not recommended**

*** Wormser et al. CID 2006; 43:1089-134**

IDSA Guidelines: Recommended Lyme Disease Antibiotics

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 *d* 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)

Refer to paper for footnotes:
Wormser et al. CID 2006;43:1089-134

IDSA Guidelines: Recommended Lyme Disease Therapies

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]	…

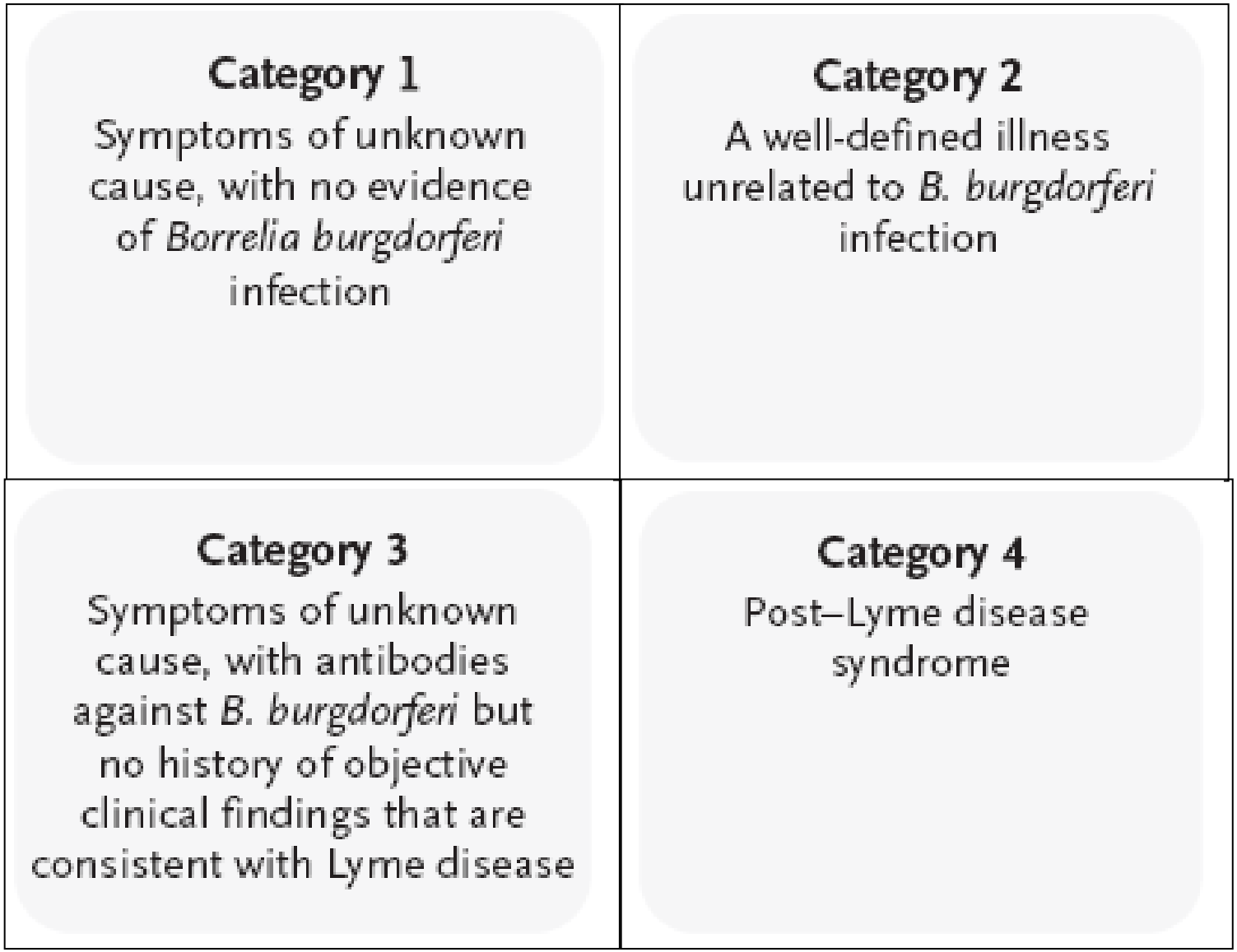
NOTE. Regardless of the clinical manifestation of Lyme disease, complete response to treatment may be delayed beyond the treatment duration. Relapse may occur with any of these regimens; patients with objective signs of relapse may need a second course of treatment.

Refer to paper for footnotes:
Wormser et al. CID 2006; 43:1089-134

Post-Lyme Disease Syndrome

- **After proper treatment for objective signs of Lyme disease**
- **Persistent (>6 months) subjective symptoms: myalgia, arthralgia, fatigue, cognitive difficulties**
- **Not due to active infection with *B. burgdorferi***
- **Causes may include:**
  - **Post-infectious inflammatory process**
  - **Coinfection**
  - **Unrelated process**

“Chronic Lyme Disease”



From Feder et al. 2007. NEJM 357:1422-30.

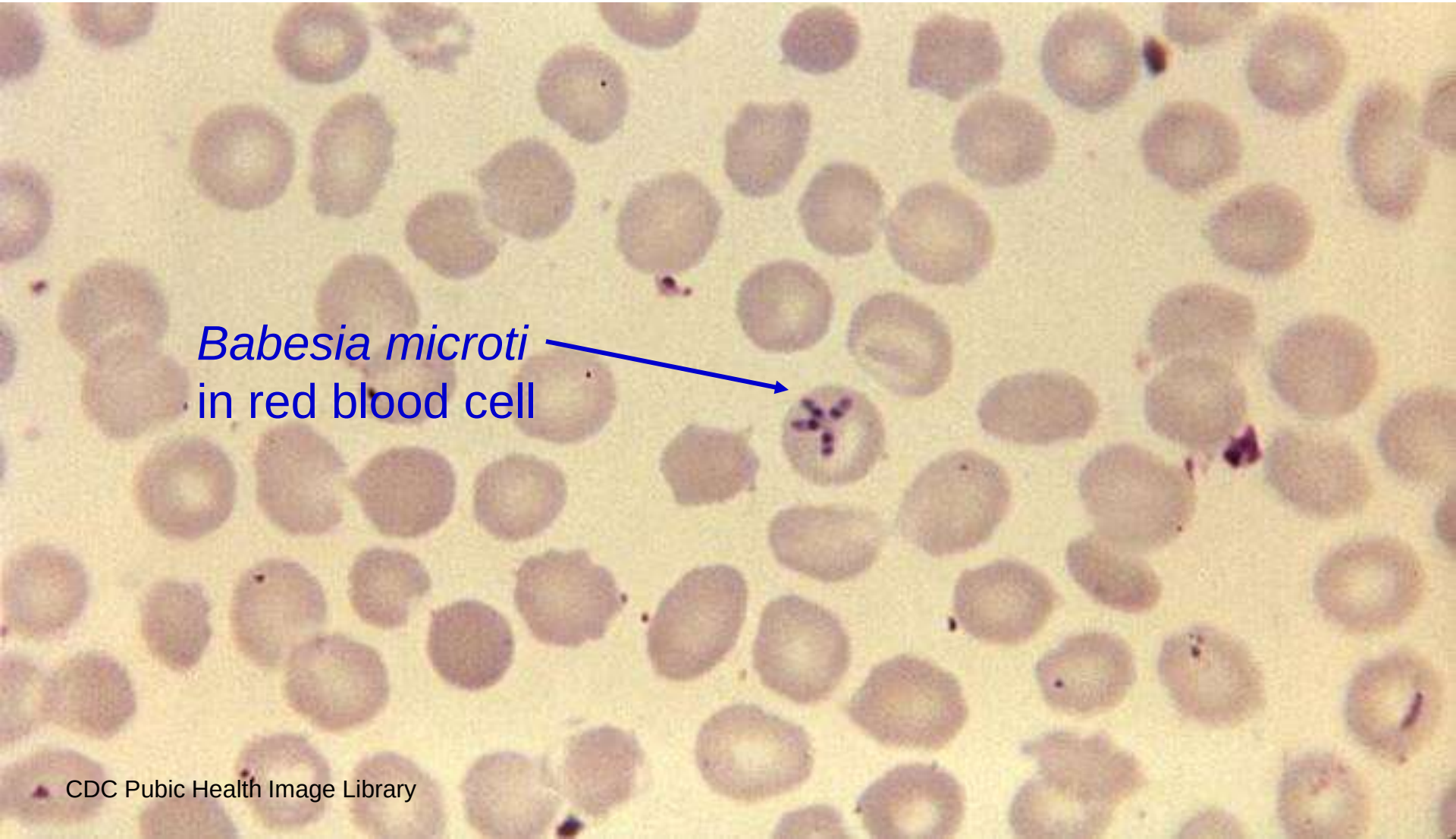
“Chronic Lyme Disease” (cont.)

- **Some patients seek long-term or repeated antibiotic therapy for persistent symptoms attributed to chronic *B. burgdorferi* infection**
- **Interpretation of tests often questionable**
- **Often lack current or previous objective evidence of Lyme disease**
- **In 2009, MDH *Clostridum difficile* surveillance detected a *C. difficile*-associated fatality in a woman receiving prolonged antibiotic therapy for Lyme disease (CID 2010;51[3]:369-70)**

Tick Bite Prophylaxis

- **200-mg dose of oral doxycycline, *when***
  - **Tick is a blacklegged tick (deer tick)**
  - **Tick was attached at least 36 hours**
  - **Doxycycline can be started <72 hours after removing tick**
  - **20% or more of local ticks infected**
  - **Patient is adult or child ≥ 8 years of age**
- **87% efficacy in preventing Lyme disease (NEJM 2001;345:79-84)**
- **Only studied for Lyme disease**

Babesiosis



CDC Pubic Health Image Library

Babesiosis Signs & Symptoms

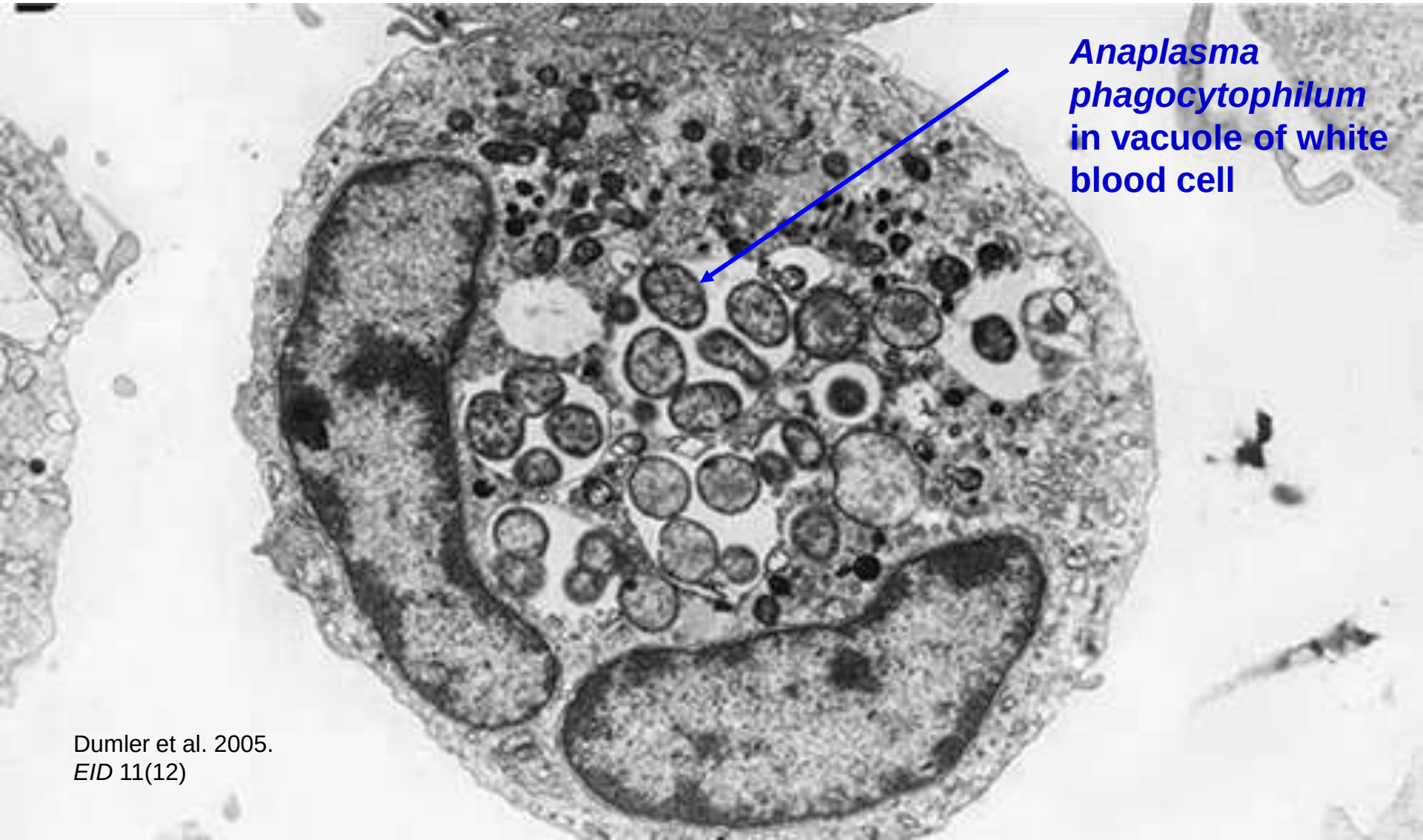
- **Agent: *Babesia microti*, other *Babesia* spp.**
- **Many infections are asymptomatic, especially in young or healthy individuals**
- **Symptomatic persons can have fever, chills, headache, muscle aches, fatigue, loss of appetite, anemia, low platelets**
- **Severe infections leading to organ failure and death can occur (most likely if elderly, asplenic, or otherwise immune compromised)**
- **Persistent infections can occur in symptomatic or asymptomatic individuals**

Babesiosis Diagnosis and Treatment

- **Diagnostic tests**
  - **Ideally order PCR plus either peripheral blood smear or serology**
- **Treatment**
  - **Milder cases: Atovaquone-azithromycin**
  - **Severe cases: Clindamycin-quinine**
    - **May need red blood cell transfusion**
    - **With certain forms of immune compromise, multiple treatment courses may be necessary***

***Krause et al 2008. CID 46:370-6**

Human Anaplasmosis/Ehrlichiosis



Dumler et al. 2005.
EID 11(12)

Anaplasmosis versus Ehrlichiosis

- **Anaplasmosis (*Anaplasma phagocytophilum*)**
  - **Expected in MN**
  - **Affects granulocytes (neutrophils)**
- **Ehrlichiosis (*Ehrlichia chaffeensis*)**
  - **Affects agranulocytes (monocytes)**
  - **NOT expected in MN**
- **Ehrlichiosis (*Ehrlichia muris*-like [EML] agent)**
  - **Expected in MN**

Anaplasmosis/Ehrlichiosis Signs and Symptoms

- **Many infections are asymptomatic, especially in young or healthy individuals**
- **Symptomatic persons have acute onset within 3-21 days after tick bite**
  - **High fever, chills, shaking, severe headache, muscle aches**
  - **Low white blood cells, low platelets, or elevated liver enzymes**
- **Severe complications (e.g. organ failure) and death can occur**

Anaplasmosis/Ehrlichiosis Diagnosis and Treatment

- **Diagnostic tests**
  - **Order PCR plus either peripheral blood smear or serology**
  - **Serologic cross-reactivity occurs between *Anaplasma*, *E. chaffeensis*, and EML agent; to differentiate, compare strength of titers or, ideally, order PCR**
- **Treatment**
  - **Begin empiric treatment with doxycycline for suspect cases while test results pending**
  - **Cases usually improve within 3 days**

Powassan (POW) Disease

- **Agent: Powassan virus (POWV), flavivirus closely related to West Nile virus (WNV);**
  - **Lineage II strain ("deer tick virus") carried by blacklegged ticks**
- **Manifestations**
  - **Encephalitis or meningitis: of known cases, 10-15% die; half have long-term sequelae**
  - **Some infections may cause only febrile illness or be asymptomatic**
- **Rarely identified: ~60 cases in N. America, 1958-2010**

POW Diagnosis

- **Available tests**
  - **Serology: POWV-specific IgM and IgG**
  - **Molecular: PCR**
  - **Specimens: serum, CSF**
- **Few laboratories in the U.S. offer POWV testing**
  - **State public health labs or Centers for Disease Control and Prevention (CDC)**

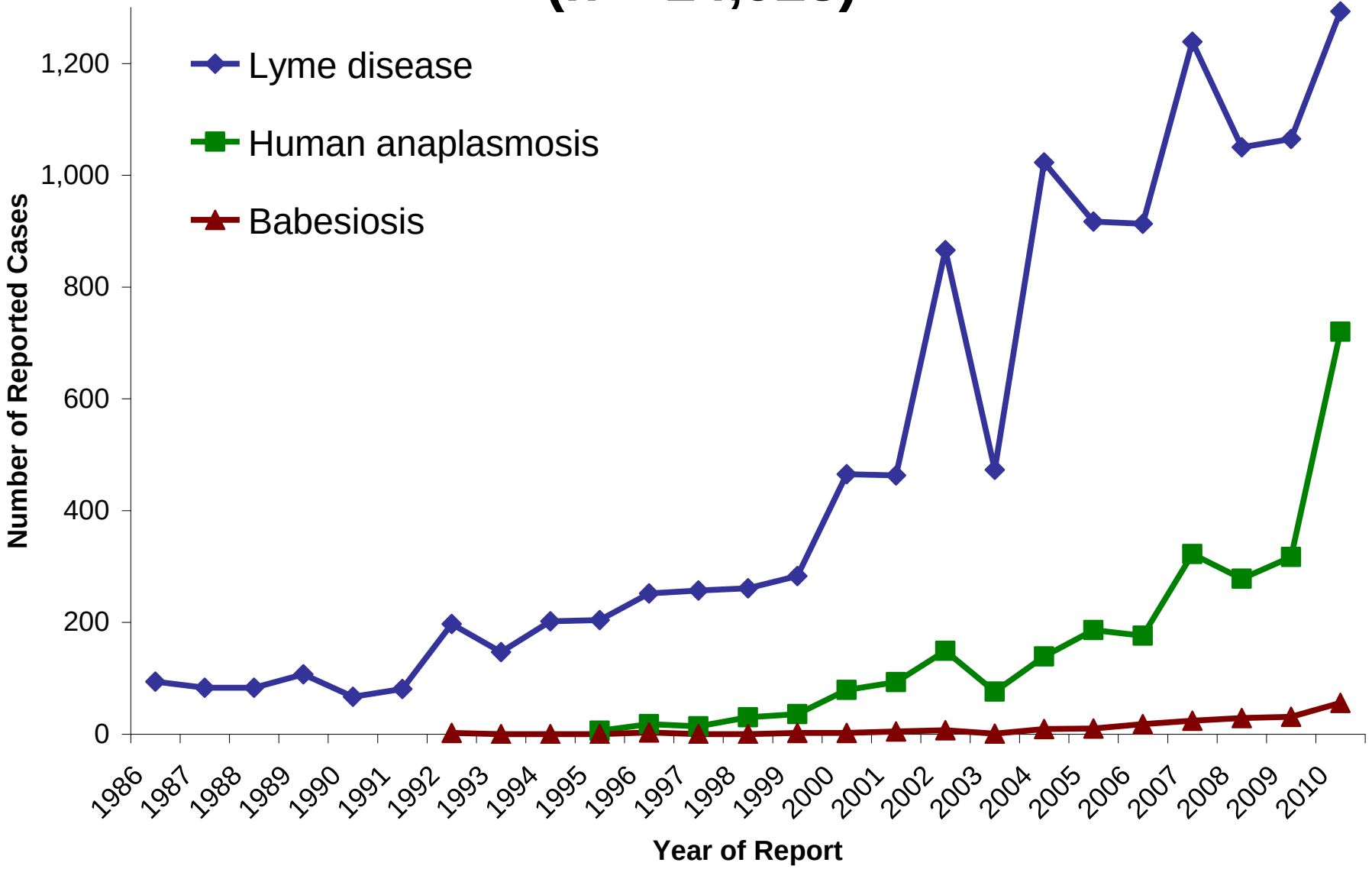
Rocky Mountain Spotted Fever (RMSF)

RMSF

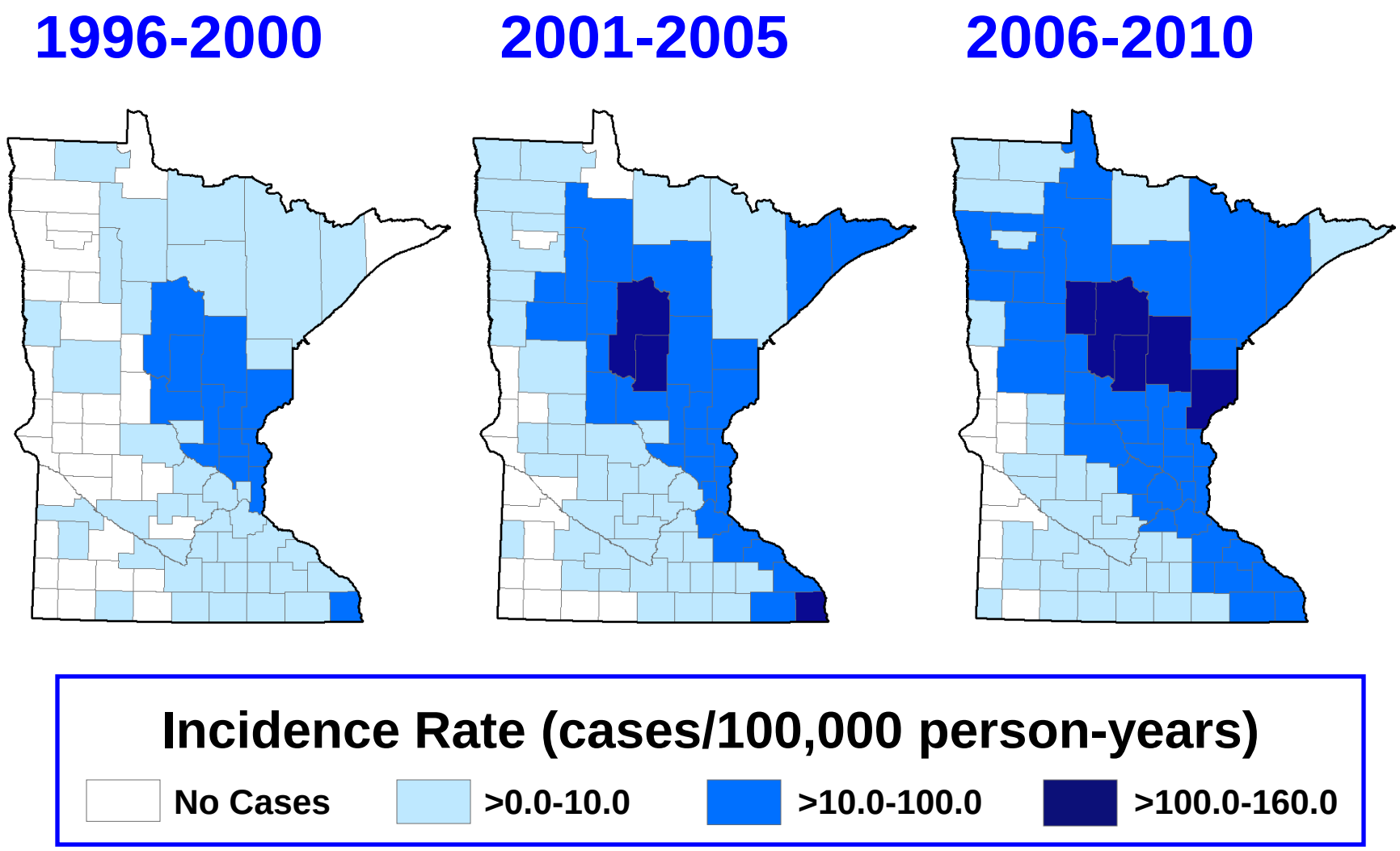
- **Agent: *Rickettsia rickettsii***
- **Classic illness: maculopapular or petechial rash, fever, headache, thrombocytopenia**
- **Suspect RMSF for patients with this presentation and tick/outdoor exposure**
  - **Note that *rash is not always present* when fever first arises**
- ***Do not delay treatment* with tetracycline if RMSF is suspected, even for young children**
  - **Prognosis and severity markedly worsen if docycycline not started by Day 5 of illness**

Epidemiology of TBDs in Minnesota

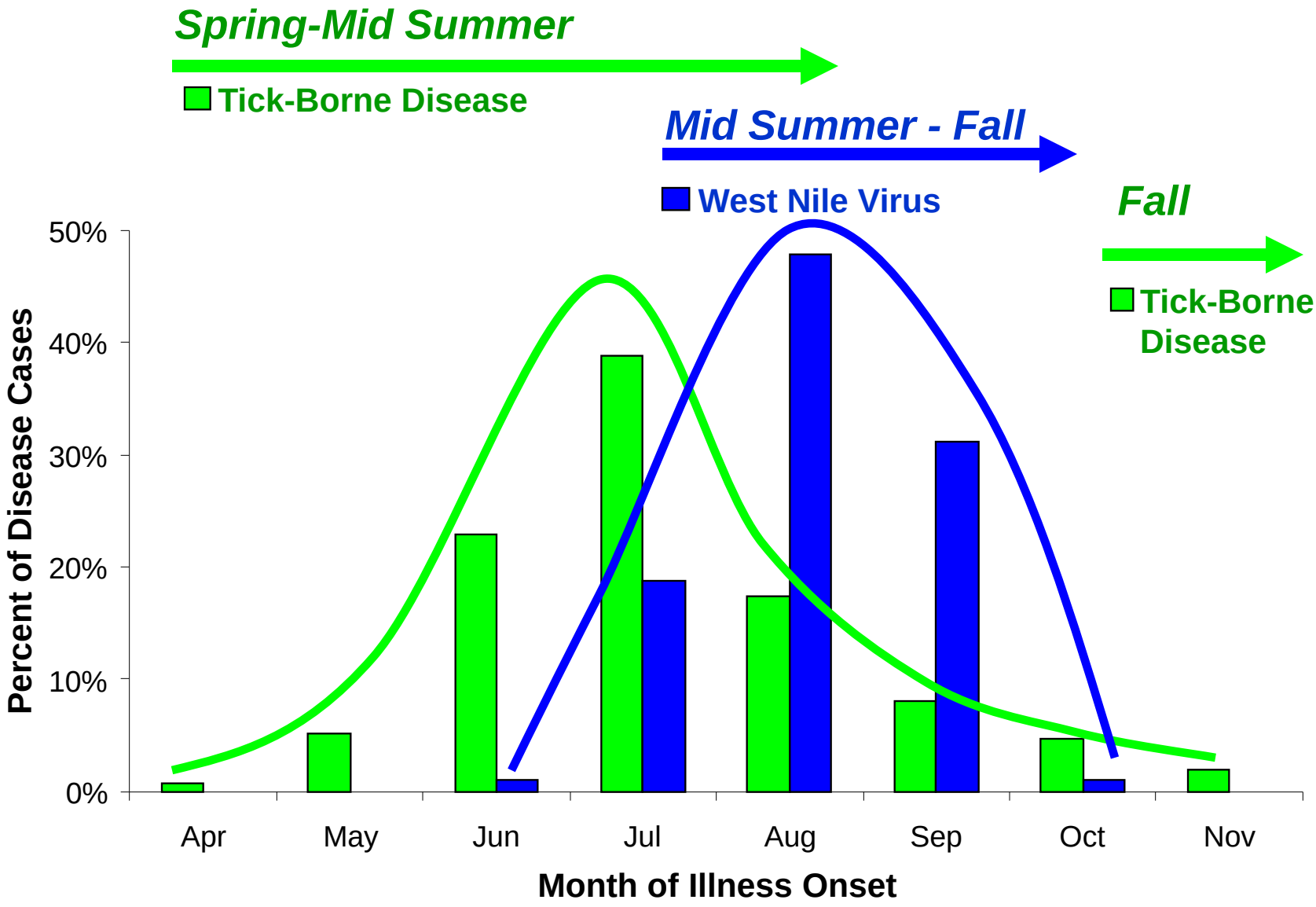
Reported Tick-Borne Disease Cases, MN, 1986-2010 (n = 14,923)



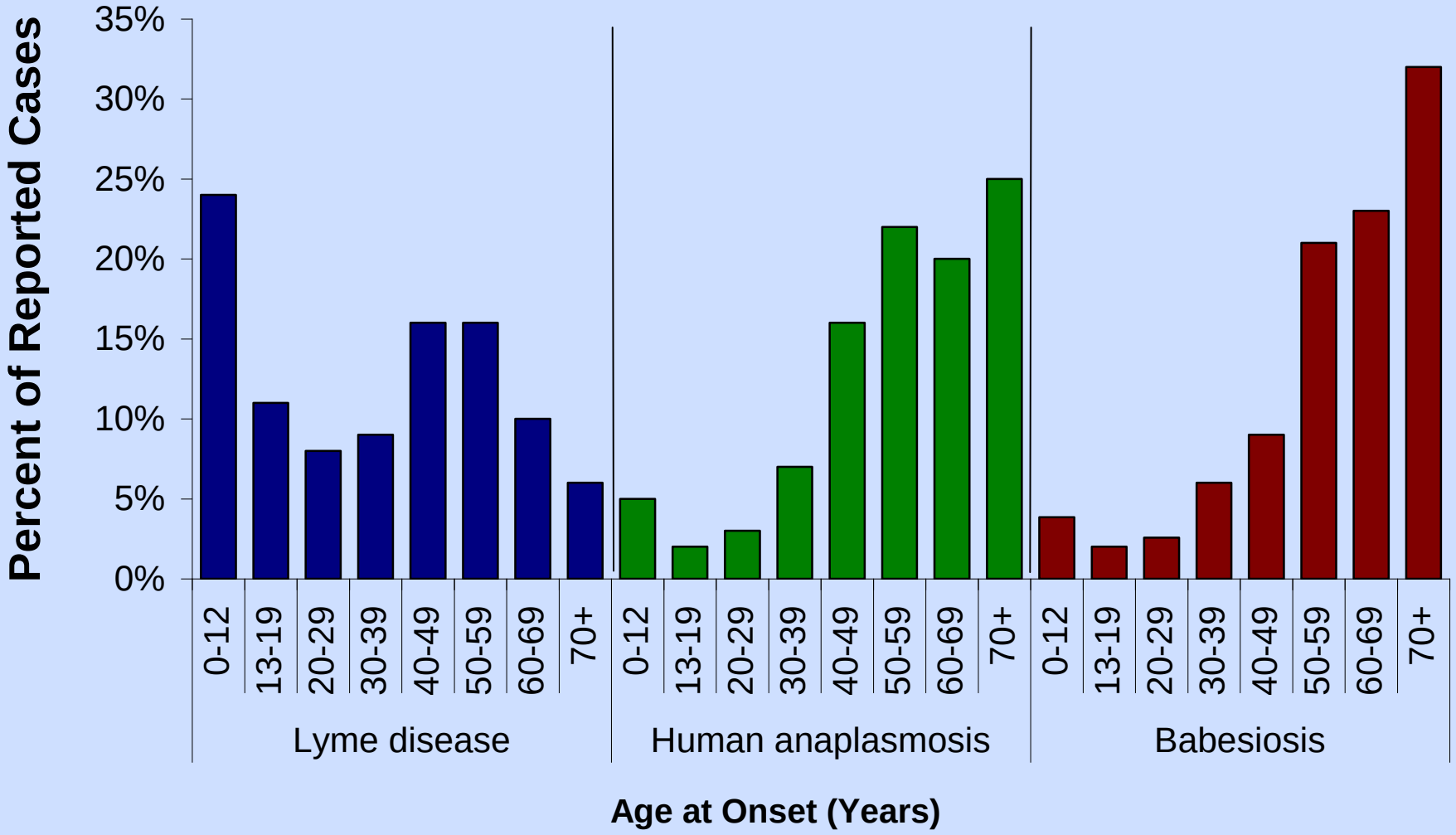
Distribution of Lyme Disease Cases by County of Residence, MN, 1996-2010



Vector-Borne Disease Cases by Month of Onset, MN, 1986-2009

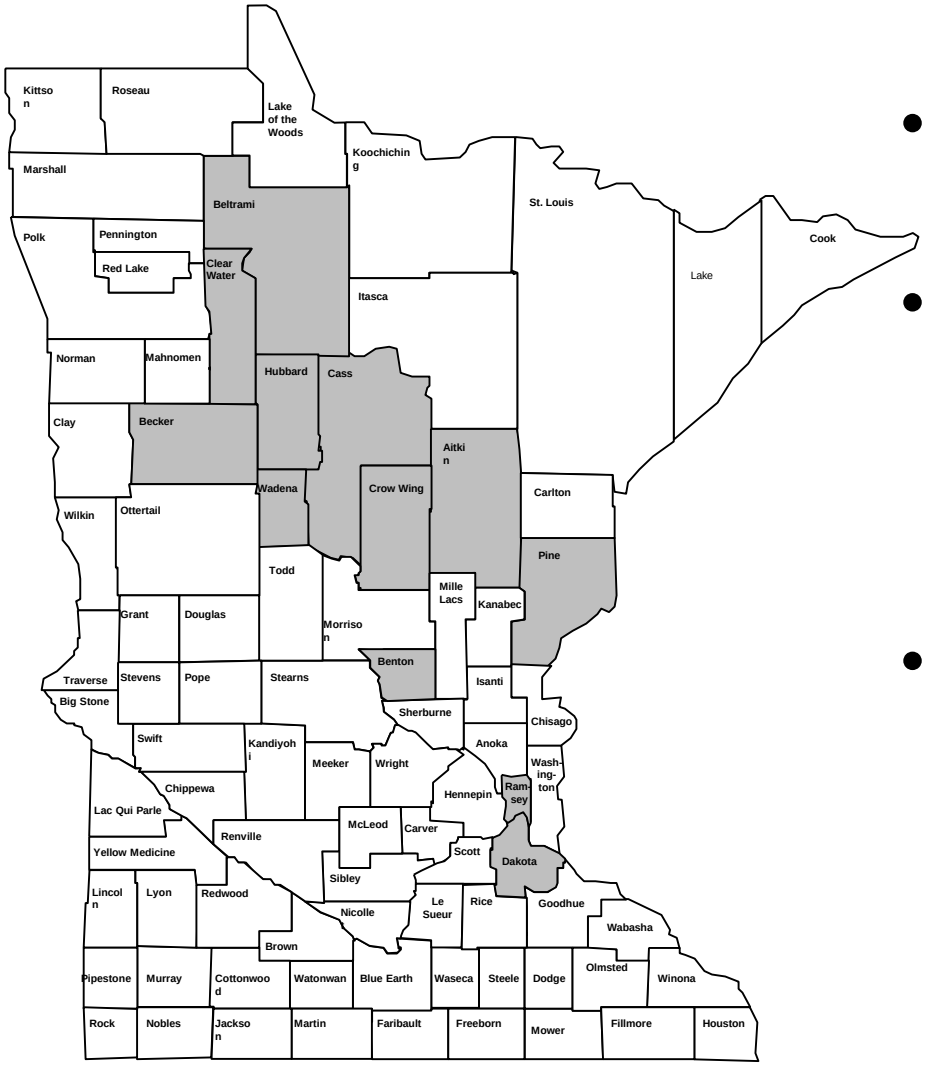


Reported Tick-Borne Disease Cases by Age at Onset, Minnesota, 1999-2008 (n = 9,247*)



** Excluding cases with unknown age*

Human Ehrlichiosis due to EML Agent: MN, 2009-2011

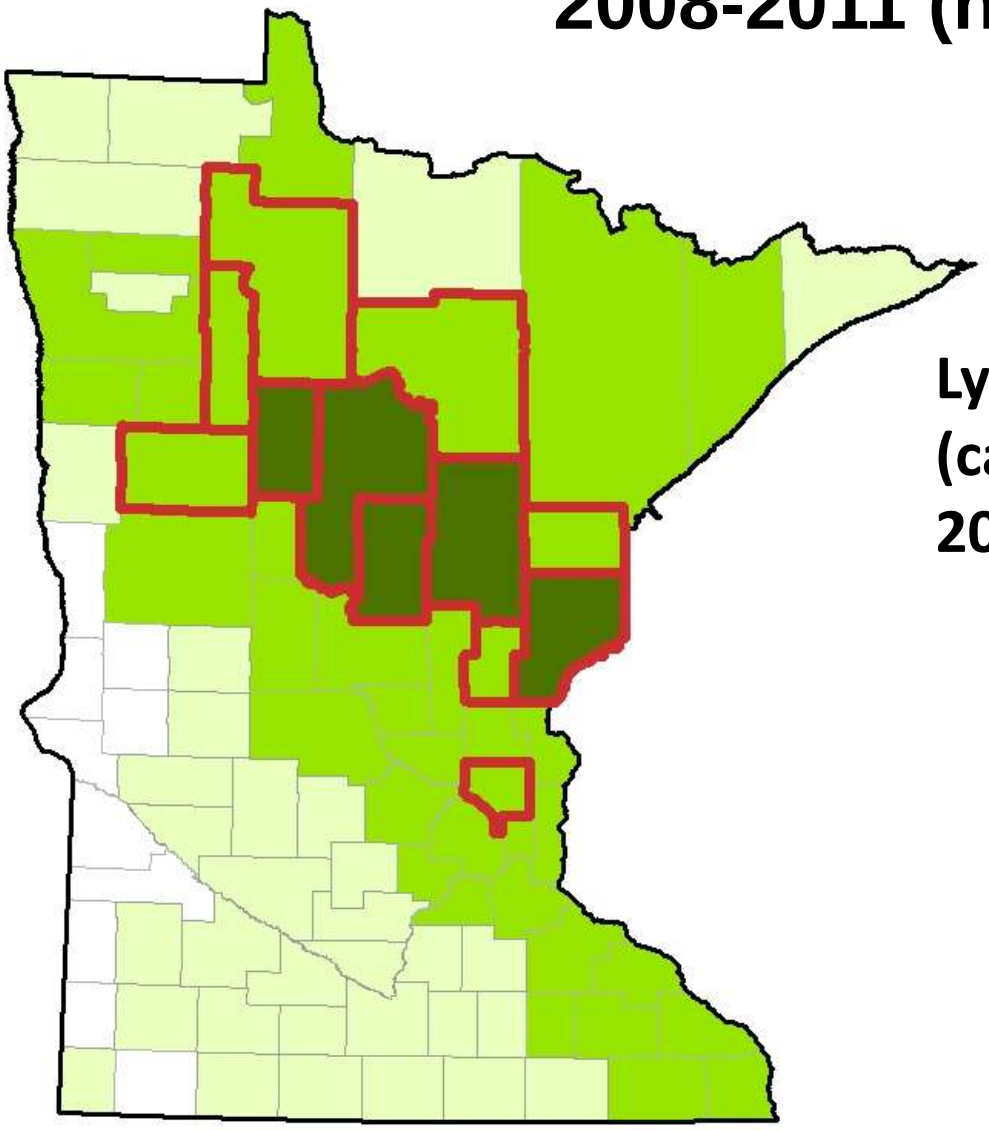


- **18 cases, 2009-2011**
- **EML identified by PCR performed by Mayo Medical Labs**
- **Exposed in areas of MN (grey on map) or Wisconsin endemic for blacklegged ticks and Lyme disease**

POW in MN, 2008-2011

- 2008-2011: 17 cases (11 in 2011)
- Severity
  - 10 encephalitis (1 death), 5 meningitis
  - 2 fever
  - 41% had sequelae
- Median age 49 years (range, 3 mos – 70 yrs)
- 82% male
- 35% immunosuppressed

POW Cases by Counties of Exposure, 2008-2011 (n=17*)



Powassan Case Exposure Counties

Lyme Disease Incidence Rate (cases/100,000 person-years), 2006-2010

- 0.0
- 0.1 – 10.0
- 10.1 – 100.0
- 100.1 – 130.0

RMSF in MN

- Thought to be rare in MN
  - Most reported cases have recent travel histories to endemic states or unconvincing illnesses or titers
- One PCR-confirmed fatal case reported in 2009 from Minnesota (Dakota County) in a pediatric case with no travel
- Primary vector (dog/wood tick) very common throughout MN in spring, early summer
- Also carried by brown dog tick, which can be in dog kennels year-round

TBD Risk from Blood Transfusions, Minnesota

- **Babesiosis: Increased numbers of transfusion-associated cases in recent years in MN and nationwide**
- **HA: Two well-documented cases in MN, 2007-2008**
- **POW: plausible, although no transfusion-acquired cases identified**

- **No screening of donated blood products performed routinely at this time for TBDs**

Prevention Messages for Your Patients

Avoid Tick Bites

- **Be aware of high-risk times and places**
- **Walk in the center of trails to avoid picking up ticks from brush**
- **Wear long pants, light-colored clothing, and repellent**
- **Perform tick checks**
- **Control ticks at home**

Use Effective Tick Repellents

- **DEET**
  - **Use product with up to 30% DEET**
  - **Apply to skin or clothing**
  - **Focus below the knees**

- **Permethrin**
  - **Apply to clothing only**
  - **Lasts through multiple washings**
  - **Good choice for people outside frequently**

Control Blacklegged Ticks at Home

- **Modify landscape**
  - **Remove leaf litter and brush from yard**
  - **Construct landscape barrier between lawn and woods**

- **Apply acaricide (pesticide) to low-lying vegetation**

References

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For More Information

Minnesota Department of Health

651-201-5414

David.Neitzel@state.mn.us

www.health.state.mn.us