

Minnesota Tick-Borne Diseases

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Infectious Disease Update

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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	<i>Borrelia burgdorferi</i>	Bacterium (spirochete)
Babesiosis	<i>Babesia microti</i>, <i>Babesia</i> spp.	Protozoan
Human anaplasmosis (HA)	<i>Anaplasma phagocytophilum</i>	Bacterium (Rickettsial)
Human ehrlichiosis (HE)	<i>Ehrlichia muris</i>-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



**Blacklegged Tick
(Deer Tick)
Nymph**



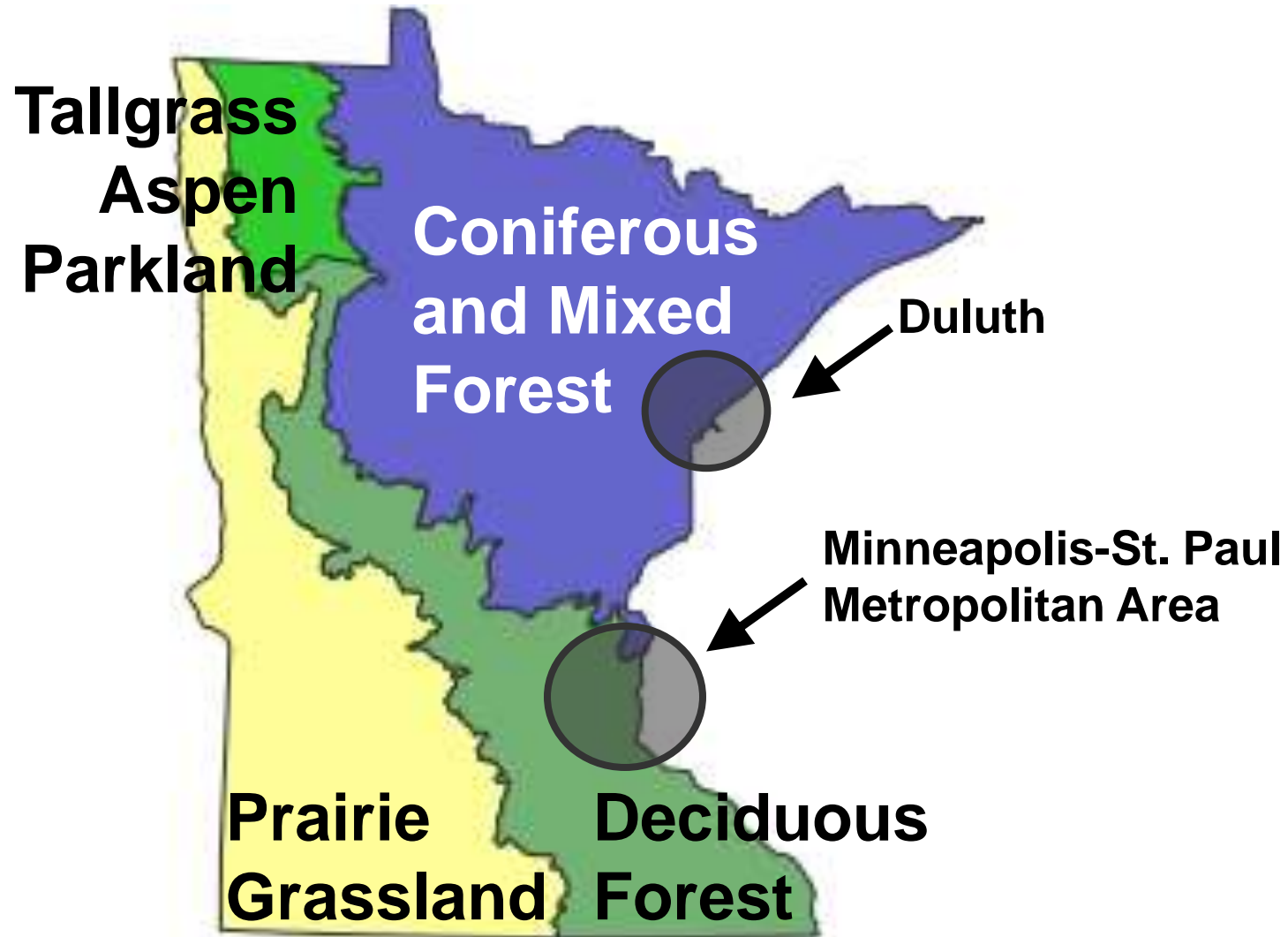
Engorged Blacklegged Tick (Deer Tick)



Blacklegged Tick Habitat

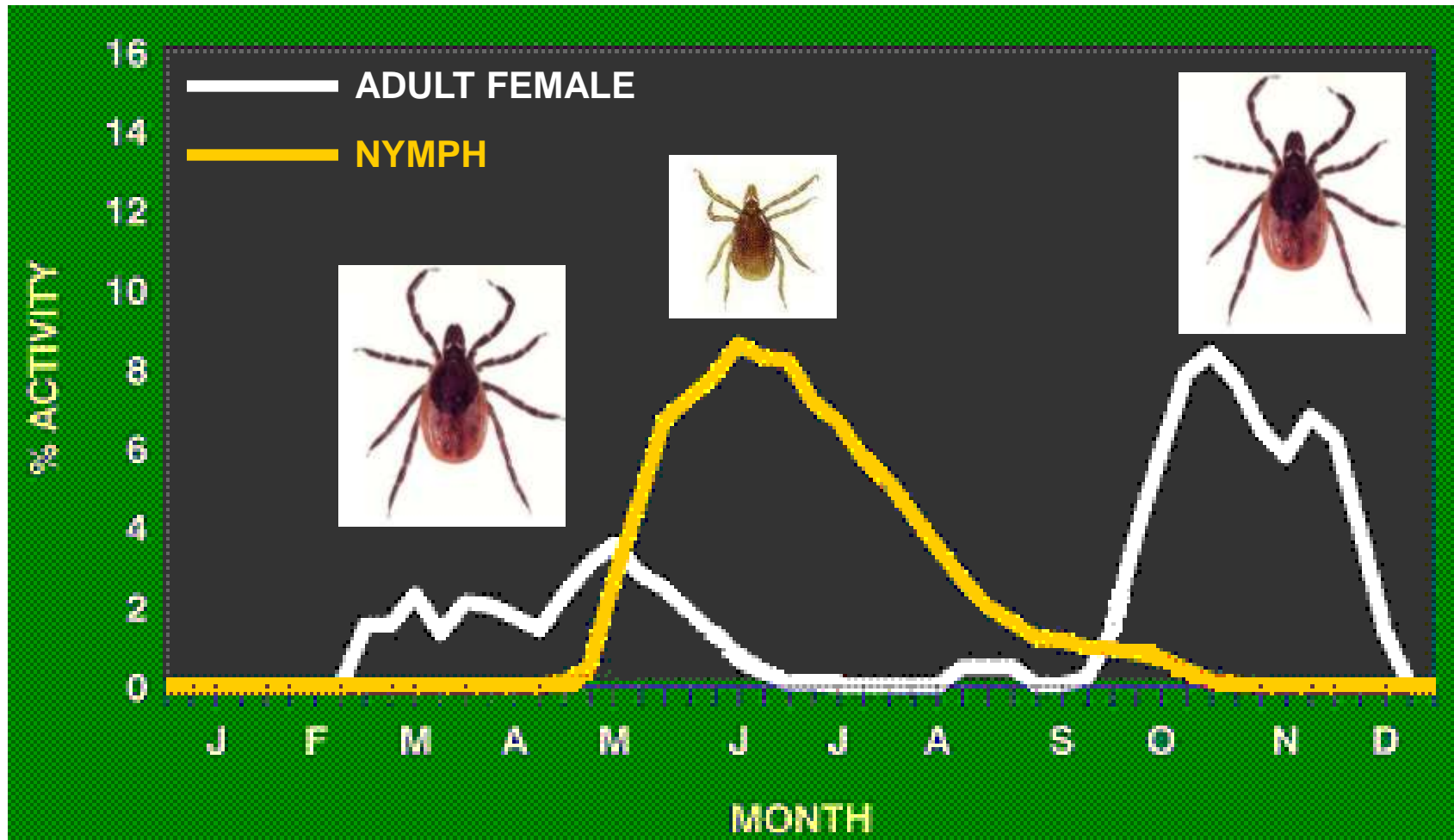


Minnesota Biomes



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
<p data-bbox="92 439 568 645">American dog tick (<i>Dermacentor variabilis</i>)</p> <p data-bbox="92 708 467 828">-Very common in MN</p>	<p data-bbox="1064 439 1487 619">Rocky Mountain spotted fever (RMSF)</p>	<p data-bbox="1534 439 1796 548"><i>Rickettsia rickettsii</i></p>
<p data-bbox="92 911 452 1116">Lone star tick (<i>Amblyomma americanum</i>)</p> <p data-bbox="92 1179 819 1379">-Not common In MN, but isolated specimens have been found</p>	<p data-bbox="1064 911 1367 1105">Human ehrlichiosis (HE)</p>	<p data-bbox="1534 911 1835 1019"><i>Ehrlichia chaffeensis</i></p>

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 <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)

**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 \geq 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”

Category 1

Symptoms of unknown cause, with no evidence of *Borrelia burgdorferi* infection

Category 2

A well-defined illness unrelated to *B. burgdorferi* infection

Category 3

Symptoms of unknown cause, with antibodies against *B. burgdorferi* but no history of objective clinical findings that are consistent with Lyme disease

Category 4

Post-Lyme disease syndrome

“Chronic Lyme Disease” (cont.)

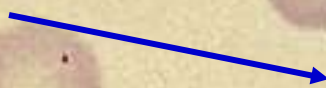
- **Some patients seek long-term or repeated antibiotic therapy for persistent symptoms attributed to chronic *B. burgdorferi* infection**
- **Interpretation of tests often questionable**
- **Often lack current or previous objective evidence of Lyme disease**
- **In 2009, MDH *Clostridium difficile* 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 \pm 8 years of age**
- **87% efficacy in preventing Lyme disease (NEJM 2001;345:79-84)**
- **Only studied for Lyme disease**

Babesiosis

Babesia microti
in red blood cell



Babesiosis Signs & Symptoms

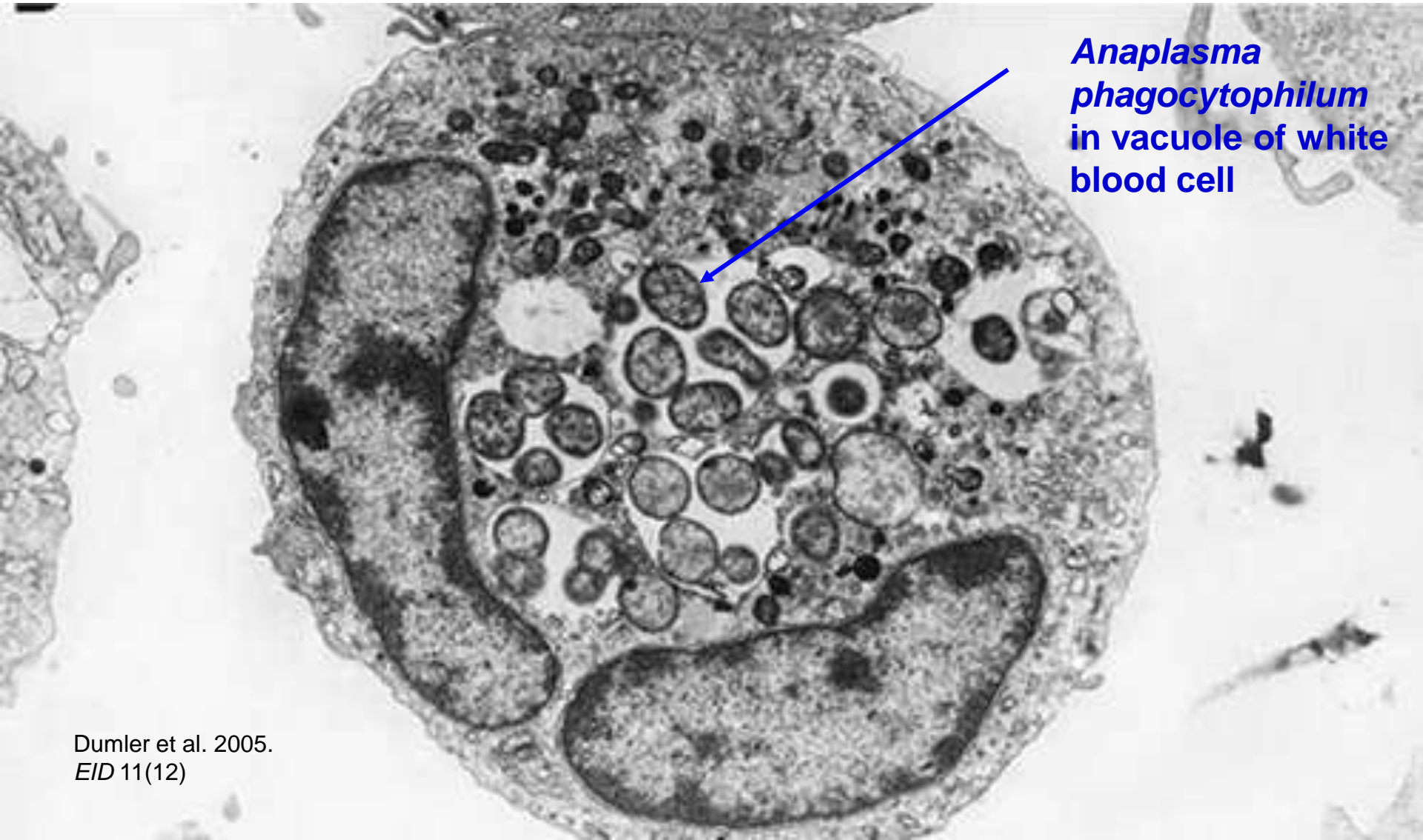
- **Agent: *Babesia microti*, other *Babesia* spp.**
- **Many infections are asymptomatic, especially in young or healthy individuals**
- **Symptomatic persons can have fever, chills, headache, muscle aches, fatigue, loss of appetite, anemia, low platelets**
- **Severe infections leading to organ failure 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



*Anaplasma
phagocytophilum*
in vacuole of white
blood cell

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)

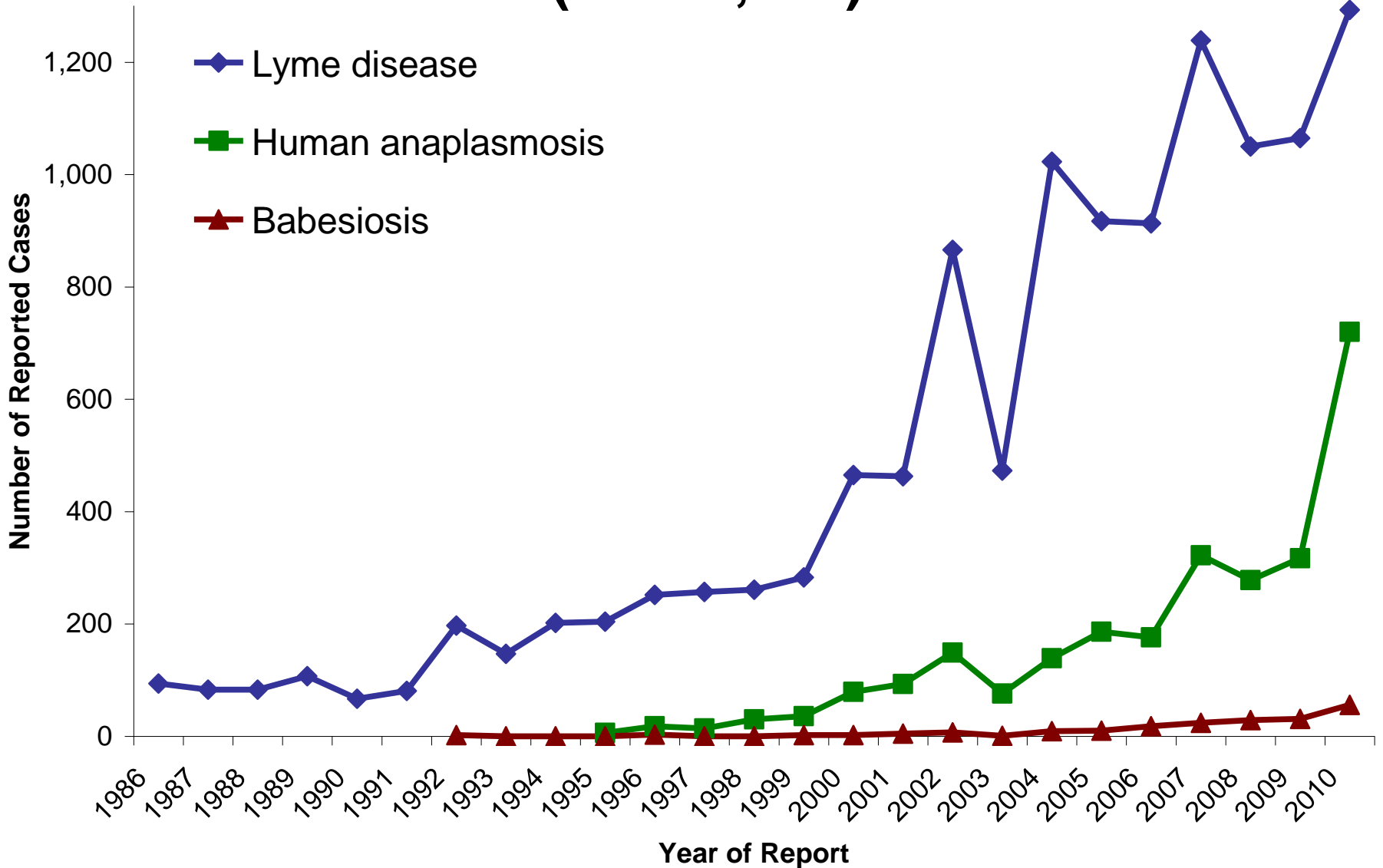


RMSF

- **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**

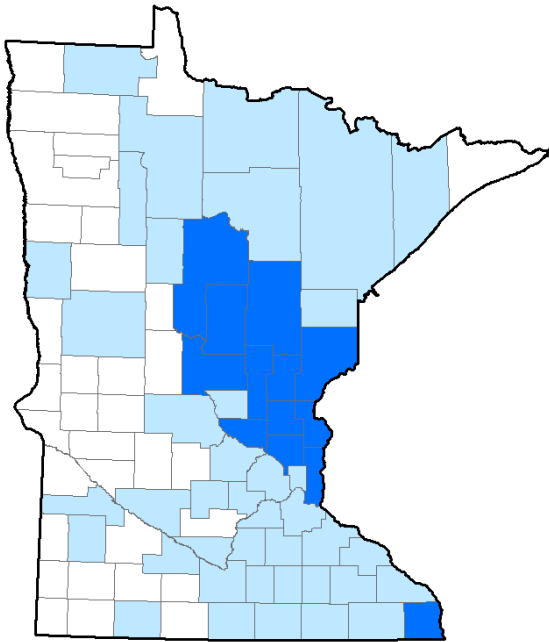
Epidemiology of TBDs in Minnesota

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

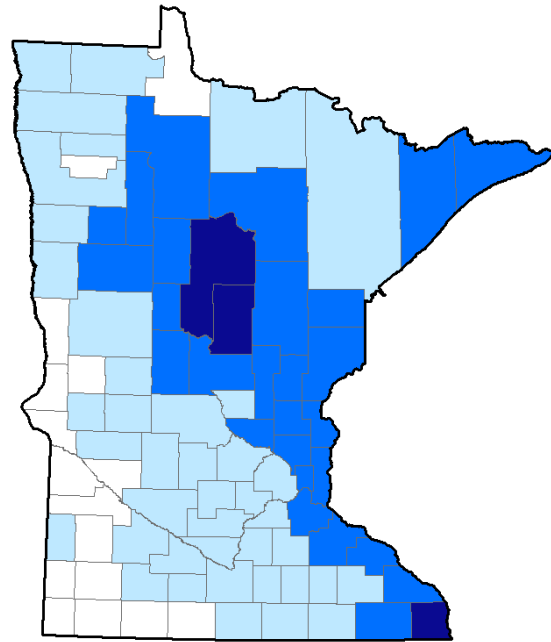


Distribution of Lyme Disease Cases by County of Residence, MN, 1996-2010

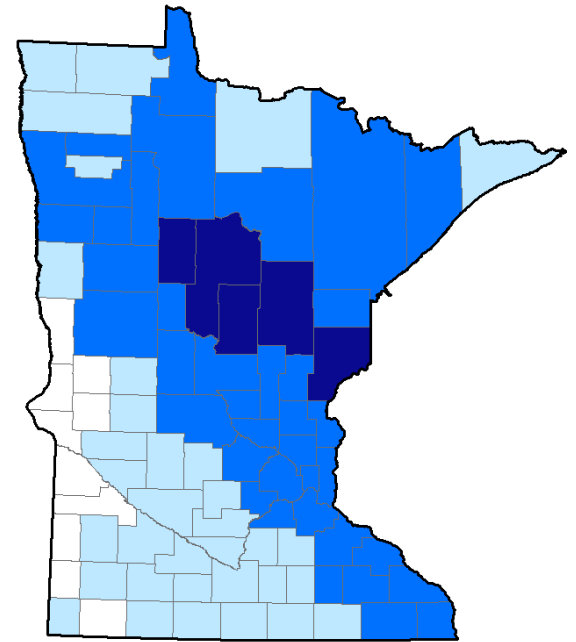
1996-2000



2001-2005



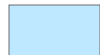
2006-2010



Incidence Rate (cases/100,000 person-years)



No Cases



>0.0-10.0

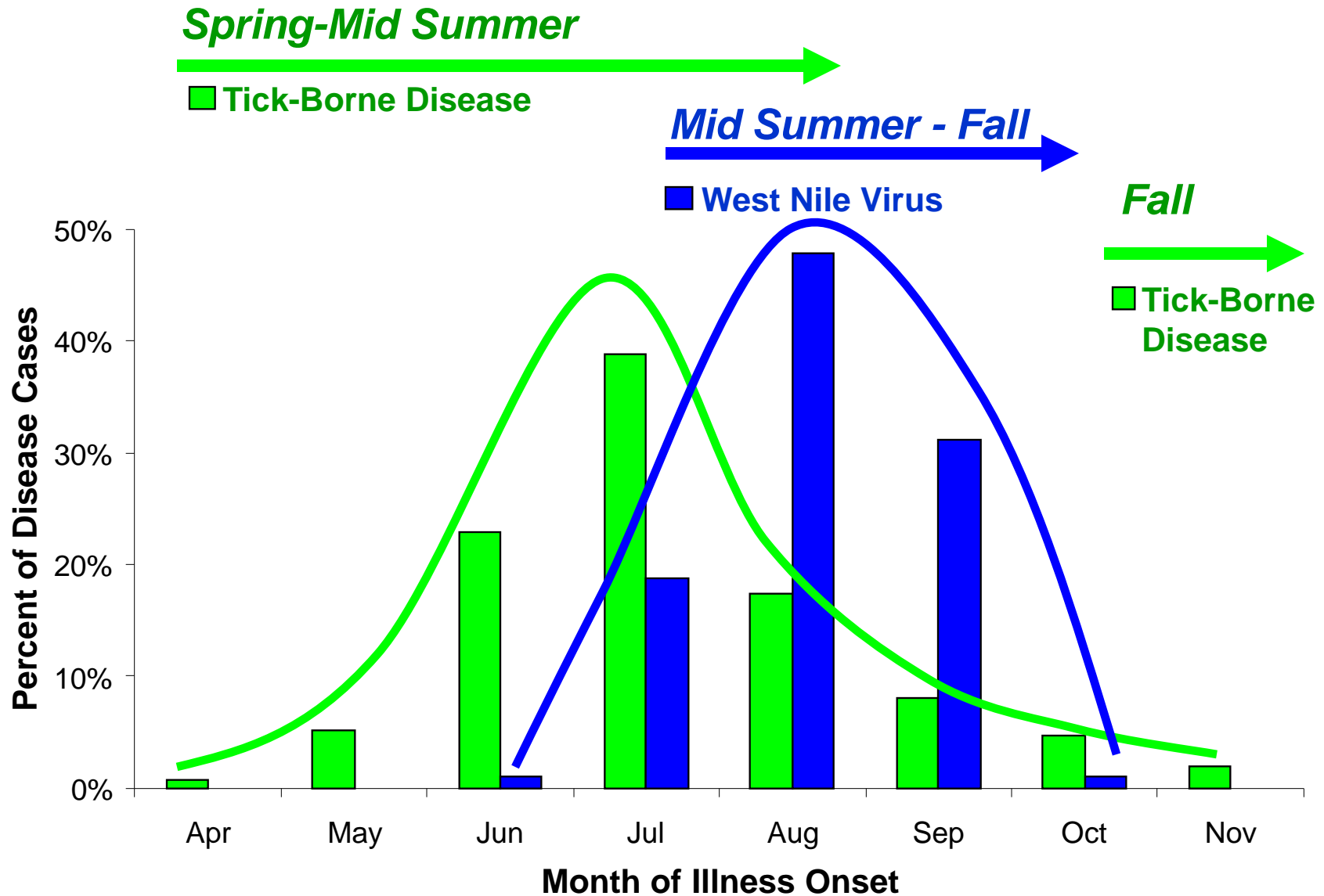


>10.0-100.0

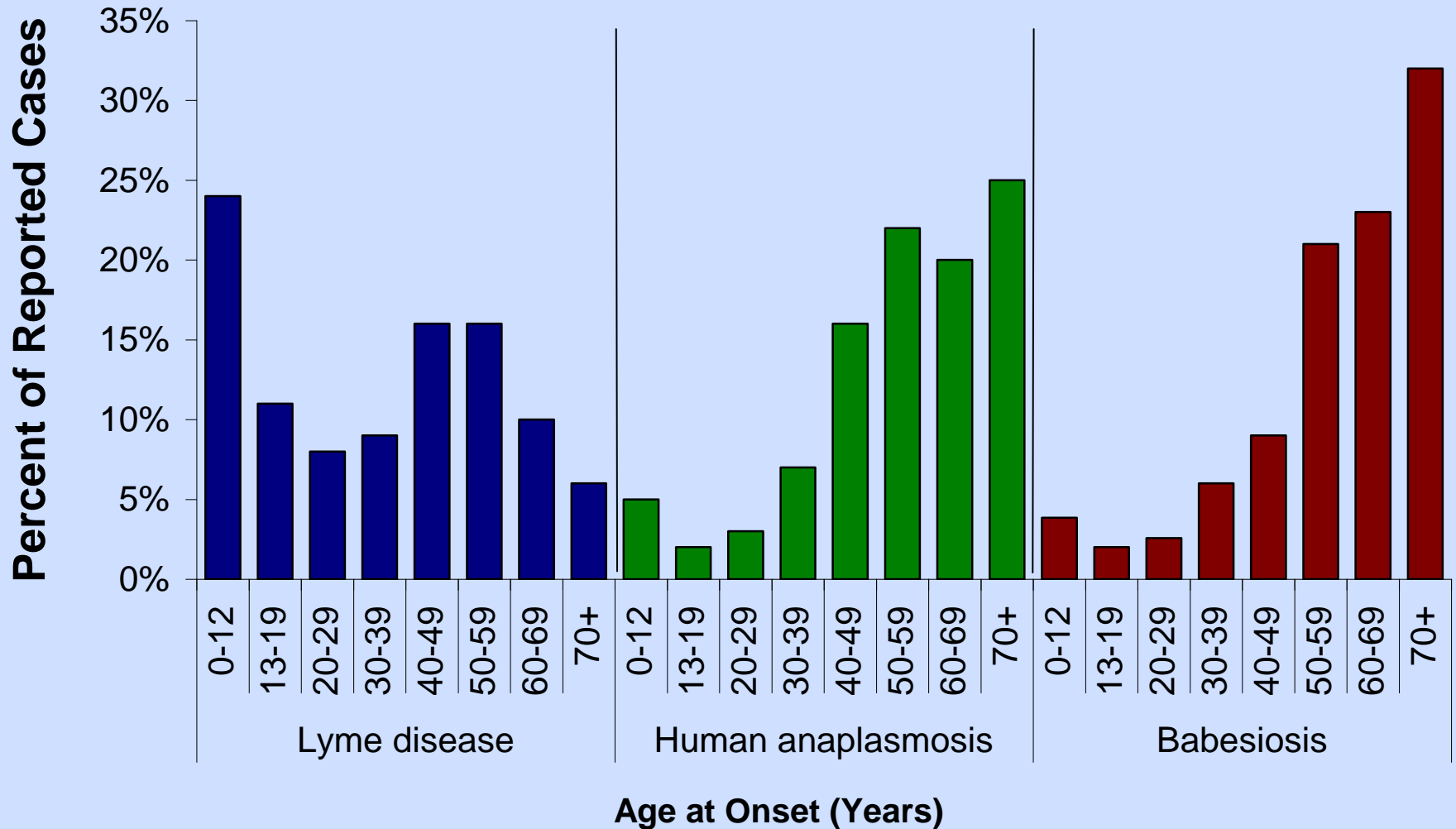


>100.0-160.0

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

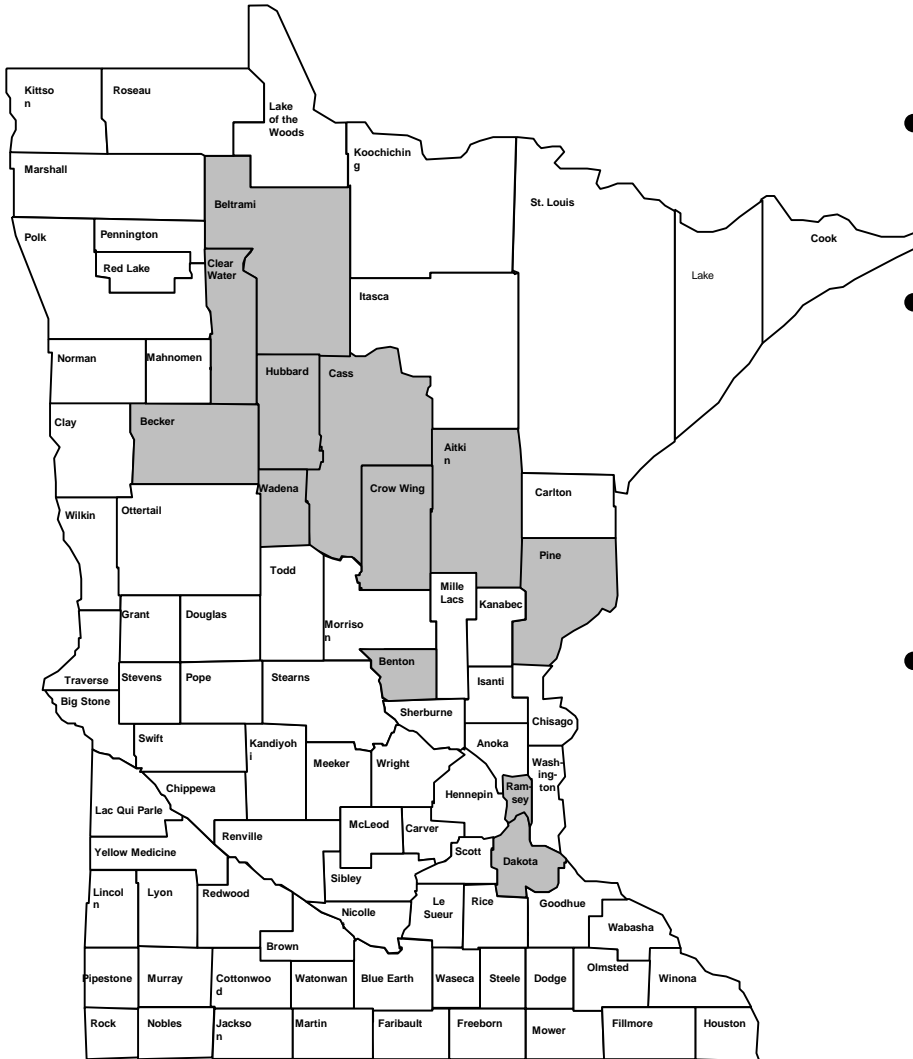


Reported Tick-Borne Disease Cases by Age at Onset, Minnesota, 1999-2008 (n = 9,247*)



* Excluding cases with unknown age

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

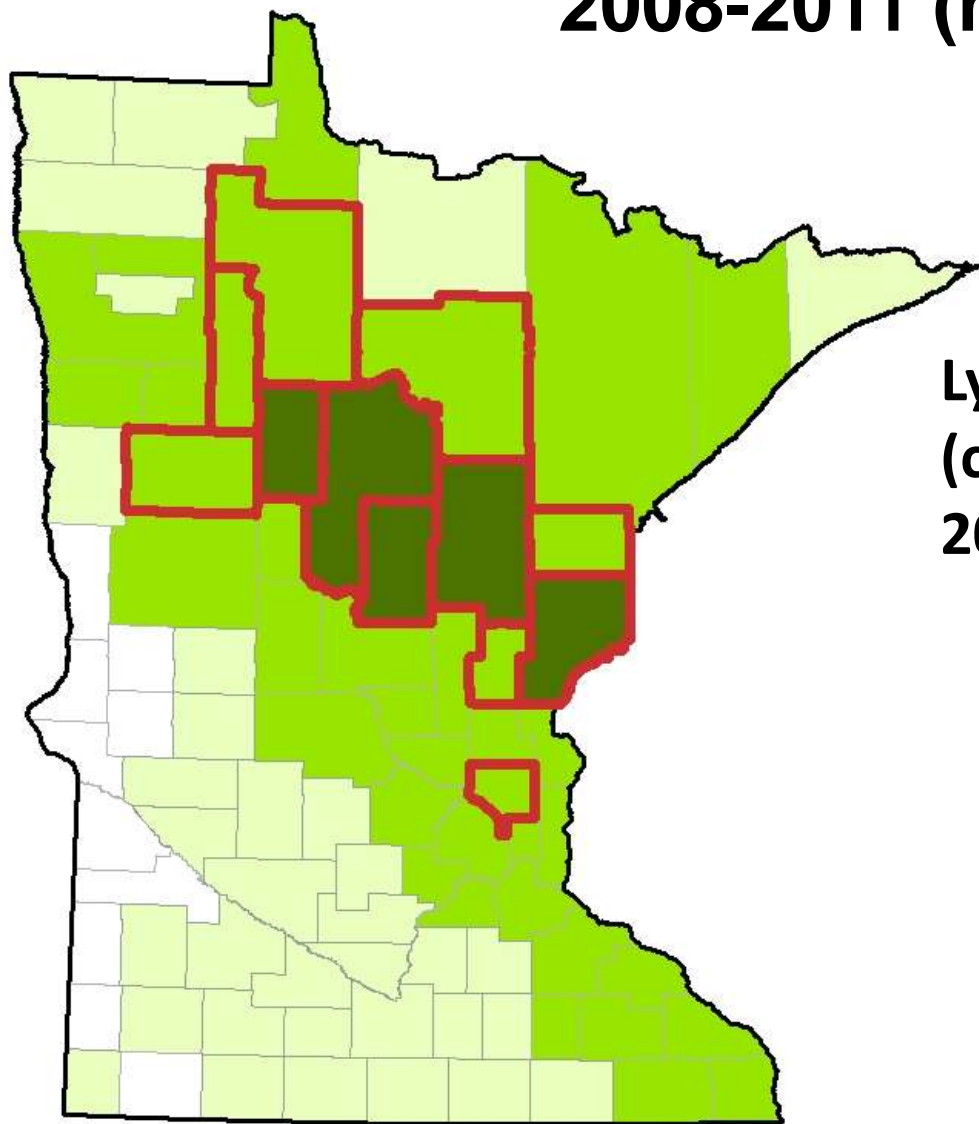


- **18 cases, 2009-2011**
- **EML identified by PCR performed by Mayo Medical Labs**
- **Exposed in areas of MN (grey on map) or Wisconsin endemic for blacklegged ticks and Lyme disease**

POW in MN, 2008-2011

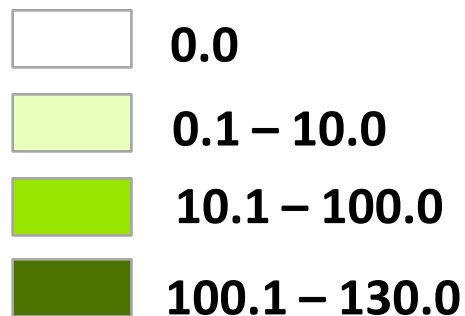
- **2008-2011: 17 cases (11 in 2011)**
- **Severity**
 - **10 encephalitis (1 death), 5 meningitis**
 - **2 fever**
 - **41% had sequelae**
- **Median age 49 years (range, 3 mos – 70 yrs)**
- **82% male**
- **35% immunosuppressed**

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



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

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