Minnesota Tick-Borne Diseases

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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

<table>
<thead>
<tr>
<th>Disease</th>
<th>Agent</th>
<th>Type of Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lyme disease</td>
<td><em>Borrelia burgdorferi</em></td>
<td>Bacterium (spirochete)</td>
</tr>
<tr>
<td>Babesiosis</td>
<td><em>Babesia microti,</em> <em>Babesia spp.</em></td>
<td>Protozoan</td>
</tr>
<tr>
<td>Human anaplasmosis (HA)</td>
<td><em>Anaplasma phagocytophilum</em></td>
<td>Bacterium (Rickettsial)</td>
</tr>
<tr>
<td>Human ehrlichiosis (HE)</td>
<td><em>Ehrlichia muris</em>-like (EML) agent</td>
<td>Bacterium (Rickettsial)</td>
</tr>
<tr>
<td>Powassan</td>
<td>Powassan virus</td>
<td>Virus</td>
</tr>
</tbody>
</table>
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

- Coniferous and Mixed Forest
- Tallgrass Aspen Parkland
- Prairie Grassland
- Deciduous Forest

Modified from Minnesota DNR, [http://www.dnr.state.mn.us/biomes/index.html](http://www.dnr.state.mn.us/biomes/index.html)
Seasonality of *Ixodes scapularis* Host-Seeking Activity

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

<table>
<thead>
<tr>
<th>TICK</th>
<th>DISEASE</th>
<th>AGENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>American dog tick</td>
<td>Rocky Mountain spotted fever</td>
<td>Rickettsia rickettsii</td>
</tr>
<tr>
<td>((Dermacentor variabilis))</td>
<td>(RMSF)</td>
<td></td>
</tr>
<tr>
<td>-Very common in MN</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lone star tick</td>
<td>Human ehrlichiosis</td>
<td>Ehrlichia chaffeensis</td>
</tr>
<tr>
<td>((Amblyomma americanum))</td>
<td>(HE)</td>
<td></td>
</tr>
<tr>
<td>-Not common in MN, but isolated specimens have been found</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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

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

Refer to paper for footnotes: Wormser et al. CID 2006;43:1089-134
## IDSA Guidelines: Recommended Lyme Disease Therapies

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

**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 ≥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

CDC Public 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

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)

Images: http://www.cdc.gov/ncidod/dvrd/rmsf/Signs.htm
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 doxycycline not started by Day 5 of illness
Epidemiology of TBDs in Minnesota
Reported Tick-Borne Disease Cases, MN, 1986-2010
(n = 14,923)

Year of Report
Number of Reported Cases
Lyme disease
Human anaplasmosis
Babesiosis
Distribution of Lyme Disease Cases by County of Residence, MN, 1996-2010

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

- No Cases
- >0.0-10.0
- >10.0-100.0
- >100.0-160.0

1996-2000

2001-2005

2006-2010
Vector-Borne Disease Cases by Month of Onset, MN, 1986-2009

Spring-Mid Summer
- Tick-Borne Disease

Mid Summer - Fall
- West Nile Virus

Fall
- Tick-Borne Disease

Percent of Disease Cases

Month of Illness Onset

Apr | May | Jun | Jul | Aug | Sep | Oct | Nov
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*)

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

• Krause et al. Persistent and relapsing babesiosis in immunocompromised patients. CID 2008; 46(3);370-6.