Tick-Borne Illnesses in Michigan

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They’re Coming!
Warmer Weather = Growing Problem

Tick-borne Lyme disease exploding into Michigan; human cases up 5-fold

Keith Matheny, Detroit Free Press
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CREEPING AND CRAWLING INTO MICHIGAN
The blacklegged or deer ticks that carry Lyme disease have steadily made inroads into Michigan in recent years. The expansion of the ticks’ range correlates with a similar expansion in human cases of Lyme disease in the state over the same time period.

<table>
<thead>
<tr>
<th>Year</th>
<th>Blacklegged Ticks, by County</th>
<th>Report</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998</td>
<td>5 Established 22 Reported</td>
<td></td>
</tr>
<tr>
<td>2007</td>
<td>12 Established 26 Reported</td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td>24 Established 18 Reported</td>
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Michigan Lyme Disease Risk Map: 2018
Lyme disease is an emerging disease transmitted by the blacklegged tick in Michigan. Local risk for Lyme disease varies depending on whether infected ticks are in the area. Several local and state agencies partner to conduct surveillance for Lyme disease in people and animals. The below map classifies risk upon field collected and infected animals and reported human cases of Lyme disease in Michigan (see the legend for specific details). The map is updated as new information becomes available.

For more information about Lyme disease prevention, visit www.michigan.gov/lyme
Most Important Tick-Borne Diseases in the U.S.

- Lyme disease (becoming common in MI)
- Anaplasmosis (rare in MI)
- Babesiosis (rare in MI)
- Ehrlichiosis (rare in MI)
- Rocky Mountain Spotted Fever (rare in MI)
American Dog tick  
*Dermacentor variabilis*

The American Dog tick is by far the most common tick found in Michigan. It is active from early May-November. It will readily bite humans and our companion animals. This species is the vector of Rocky Mountain spotted fever and tularemia, and is easily distinguished by its ornate scutum.

Woodchuck tick  
*Ixodes cookei*

Often confused with the Black-legged tick, *Ixodes cookei* is common in Michigan and will readily bite dogs and humans. People and pets will often come in contact near the dens of animals (skunks, woodchucks) in wooded environments. This species is the vector of Powassan encephalitis.

Black-legged tick  
*Ixodes scapularis*

Emerging as a serious public health concern in Michigan, the Black-legged tick is the vector of Lyme disease, granulocytic anaplasmosis, and babesiosis. This tick readily quests for hosts in the low vegetation of forests with abundant small mammals and white tailed deer; accumulating along human and game trails. See the map below for the currently known distribution.

Lone Star tick  
*Amblyomma americanum*

Known by its distinctive "Lone Star" marking, this tick is becoming more prevalent in Michigan. It will readily bite people and our companion animals, and is the vector of monocytic ehrlichiosis and tularemia. This tick is common in wooded areas with populations of white-tailed deer.

Brown Dog tick  
*Rhipicephalus sanguineus*

Also known as the Kennel tick, this species is unique in its ability to survive and breed in indoor environments. It is the vector of Rocky Mountain spotted fever, canine babesiosis and canine ehrlichiosis. Hygienic practices in shelters/kennels can prevent infestations.
Tick Identification

Actual Size Comparison
- Blacklegged (Deer) tick
- American dog (Wood) tick
- Lone star tick
  - Female, Male, Nymph, Larva

Tick removal tips

Common ticks found in Michigan
From left to right: Blacklegged tick nymph, Blacklegged tick female, Lone star tick female, American Dog tick female

www.michigan.gov/lyme
Ixodes scapularis

Vector for:
1) Lyme disease
2) Anaplasmosis
3) Babesiosis
Lyme Disease

• 1977: cluster of suspected JRA cases in Lyme, Connecticut
• 1981: causative agent discovered by Willy Burgdorfer
  – Spirochete named *Borrelia burgdorferi*
In 2014, 96% of confirmed Lyme disease cases were reported from 14 states:

- Connecticut
- Delaware
- Maine
- Maryland
- Massachusetts
- Minnesota
- New Hampshire
- New Jersey
- New York
- Pennsylvania
- Rhode Island
- Vermont
- Virginia
- Wisconsin

<table>
<thead>
<tr>
<th>Year</th>
<th>MI Cases</th>
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<tbody>
<tr>
<td>2010</td>
<td>76</td>
</tr>
<tr>
<td>2011</td>
<td>89</td>
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<tr>
<td>2012</td>
<td>80</td>
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<td>2013</td>
<td>114</td>
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<tr>
<td>2014</td>
<td>93</td>
</tr>
<tr>
<td>2015</td>
<td>125</td>
</tr>
<tr>
<td>2016</td>
<td>159</td>
</tr>
</tbody>
</table>
Life cycle & epidemiology

- Primary reservoirs:
  - Nymph: white-footed mouse
  - Adulte: white-tailed deer
- Vast majority of cases: May - August
- *B. burgdorferi* rarely transmitted with <48 hours of attachment
Early Localized Disease

- Erythema migrans (EM, bull’s eye rash)
- Occurs in approx 80% at site of tick bite within 7 – 14 days
- Can be associated with fever, malaise, flu-like symptoms
EM rash variations

- Classic EM: Circular red rash with central clearing that slowly expands
- Bluish hue without central clearing
- Red, expanding lesion with central crust
- Red, oval-shaped plaque on trunk
- Red-blue lesion with central clearing on back of knee
- Early disseminated Lyme disease: multiple red lesions with dusky centers
Early Disseminated Disease

- Occurs several weeks to months post-exposure
- Fever or flu-like syndrome common
- Cutaneous:
  - Multiple erythema migrans lesions
Early Disseminated Disease

- Neurologic manifestations (15%):
  - Occur weeks to months after exposure
  - Cranial nerve palsies
    - **Most commonly facial nerve**
    - Can be unilateral or bilateral
  - Lymphocytic meningitis
    - Similar to viral meningitis picture
  - Radiculoneuritis
    - Can mimic sciatica
    - Most commonly missed symptom
Early Disseminated Disease

• Cardiac manifestations (5%):
  – Occur weeks to months after exposure
  – New AV heart block
    • 1\textsuperscript{st} to 3\textsuperscript{rd} degree
    • Can fluctuate rapidly
  – Myopericarditis
    • Rare
    • Usually mild
Late Lyme Disease

Occurs months to years after exposure:

• Arthritis (common):
  – Intermittent attacks of pauciarticular pain & swelling
  – Usually large joints (classically knee)

• Neuro (rare, controversial):
  – Encephalopathy
  – Polyneuropathy
Post-Lyme Disease Syndrome

• No well-accepted definition
• Generally refers to persistent & disabling symptoms after treatment of Lyme (fatigue, malaise, arthralgias, myalgias)
• No data to suggest persistent or latent infection in these cases
• No role for antibiotics in management
Lyme Disease Diagnosis

- Erythema migrans = pathognomonic (treat, don’t test)
- Other cases: 2-tier testing (ELISA screen → confirmatory Western Blot)
  - ELISA false positives common (antigen cross-reacts with several other organisms)
  - Western Blot: + IgM with ≥ 4 weeks of symptoms highly likely to represent false positive. Send IgG alone if symptoms for ≥ 4 wks
- Testing utility dependent on pre-test probability
Lyme Testing Algorithm

Two-Tiered Testing for Lyme Disease

First Test
- Enzyme Immunoassay (EIA)
- Immunofluorescence Assay (IFA)

Second Test
- Signs or symptoms ≤ 30 days
  - IgM and IgG Western Blot
- Signs or symptoms > 30 days
  - IgG Western Blot ONLY

Consider alternative diagnosis OR
If patient with signs/symptoms consistent with Lyme disease for ≤ 30 days, consider obtaining a convalescent serum

National Center for Emerging and Zoonotic Infectious Diseases
Division of Vector Borne Diseases | Bacterial Diseases Branch
Lyme Western Blot

• IgG Western Blot requires **AT LEAST** 5 positive bands per CDC criteria
Lyme Disease Treatment

• Prophylaxis for *Ixodes* tick bite: doxycycline 200 mg x 1
  • Used for attached tick

• Early disease:
  – Doxycycline 100mg BID x 14 days
  – Alternatives: amoxicillin 500mg TID or cefuroxime

• Early disseminated disease:
  – Doxycycline x 14 – 28 days
  – Meningitis or advanced heart block: IV ceftriaxone x 28 d

• Late disease:
  – Arthritis: doxycycline x 28 days
  – Neurologic: IV ceftriaxone x 28 days

Jarisch-Herxheimer reaction in about 15% of early disseminated dz
What is the risk after a tick bite in endemic areas?

<table>
<thead>
<tr>
<th>Tick Stage and Engorgement Status</th>
<th>Doxycycline Group (N=235)</th>
<th>Placebo Group (N=247)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nymphal</td>
<td>1/124 (0.8)</td>
<td>8/142 (5.6)</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td>Partially engorged</td>
<td>1/78 (1.3)</td>
<td>8/81 (9.9)</td>
<td>0.03</td>
</tr>
<tr>
<td>Unfed (flat)</td>
<td>0/43</td>
<td>0/59</td>
<td>1.00</td>
</tr>
<tr>
<td>Adult female</td>
<td>0/100</td>
<td>0/97</td>
<td>1.00</td>
</tr>
<tr>
<td>Partially engorged</td>
<td>0/28</td>
<td>0/36</td>
<td>1.00</td>
</tr>
<tr>
<td>Unfed (flat)</td>
<td>0/66</td>
<td>0/57</td>
<td>1.00</td>
</tr>
<tr>
<td>Larval</td>
<td>0/10</td>
<td>0/8</td>
<td>1.00</td>
</tr>
<tr>
<td>Adult male</td>
<td>0/1</td>
<td>0/0</td>
<td>1.00</td>
</tr>
<tr>
<td>All</td>
<td>1/235 (0.4)</td>
<td>8/247 (3.2)</td>
<td>&lt;0.04</td>
</tr>
</tbody>
</table>

*P values were derived by the two-tailed Fisher’s exact test.
Anaplasmosis: formerly known as human granulocytic ehrlichiosis (HGE)

- *Anaplasma phagocytophilum* – intracellular GNR that infects neutrophils
- 2 – 25% *I. scapularis* ticks coinfected with *B. burgdorferi* & *A. phagocytophilum*
- Similar epi to Lyme (shared vector)
- Approx 2,000 cases annually.
Anaplasmosis

• Incubation: 7-10 days
• Presentation: wide spectrum of severity
  – Fevers, malaise, myalgias, headaches (flu-like)
  – Rash is rare
  – Labs: leukopenia, thrombocytopenia, elevated AST/ALT
• Diagnosis: if clinical suspicion, start tx!
  – morulae in PMN cytoplasm (50% sensitive)
  – serology only helpful retrospectively
  – PCR most sensitive for acute disease (send out)
• Treatment: doxycycline x 10 d
Babesiosis: our very own malaria cousin

• *Babesia microti*: erythrocyte-infecting protozoa
• Same Ixodes vector as Lyme & Anaplasma
• Hyperendemic in coastal counties & islands of southern New England
• Reports of transmission via blood transfusion
• Approx 1,800 cases annually
Babesiosis

- Incubation: **1-6 wks**
- Presentation: **wide spectrum of severity**
  - Typical picture: fever, chills, malaise, weakness, HA
  - Labs: **hemolysis** (low Hb, haptoglobin, high LDH & total bili)
  - Exam: jaundice, hepatosplenomegaly if severe
  - Complications: ARDS, DIC, AKI, CHF, splenic rupture

- Risk factors for severe disease:
  - **Splenectomy**
  - Immunocompromised state
  - Advanced age
Babesiosis

• Dx: blood smear is gold standard
  – Ring or pear-shaped organisms in rbcs
  – “Maltese cross” tetrad
  – Occas extra-erythrocytic organisms
  – PCR: more sensitive for very low-level parasitemia

Treatment
• Mild/mod disease: azithromycin + atovaquone
• Severe disease: clindamycin + quinine
Ehrlichiosis

LONE STAR TICK
*Amblyomma americanum*

Where found: Widely distributed in the southeastern and eastern United States.

Transmits: *Ehrlichia chaffeensis* and *Ehrlichia ewingii* (which cause human ehrlichiosis), tularemia, and STARI.

Comments: A very aggressive tick that bites humans. The adult female is distinguished by a white dot or “lone star” on her back. Lone star tick saliva can be irritating; redness and discomfort at a bite site does not necessarily indicate an infection. The nymph and adult females most frequently bite humans and transmit disease.

Reported Ehrlichiosis distribution 2014, CDC
Anaplasmosis & Ehrlichiosis: very similar diseases
**Ehrlichia chaffeensis & ewingii**

- Intracellular GNRs that infect monocytes
- Clinical picture & treatment virtually identical to anaplasmosis
- Diagnosis: if clinical suspicion, start tx!
  - morulae seen in monocyte cytoplasm (only 20-30% sensitive)
  - serology only helpful retrospectively
  - PCR most sensitive for acute disease (send out)
STARI – Mimicker of Lyme Disease

– Associated with lone star tick bite
– Occurs in Southcentral US
– Typical erythema migrans lesion and mild flu-like symptoms
– Negative Lyme serology
– Treatment: same as early Lyme (doxy x 10 d)
– No known long-term complications

Suspected pathogen: *Borrelia lonestari*
Rocky Mountain Spotted Fever

**AMERICAN DOG TICK**
*Dermacentor variabilis*

*Where found:* Widely distributed east of the Rocky Mountains. Also occurs in limited areas on the Pacific Coast.

*Transmits:* Tularemia and Rocky Mountain spotted fever.

*Comments:* The highest risk of being bitten occurs during spring and summer. Dog ticks are sometimes called wood ticks. Adult females are most likely to bite humans.
Rocky Mountain Spotted Fever

- *Rickettsia rickettsii* – intracellular GNR with tropism for vascular endothelium
- Incubation: 5-7 days
- Symptoms: fever, malaise, myalgias, HA, abd pain
- Signs:
  - Petechial rash is hallmark: begins distally then spreads centrally. Examine palms & soles.
- Rash often lags other signs/symptoms by 3-5 days
Rocky Mountain Spotted Fever

- Labs:
  - ↓ platelets
  - ↑ AST/ALT
  - CSF: lymphocytic pleocytosis

- Dx: largely clinical
  - Serology insensitive in 1st 2 wks of illness
  - PCR of skin bx can be helpful but serum PCR insensitive

Complications: distal extremity necrosis, ARDS, GI bleeding
RMSF

• Treatment:
  – **Start immediately** if you have clinical suspicion (even if rash is absent)
  – Doxycycline is treatment of choice
  – Should note clinical improvement within 72 hrs
  – Chloramphenicol is alternative agent for pregnant women
Less Common Tick-Borne Diseases

- Heartland Virus
  - Vector: lone star tick
- Powassan encephalitis
  - Vector: black legged tick
- Tularemia
  - Pathogen: *Francisella tularensis*
  - Vector: American Dog tick & Lone Star Tick
- Relapsing Fever
  - Pathogen: *Borrelia spp.*
  - Vector: argasid (soft body) ticks
- Spotted Fever
  - Pathogen: *Rickettsia parkeri*
  - Vector: Gulf Coast tick
How to remove a tick

Items you will not need:

1. Use fine-tipped tweezers to grasp the tick as close to the skin's surface as possible.

2. Pull upward with steady, even pressure. Don't twist or jerk the tick; this can cause the mouth-parts to break off and remain in the skin. If this happens, remove the mouth-parts with tweezers. If you are unable to remove the mouth easily with clean tweezers, leave it alone and let the skin heal.

3. After removing the tick, thoroughly clean the bite area and your hands with rubbing alcohol, an iodine scrub, or soap and water.

4. Dispose of a live tick by submerging it in alcohol, placing it in a sealed bag/container, wrapping it tightly in tape, or flushing it down the toilet. Never crush a tick with your fingers.
How to prevent tick bites

Protect Yourself Against Lyme Disease in Spring, Summer, and Fall

1. Walk in the middle of trails, away from tall grass and bushes.
2. Wear a long-sleeved shirt.
3. Wear white or light-colored clothing to make it easier to see ticks.
4. Wear a hat.
5. Spray tick repellent on clothes and shoes before entering woods.
6. Wear long pants tucked into high socks.
7. Wear shoes—no bare feet or sandals.

Chemical Class and Type:
- Permethrin is an acronym for the permethrin chemical group.
- It is a synthetic pyrethroid, a class of insecticides and acaricides.
- It is non-systemic and non-toxic to non-target insects.

Physical / Chemical Properties:
- Appearance: White to yellowish-white crystalline powder
- Odor: Odorless
- Melting point: 180-182°C (356-356°F)
- Density: 1.0 g/mL
- Solubility: Water: < 1 mg/mL

Uses:
- Permethrin is used as an insect repellent to prevent tick bites and other insect bites such as mosquitoes.

Molecular Structure - Permethrin

DEET (N,N-diethyl-m-toluamide)

Warning: Use only as directed. Use in accordance with local, state, and federal regulations. Store in a cool, dry place away from children and pets.
Take Home Points

• Risk of tick-borne illness is heavily dependent on geography & seasonality
• Diagnosis of acute disease largely clinical
• Do not wait for confirmatory testing to initiate treatment of acute disease
• Doxycycline is treatment of choice for most tick-borne illnesses (exception: babesiosis, Lyme meningitis or carditis)
References


• Mandell, Douglass, and Bennett’s Principles and Practice of Infectious Diseases. Lyme Borreliosis Chapter.


• Thorner et al. Rocky Mountain Spotted Fever. CID 1998.

A 45 year old man presents to your Providence, RI office in early June with the skin lesion shown below. He feels fine and has no other symptoms or abnormalities on exam. He gardens outdoors frequently but does not remember sustaining any recent tick bites. What is the most appropriate next step?

- check Lyme serology
- prescribe doxycycline 200 mg x 1 dose
- check serology for anaplasma
- prescribe doxycycline 100 mg bid x 14 days
- prescribe cephalexin 500 mg 4xd x 7 days
A 46 yo woman with a PMHx of HTN, hypothyroidism, depression presents with 5 months of fatigue, headaches, and arthralgias of wrists, elbows, knees, and ankles. She denies fevers or chills. Skin, joint, and neuro exams are unremarkable. She sustained several tick bites the summer prior to the onset of her symptoms. Lyme testing performed by another provider revealed a positive ELISA and IgM Western Blot but a negative IgG Western Blot. What is the most likely interpretation of test results?

a) positive for chronic Lyme disease
b) false positive ELISA and IgM Western Blot
c) delayed seroconversion of acute Lyme
d) cross reactivity with anaplasma serology
e) none of the above
A 55 yo healthy woman presents with one week of low-grade fevers, chills, myalgias, and headache. She spent several days camping in southern New Jersey three weeks prior to the onset of her symptoms. Exam is notable for temperature 99.5F and conjunctival pallor. No rashes or abnormal skin findings. Labs reveal WBC 7.2, Hb 8.9, platelets 130K, T bili 1.8, LDH 460, haptoglobin 9. Serologic tests for Lyme and anaplasma are negative. Blood smear shows intra-erythrocytic ring forms in 2% of red blood cells.

What is the most appropriate treatment?
a) doxycycline  
b) quinine and clindamycin  
c) ceftriaxone  
d) artemether and lumefantrine  
e) atovaquone and azithromycin
60 year old man with a history of diabetes presents with 3 weeks of low-grade fevers, chills, fatigue, mild headache, and loss of appetite. He was prescribed a one week course of levofloxacin by his PCP two weeks ago without improvement. His symptoms began one week after returning from a fishing trip in Arkansas. He sustained multiple mosquito bites and brushed off several ticks that had a central white dot on their body. Exam reveals T 99.9 and mild diaphoresis but otherwise normal. Labs notable for WBC 5.8, Hb 11.9, platelets 120,000. AST 95, ALT 117, alk phos 353, T bili 2. Creatinine 0.99. What is the most likely etiology of his symptoms?

a) Anaplasma phagocytophilum
b) Ehrlichia chaffeensis
c) Francisella tularensis
d) Borrelia burgdorferi
e) Rickettsia ricketsii