



School of Medicine

University of Missouri

Tickborne infections in Missouri: Diagnostic caveats

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Disclosures

Member of the American Board of Internal Medicine (ABIM)
Infectious Disease Longitudinal Knowledge Assessment Item-
Writing Task Force

Case # 1

- A 48-year-old woman with no significant PMH presents to the office with a 2 month-history of progressive fatigue and body aches. She reports a “brain fog” that is making completion of work tasks difficult. No fevers, night sweats, weight loss or rashes. No history of COVID-19 infection (up-to-date on COVID-19 vaccination). Never travelled outside of Missouri. Physical exam is unremarkable.
- After initial tests including CBC, CMP and CRP returned normal, her PCP ordered “tick panel” after she reported multiple tick bites in recent months.
- Lyme ELISA is positive. Western blot IgM positive, IgG negative. The PCP prescribes doxycycline x 21 days. Patient is referred to Infectious Diseases for persistent symptoms after completion of doxycycline.

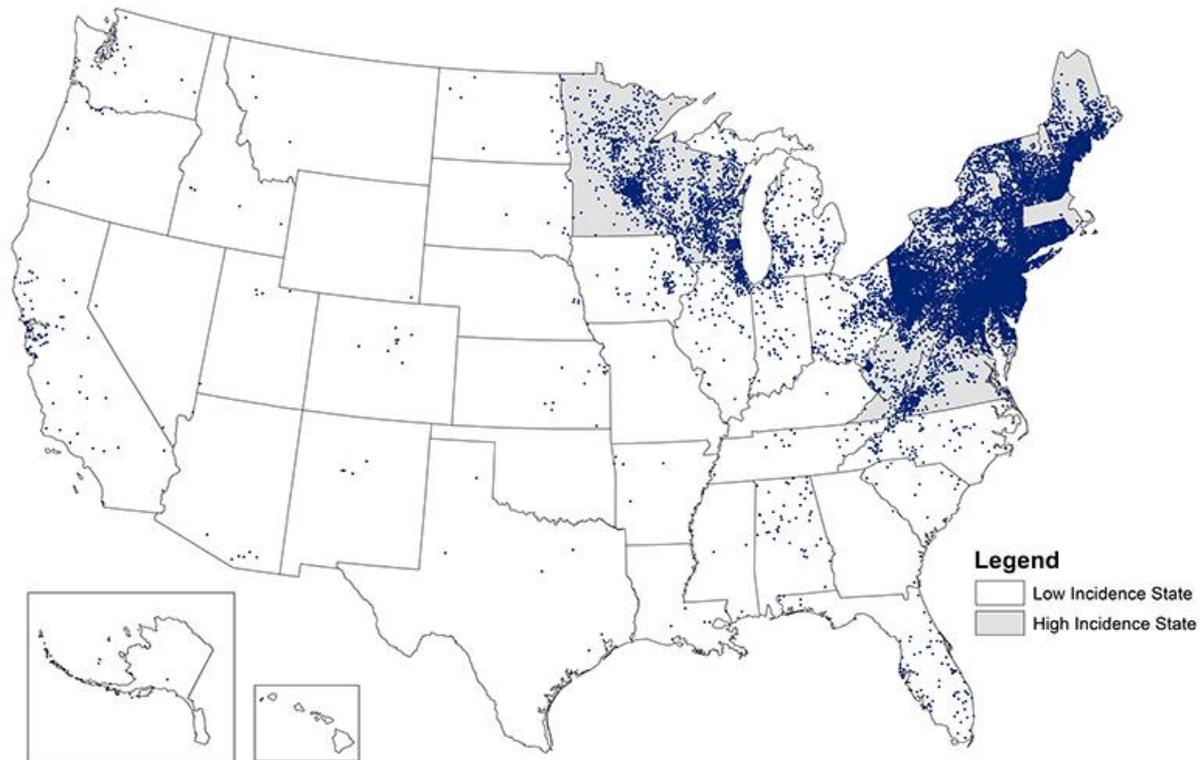
#1

Do not routinely order “tick-borne disease panels”

- These usually include antibody testing for multiple tick-borne infections which may or may not be endemic in Missouri
- These panels may include serologic testing for *Anaplasma phagocytophilum*, *Babesia microti* and *Borrelia burgdorferi*.



Reported Cases of Lyme Disease – United States, 2019. Source: CDC



Lyme disease is not endemic in Missouri

RESEARCH ARTICLE

Using citizen science to describe the prevalence and distribution of tick bite and exposure to tick-borne diseases in the United States

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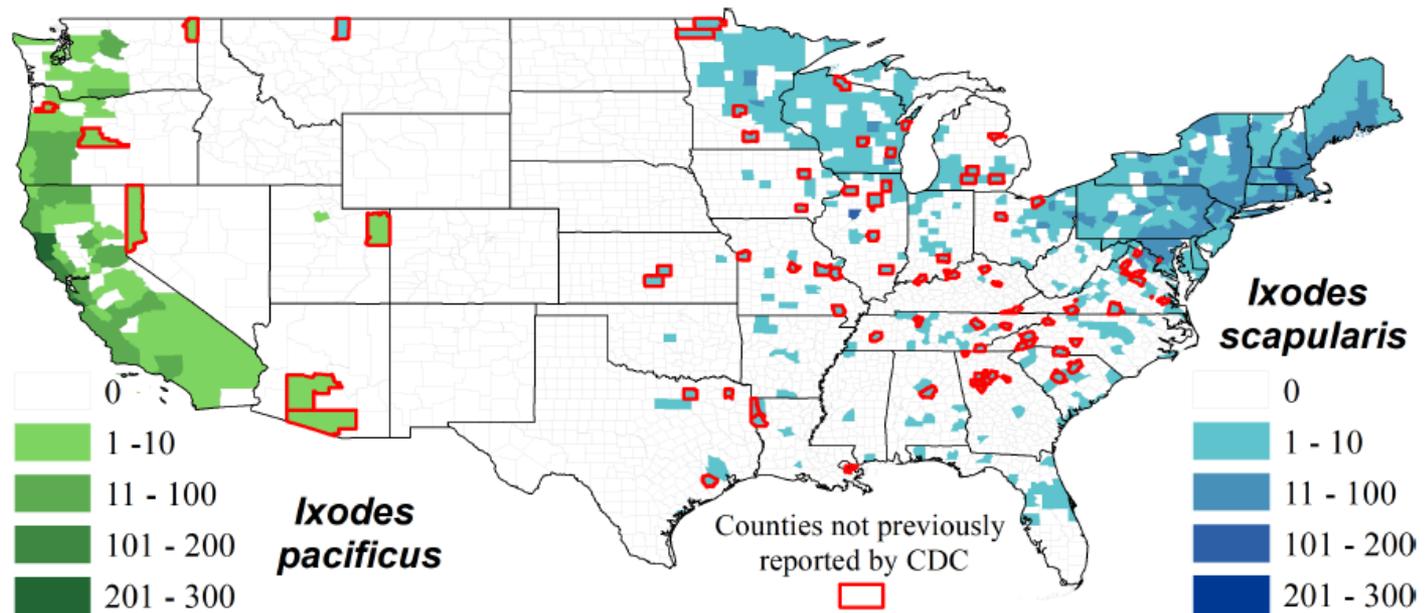


Fig 2. The county level distribution of *I. pacificus* and *I. scapularis* based on location data collected by citizen scientists. Counties outlined in red did not have previous records according to [12], no records include travel history of the submitter.

Table 4. Prevalence of *A. phagocytophilum*, *Bab. microti*, *B. burgdorferi*, and *B. miyamotoi* for *Ixodes scapularis* and *I. pacificus* ticks by state.

| | n | <i>A. phagocytophilum</i> | <i>Bab. microti</i> | <i>B. burgdorferi</i> | <i>B. miyamotoi</i> |
|--------------------------|-----|---------------------------|-------------------------|-----------------------------|------------------------|
| <i>Ixodes scapularis</i> | | | | | |
| Alabama | 7 | 0 / 7 (0, 0–43.9) | 1 / 7 (14.3, 0.8–58) | 0 / 7 (0, 0–43.9) | 0 / 7 (0, 0–43.9) |
| Arkansas | 12 | 0 / 12 (0, 0–30.1) | 1 / 12 (8.3, 0.4–40.2) | 0 / 12 (0, 0–30.1) | 0 / 12 (0, 0–30.1) |
| Connecticut | 120 | 8 / 120 (6.7, 3.1–13.1) | 6 / 120 (5, 2–11) | 26 / 120 (21.7, 14.9–30.3) | 1 / 120 (0.8, 0–5.2) |
| Delaware | 10 | 0 / 10 (0, 0–34.5) | 0 / 10 (0, 0–34.5) | 1 / 10 (10, 0.5–45.9) | 0 / 10 (0, 0–34.5) |
| Florida | 25 | 0 / 25 (0, 0–16.6) | 0 / 25 (0, 0–16.6) | 1 / 25 (4, 0.2–22.3) | 0 / 25 (0, 0–16.6) |
| Georgia | 15 | 0 / 15 (0, 0–25.3) | 0 / 15 (0, 0–25.3) | 1 / 15 (6.7, 0.3–34) | 0 / 15 (0, 0–25.3) |
| Illinois | 149 | 8 / 149 (5.4, 2.5–10.7) | 0 / 149 (0, 0–3.1) | 9 / 149 (6, 3–11.5) | 0 / 149 (0, 0–3.1) |
| Indiana | 36 | 1 / 36 (2.8, 0.1–16.2) | 2 / 36 (5.6, 1–20) | 2 / 36 (5.6, 1–20) | 0 / 36 (0, 0–12) |
| Iowa | 13 | 0 / 13 (0, 0–28.3) | 0 / 13 (0, 0–28.3) | 1 / 13 (7.7, 0.4–37.9) | 0 / 13 (0, 0–28.3) |
| Kansas | 3 | 0 / 3 (0, 0–69) | 0 / 3 (0, 0–69) | 0 / 3 (0, 0–69) | 0 / 3 (0, 0–69) |
| Kentucky | 6 | 0 / 6 (0, 0–48.3) | 0 / 6 (0, 0–48.3) | 0 / 6 (0, 0–48.3) | 0 / 6 (0, 0–48.3) |
| Louisiana | 14 | 0 / 14 (0, 0–26.8) | 0 / 14 (0, 0–26.8) | 1 / 14 (7.1, 0.4–35.8) | 0 / 14 (0, 0–26.8) |
| Maine | 418 | 16 / 418 (3.8, 2.3–6.3) | 7 / 418 (1.7, 0.7–3.6) | 68 / 418 (16.3, 12.9–20.2) | 1 / 418 (0.2, 0–1.5) |
| Maryland | 230 | 1 / 230 (0.4, 0–2.8) | 1 / 230 (0.4, 0–2.8) | 13 / 230 (5.7, 3.2–9.7) | 3 / 230 (1.3, 0.3–4.1) |
| Massachusetts | 543 | 50 / 543 (9.2, 7–12) | 14 / 543 (2.6, 1.5–4.4) | 146 / 543 (26.9, 23.2–30.9) | 9 / 543 (1.7, 0.8–3.2) |
| Michigan | 31 | 0 / 31 (0, 0–13.7) | 0 / 31 (0, 0–13.7) | 2 / 31 (6.5, 1.1–22.8) | 0 / 31 (0, 0–13.7) |
| Minnesota | 126 | 5 / 126 (4, 1.5–9.5) | 2 / 126 (1.6, 0.3–6.2) | 16 / 126 (12.7, 7.7–20.1) | 1 / 126 (0.8, 0–5) |
| Mississippi | 4 | 0 / 4 (0, 0–60.4) | 1 / 4 (25, 1.3–78.1) | 0 / 4 (0, 0–60.4) | 0 / 4 (0, 0–60.4) |
| Missouri | 19 | 0 / 19 (0, 0–20.9) | 0 / 19 (0, 0–20.9) | 0 / 19 (0, 0–20.9) | 0 / 19 (0, 0–20.9) |
| Montana | 1 | 0 / 1 (0, 0–94.5) | 0 / 1 (0, 0–94.5) | 0 / 1 (0, 0–94.5) | 0 / 1 (0, 0–94.5) |
| New Hampshire | 173 | 12 / 173 (6.9, 3.8–12.1) | 10 / 173 (5.8, 3–10.7) | 43 / 173 (24.9, 18.8–32.1) | 4 / 173 (2.3, 0.7–6.2) |
| New Jersey | 185 | 6 / 185 (3.2, 1.3–7.3) | 7 / 185 (3.8, 1.7–8) | 29 / 185 (15.7, 10.9–21.9) | 5 / 185 (2.7, 1–6.5) |
| New York | 947 | 40 / 947 (4.2, 3.1–5.8) | 23 / 947 (2.4, 1.6–3.7) | 177 / 947 (18.7, 16.3–21.4) | 10 / 947 (1.1, 0.5–2) |
| North Carolina | 38 | 0 / 38 (0, 0–11.4) | 0 / 38 (0, 0–11.4) | 2 / 38 (5.3, 0.9–19.1) | 1 / 38 (2.6, 0.1–15.4) |
| Ohio | 182 | 3 / 182 (1.6, 0.4–5.1) | 0 / 182 (0, 0–2.6) | 12 / 182 (6.6, 3.6–11.5) | 2 / 182 (1.1, 0.2–4.3) |

#2

Lyme serology can be falsely positive

- Look for other causes of fatigue, pain and other non-specific symptoms.
- If the patient has not travelled to a Lyme-endemic area, most probably it is not Lyme disease.



#2

Lyme serology can be falsely positive

- 10% of men and 15% of women were either exhausted or very tired either everyday or most days in the previous 3 months
- 17% of men and 21% of women often had pain in the previous 3 months
- In non-endemic areas, the pre-test probability is low -> low positive predictive value -> **false positives**

Blackwell D, Clark T. QuickStats: percentage of adults who often felt very tired or exhausted in the past 3 months, by sex and age group—National Health Interview Survey, United States, 2010-2011.

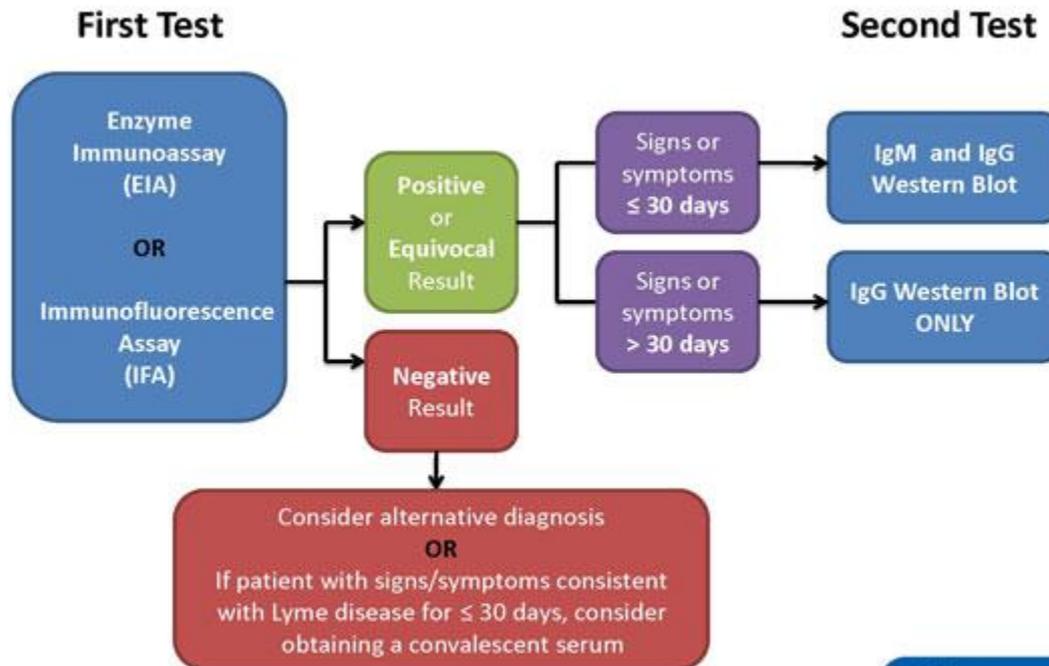
Blackwell D, Clark T. Quick Stats: percentage of adults aged 18 years who often had pain in the past 3 months, by sex and age group—National Health Interview Survey, United States, 2010-2011.



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Previous Standard Lyme Testing Algorithm

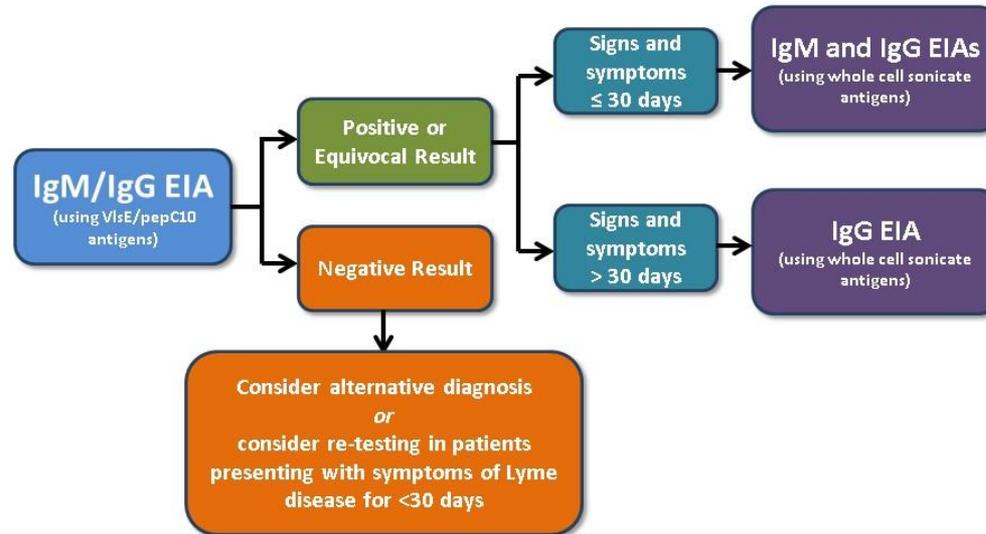
Two-Tiered Testing for Lyme Disease



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



Modified Two-Tier Testing Algorithm



Case # 2

- A 38-year-old woman with no significant PMH presents to the ED with headache, chills and fatigue x 5 days. No rashes. Physical exam is remarkable for temperature of 39 Celsius.
- She lives in Sedalia, MO and has not travelled outside Missouri in more than 10 years. She enjoys gardening and hiking. Does not recall tick bites this Summer.
- Labs are significant for leukopenia (total WBC 2K, lymphopenia 700), thrombocytopenia and elevated liver enzymes. CXR unremarkable. HIV and Hep C screening negative.
- Ehrlichiosis is highly suspected. What test would you order to confirm your suspicion?



- a. *Ehrlichia* IgG/IgM
- b. *Ehrlichia* PCR
- c. Peripheral blood smear

#3

***Ehrlichia* PCR is the preferred testing in suspected ehrlichiosis.**

- High sensitivity during first week of illness.
- Sensitivity decreases after initiation of doxycycline
- Very specific



#4

***Ehrlichia* serology requires careful interpretation.**

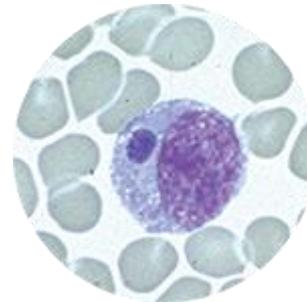
- They may be negative in the acute phase of the infection (7-10 days of illness)
- They may be used for retrospective diagnosis if repeated 2-4 weeks later (four-fold rise in IgG titers)
- IgG may remain positive for a long time.



#5

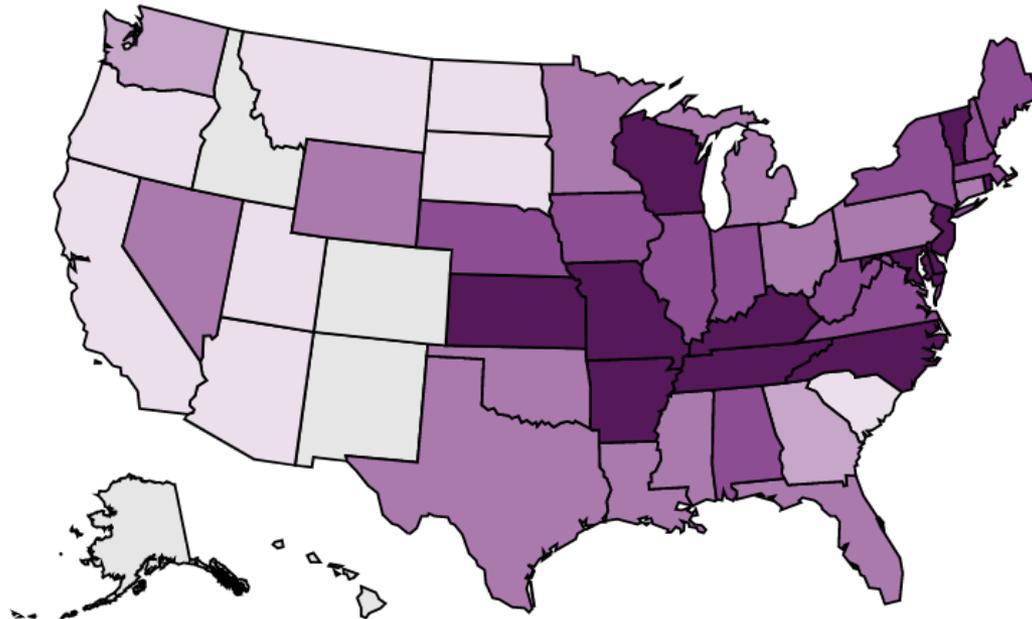
Peripheral blood smear could assist in the diagnosis but low yield

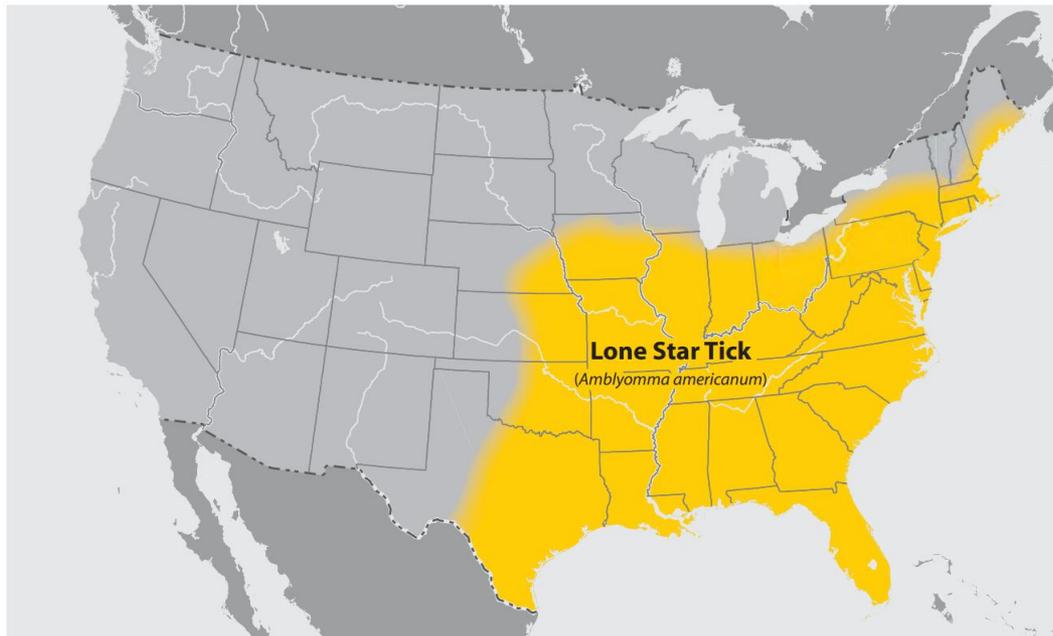
- Morulae can be detected in 20% of patients
- Monocytes – *E. chaffeensis*
- Granulocytes – *E. ewingii*



Annual incidence (per million population) of reported *Ehrlichia chaffeensis* ehrlichiosis—United States for 2019

● 0 ● 0 to <0.3 ● 0.3 to <4.0 ● 4.0 to <11.1 ● 11.1+ ● Not notifiable





ABOUT THIS MAP: This map shows the extent of established *Amblyomma americanum* tick populations, commonly known as lone star ticks. However, tick abundance within this area varies locally. The map does not represent the risk of contracting any specific tickborne illness. Please consult your local health department or USDA Cooperative Extension office to learn about the risks of tickborne disease in your local area. Rev. 07/2011.

National Center for Emerging and Zoonotic Infectious Diseases
Division of Vector-Borne Diseases



Case # 3

- A 50-year-old man with PMH of HTN presents to his PCP with worsening fatigue for 3 months. No history of rashes or fever. Physical exam is normal.
- He is from Mexico, MO. He owns a landscape company. He has had multiple tick bites.
- Labs including CBC, CMP, TSH and CRP are normal. HIV and Hep C screening negative.
- PCP orders a tick panel which returns with positive RMSF IgM. He is prescribed doxycycline x 14 days but the fatigue has not improved. He is referred to ID clinic for persistent symptoms.



Case # 4

- A 60-year-old man with PMH of HTN and T2DM presents to his PCP with fever for 2-3 days. A new rash started today around his ankles and wrists, and he reports a new headache and muscle aches.
- He lives in Columbia, MO. He reports multiple ticks have been attached when walking around his 5-acre property
- Physical exam remarkable for temperature of 102.1 F and HR 90. The rash in ankles and wrists is erythematous and macular.
- Labs show normal WBC, hyponatremia and elevated liver enzymes. Ehrlichia PCR was negative. RMSF serology was negative.



Which patient has RMSF?

- a. Case 3
- b. Case 4

#6 The diagnosis of RMSF is clinical based on presentation.

- RMSF serology (antibodies against Rickettsia) can be negative in the first 1-2 weeks of illness.
- Convalescent titers 2-3 weeks after onset of symptoms can help make retrospective diagnosis: 4-fold increase in IgG titers
- IgM alone should not be used to make diagnosis of RMSF. Possibility of false-positive.



Take home messages

- Fatigue and non-specific symptoms are likely not caused by an acute tickborne infection.
- Lyme is not endemic in Missouri. Testing for Lyme disease should not be done unless history of travel to endemic area.
- *Ehrlichia* PCR is the best test for diagnosis of ehrlichiosis.
- The diagnosis of RMSF is mostly clinical. Serology with acute and convalescent titers can aid in retrospective diagnosis.



Thank you!

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