TO: Primary care providers, infectious disease, laboratories, infection control, and public health

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RE: TICK-BORNE DISEASES IN NEBRASKA

DATE: April 20, 2018

The arrival of spring marks the beginning of another tick season. In the interest of public health and prevention, our office seeks to inform Nebraska health care providers about the known tick-borne diseases in our state.

Key messages for Nebraska clinicians:

**Spotted fever rickettsia including Rocky Mountain spotted fever (RMSF)**

Our office receives reports of from 6 to 31 patients with spotted fever rickettsia every year. Health care providers risk overlooking this diagnosis because of its rarity. RMSF NEEDS TO BE A DIAGNOSTIC CONSIDERATION IN ANY PERSON WITH A FEVER AND A HISTORY OF EXPOSURE TO ENVIRONMENTS WHERE TICKS MIGHT BE PRESENT. The skin rash is not always present when the patient first presents to a physician. **This disease is frequently overlooked or misdiagnosed, with numerous reports of serious and sometimes fatal consequences.** Nebraska experienced a fatal case of RMSF in 2015 where the diagnosis was missed and treatment was delayed until the disease was well advanced.

Laboratory diagnosis is made by detecting a rise in antibody titer to *Rickettsia rickettsii* between acute and convalescent sera. **Treatment requires tetracycline-class of antibiotics or chloramphenicol. Tetracycline-class treatment is recommended for persons of all ages, including children.** Beta lactam antibiotics and fluoroquinolones are contraindicated. Immediate empiric therapy is recommended and should not be delayed while awaiting diagnostic results.

**Tularemia**

Tularemia is caused by *Francisella tularensis*. This agent is found in nature in rabbits, muskrats, prairie dogs and other rodents. Human infection occurs through several routes, including tick or deer fly bites, skin contact with infected animals, bites from infected cats, ingestion of
contaminated water, or inhalation of contaminated dusts or aerosols. Nebraska reported 24, 11, and 7 cases in 2015, 2016, and 2017, respectively.

Disease following a tick bite or deerfly bite is usually ulceroglandular. Diagnosis can be made by isolation of *F. tularensis* in a clinical specimen or by a four-fold rise between acute and convalescent serum antibody titers. In patients that present with symptoms and/or history highly suggestive of tularemia, clinicians should consider culture which will facilitate typing if an isolate is recovered. For surveillance purposes, typing of isolates is highly advantageous. If tularemia is suspected, laboratory staff should be alerted to ensure safety precautions are in place to prevent infection in the lab workers. Although tularemia can be life-threatening, most infections are successfully treated with antibiotics. While streptomycin is the drug of choice, gentamicin is an acceptable alternative. Tetracyclines may be a suitable alternative to aminoglycosides for patients who are less severely ill.

**Ehrlichiosis**

Ehrlichiosis is caused by *Ehrlichia chaffeensis*, an intracellular bacterium that grows within cytoplasmic phagosomes of white blood cells, and can cause leukopenia. This bacteria is transmitted via the tickbite of *Amblyomma americanum* (“Lone star tick”). Symptoms may include severe malaise, fever and headache. If left untreated, the illness may progress with hypotension, coagulopathy, hemorrhage of internal organs and renal failure. Nebraska sees from zero to seven cases per year. In 2017 3 cases were reported.

Diagnosis can be made by identifying the classic inclusion or morulae in the cytoplasm of monocytes or macrophages. Confirmation requires a four-fold rise in IgG antibody titer between acute and convalescent sera or by molecular detection of *Ehrlichia* DNA in clinical specimens. Recommended therapy is with a tetracycline-class antibiotic.

**Lyme Disease**

Lyme disease is transmitted by the tick *Ixodes scapularis* which is not yet established in Nebraska. This fact makes any diagnosis of Nebraska-acquired Lyme disease caused by *Borrelia burgdorferi* highly suspect. Lyme disease is highly regional in the United States. In 2017, Nebraska reported 13 cases to the national reportable disease system at the CDC, all cases where exposure could be determined had exposure/acquisition in regions of the country where this tick is endemic.

Serologic testing for Lyme disease requires a strict two-step process starting with an ELISA, which if positive should be followed by a Western blot. Positive serologic evidence requires both the ELISA and Western blot to be positive. This testing algorithm optimizes sensitivity and specificity in untreated patients (https://www.cdc.gov/lyme/healthcare/index.html).

**Anaplasmosis**

Anaplasmosis is caused by *Anaplasma phagocytophilum*, an intracellular bacterium that targets neutrophils, altering their function, and forms morulae within vacuoles. Symptoms are similar to ehrlichiosis and include malaise, fever, and headache. If left untreated, anaplasmosis can be fatal, even in previously healthy people. Severe clinical presentations may include difficulty breathing, hemorrhage, renal failure or neurological deficits. Like Lyme disease, anaplasmosis is highly regional and transmitted by the *Ixodes scapularis* tick. This makes any diagnosis of Nebraska-acquired anaplasmosis highly suspect. Nebraska has reported from zero to two cases annually, none for 2017. As with Lyme disease reports, these patients reported exposure/acquisition in regions of the country known to be endemic for *Ixodes scapularis* ticks.
Diagnosis can be made by identifying the classic inclusion or morulae in the cytoplasm of neutrophils or eosinophils. Confirmation requires a four-fold rise in IgG antibody titer between acute and convalescent sera or by molecular detection of *Anaplasma* DNA in clinical specimens.

**Southern Tick-Associated Rash Illness (STARI)**
A red, expanding “bull’s-eye” rash similar to those seen in patients with Lyme disease has also been observed in people bitten by *Amblyomma americanum*, often referred to as the lone-star tick. The condition has been named Southern Tick-Associated Rash illness. Occasionally patients may also experience fever, malaise and headache. Whether the lesions and illness described in patients following an *Amblyomma americanum* tick bite are infectious or allergic/toxin mediated remains speculative. Studies have shown that the rash is not caused by *Borrelia burgdorferi*, the causative agent of Lyme disease. Though once thought to be caused by another species of *Borrelia*, research has not supported this idea. While experts including CDC are uncertain as to the necessity for antibiotic treatment for this condition, since its etiology is unknown, a 21-day course of a tetracycline-class antibiotic is often prescribed (https://www.cdc.gov/stari/symptoms/index.html).

**Work in Progress: We Need Your Help**
Nebraska’s state and local health departments need the assistance of patients and doctors to accurately define the spectrum of tick-borne diseases in Nebraska. People who want ticks identified should contact the UNL Veterinary Science Department (402-472-2952). Physicians who suspect non-endemic tick-borne disease (e.g., Lyme disease, anaplasmosis, or STARI-related disease) should contact a public health official (your local health department, or Tom Safranek, M.D., State Epidemiologist) for assistance in a diagnostic work-up. Details for specimen collection and transport can be obtained by contacting the Nebraska Public Health Laboratory (Toll-Free: 1-866-290-1406).

<table>
<thead>
<tr>
<th>Tick</th>
<th>Distribution</th>
<th>Associated Illness</th>
<th>Infectious Agent</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Dermacentor variabilis</em></td>
<td>Statewide</td>
<td>Rocky Mountain spotted fever</td>
<td><em>Rickettsia rickettsii</em></td>
</tr>
<tr>
<td>(American dog tick or wood tick)</td>
<td></td>
<td>Tularemia</td>
<td><em>Francisella tularensis</em></td>
</tr>
<tr>
<td><em>Dermacentor andersoni</em></td>
<td>NW Nebraska</td>
<td>Rocky Mountain spotted fever</td>
<td><em>Rickettsia rickettsii</em></td>
</tr>
<tr>
<td><em>Amblyomma americanum</em></td>
<td>Southern and central Nebraska</td>
<td>Ehrlichiosis (formerly human monocytic ehrlichiosis)</td>
<td><em>Ehrlichia chaffeensis</em></td>
</tr>
<tr>
<td>(Lone star tick)</td>
<td></td>
<td>Southern Tick Associated Rash illness</td>
<td>Unknown etiology</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tularemia</td>
<td><em>Francisella tularensis</em></td>
</tr>
<tr>
<td><em>Ixodes scapularis</em></td>
<td>Not established in Nebraska</td>
<td>Lyme disease</td>
<td><em>Borrelia burgdorferi</em></td>
</tr>
<tr>
<td>(deer tick or blacklegged tick)</td>
<td></td>
<td>Anaplasmosis (formerly human granulocytic ehrlichiosis)</td>
<td><em>Anaplasma phagocytophilium</em></td>
</tr>
</tbody>
</table>

**Tick Distribution Associated Illness Infectious Agent**

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For more information please visit:
CDC RMSF Page: https://www.cdc.gov/rmsf/
CDC Tularemia Page: https://www.cdc.gov/tularemia/
CDC Ehrlichiosis Page: https://www.cdc.gov/ehrlichiosis/
CDC Lyme Disease Page: https://www.cdc.gov/lyme/
CDC Anaplasmosis Page: https://www.cdc.gov/anaplasmosis/index.html
CDC STARI Page: https://www.cdc.gov/stari/