

Nebraska Department of Health and Human Services

Health Alert Network

UPDATE

May 4, 2023

Tick-Borne Diseases & Nebraska

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.

Lyme Disease has been addressed in a separate HAN which can be found here:

<https://dhhs.ne.gov/han%20Documents/UPDATE04242023.pdf>

Spotted fever group rickettsia (SFR)/Rocky Mountain Spotted Fever (RMSF)

SFR is a group of related bacteria that can cause spotted fevers including RMSF. Several of these SFR have similar signs and symptoms, including fever, headache, and rash, but are often less severe than RMSF. Our office has reported a median of 8 cases (range 5-48) of SFR annually over the last 5 years (2018–2022). SFR, particularly **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. RMSF is frequently overlooked or misdiagnosed, with numerous reports of serious and sometimes fatal consequences. Nebraska has experienced fatal cases of RMSF, one each in 2015 (confirmed case), 2020 (confirmed case), and 2021 (probable case).

Diagnosis: Do not delay treatment while awaiting diagnostic test results. The optimal diagnostic test depends on the duration from symptom onset and the type of specimen(s) available for testing. RMSF is a nationally notifiable condition. Correct testing and reporting of RMSF is important to improve understanding of how common this disease is, where it occurs, and how disease trends change over time.

- *Serology:* The standard serologic test for diagnosis of RMSF is the indirect immunofluorescence antibody (IFA) assay for immunoglobulin G (IgG) using *R. rickettsii* antigen. IgG IFA assays should be performed on paired acute and convalescent serum samples collected 2–4 weeks apart to demonstrate evidence of a 4-fold seroconversion. *Persistent antibodies:* Antibodies to *R. rickettsii* might remain elevated for many months after the disease has resolved.
- *PCR:* Polymerase chain reaction (PCR) amplification is performed on DNA extracted from whole blood. *R. rickettsii* infect the endothelial cells that line blood vessels and may not circulate in large numbers in the blood until the disease has progressed to a severe phase of infection. Although a positive PCR result is helpful, a negative result does not rule out the diagnosis, and **treatment should not be withheld on the basis of a negative result**.
- *IHC and culture:* Culture and immunohistochemistry (IHC) and culture can also be performed on skin biopsies of a rash lesion, or post-mortem tissue specimens.

Treatment: **requires doxycycline.** Doxycycline 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 has reported a median of 9 cases annually (range: 5–16) over the last 5 years (2018–2022). Forms of this disease include: ulceroglandular, glandular, oculoglandular, oropharyngeal, pneumonic, and typhoidal. *Diagnosis*: made by isolation of *Francisella tularensis* in a clinical specimen or by demonstrating a 4-fold rise between acute and convalescent serum antibody titers. *Treatment*: while streptomycin is the drug of choice, gentamicin is an acceptable alternative. Doxycycline may be a suitable alternative to aminoglycosides for patients who are less severely ill.

Ehrlichiosis

Ehrlichiosis is caused most commonly by *Ehrlichia chaffeensis* (less commonly *Ehrlichia ewingii*), an intracellular bacterium that grows within cytoplasmic phagosomes of white blood cells and can cause leukopenia. This bacteria is transmitted via the tick bite of *Amblyomma americanum* (“Lone star tick”). Symptoms may include severe malaise, fever, and headache. Although rare, severe outcomes including death are possible. Nebraska reported its first ehrlichiosis-associated death in 2019 (confirmed case) and a second associated death in 2022 (probable case). Nebraska has reported a median of 7 cases annually (range: 2–19). However, with the expansion of the Lone star tick (*Amblyomma americanum*) in Nebraska, this disease is likely underdiagnosed. **In 2022, ehrlichiosis was the most frequently reported tick-borne disease in the state with 19 reported cases.** This was also the most ehrlichiosis cases ever reported in Nebraska since it became a reportable condition. Providers suspecting a SFR or RMSF diagnosis should also consider ehrlichiosis as a potential diagnosis. *Diagnosis*: confirmation requires a 4-fold rise in IgG antibody titer by immunofluorescence assay (IFA) between acute and convalescent sera or by molecular detection of *Ehrlichia* DNA in clinical specimens. Diagnosis can also be made by identifying the classic inclusion or morulae in the cytoplasm of monocytes or macrophages. *Treatment*: doxycycline.

Anaplasmosis

Like Lyme disease, anaplasmosis is transmitted by the *Ixodes scapularis* tick. Established populations (meeting CDC criteria) of this tick have been identified in Douglas, Sarpy, and Saunders counties in 2019 and Thurston County in 2021. **This fact makes it possible for anaplasmosis, caused by *Anaplasma phagocytophilum*, to be acquired in eastern Nebraska.** However, even with these established populations, Nebraska is considered a low prevalence state for anaplasmosis. At this time, local human health risk is unknown. *Diagnosis*: confirmation requires a 4-fold rise in IgG antibody titers between acute and convalescent sera or by molecular detection of *Anaplasma* DNA in clinical specimens. Diagnosis can also be made by identifying the classic inclusion or morulae in the cytoplasm of neutrophils or eosinophils. *Treatment*: doxycycline.

Heartland and Bourbon Virus

Heartland and Bourbon viruses are both RNA viruses. Heartland virus was first discovered in 2009 in Missouri and is believed to be transmitted by *Amblyomma americanum* (“Lone star tick”). Initial symptoms are similar to ehrlichiosis which include fever, fatigue, anorexia, nausea, and diarrhea. Bourbon virus was discovered in Bourbon County, Kansas in 2014. Like Heartland virus, Bourbon virus is also believed to be transmitted by *Amblyomma americanum*. Symptoms reported from patients include fever, fatigue, anorexia, nausea, vomiting, and maculopapular rash. Leukopenia, thrombocytopenia, and mild to moderate elevation of liver transaminases have also been seen in patients diagnosed with Heartland or Bourbon viruses. To date, no cases of Heartland or Bourbon virus have been identified in Nebraska residents. Infection with Heartland or Bourbon virus should be considered in patients being treated for suspected tick-borne disease who do not respond to treatment (e.g., doxycycline). *Diagnosis*: presently, no routine testing is available commercially for Heartland or Bourbon viruses. However, protocols are in place to allow people to be tested for evidence of infection through the CDC. Providers must contact their local health department to determine if suspected

patients meet CDC criteria for testing. *Treatment:* Presently, there are no vaccines or medications to prevent or treat infections with Heartland or Bourbon viruses.

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. In such patients, **the rash is not caused by *Borrelia burgdorferi***, the causative agent of Lyme disease. *Diagnosis:* STARI is diagnosed based on symptoms, geographic location, and possibility of tick bite. Because the cause of STARI is unknown, no diagnostic blood tests have been developed. *Treatment:* the potential utility of antibiotic treatment for this condition is unclear, although 21-day course of a tetracycline-class antibiotic is often prescribed (<https://www.cdc.gov/stari/symptoms/index.html>).

Alpha-gal Syndrome (red meat allergy)

Alpha-gal syndrome (AGS) is an allergy first described in 2009 to the alpha-gal molecule. Alpha-gal (galactose- α -1,3-galactose) is a sugar molecule found in most mammals (except in people, apes, and monkeys) and can be found in products made from mammals (including some medications, cosmetics, vaccines, gelatin, and milk products). Allergic reactions typically occur after people eat meat from mammals that have alpha-gal or are exposed to products made from mammals. Symptoms can appear 3–6 hours after eating meat or exposure to products containing alpha-gal, may not occur after every exposure, and may vary from person to person. Common symptoms include: rash, hives, difficulty breathing, drop in blood pressure, dizziness or faintness, nausea or vomiting, and severe stomach pain. **Alpha-gal allergies can be severe, and even life threatening.** Both children and adults can develop alpha-gal allergy, however, most cases of alpha-gal allergy appear to occur in people >50 years of age. In the US, growing evidence suggests that Alpha-gal syndrome may be triggered by the bite from a lone star (*Amblyomma americanum*) or blacklegged (*Ixodes scapularis*) tick. *Diagnosis:* The main diagnostic test for alpha-gal syndrome is a blood test looking for immunoglobulin-E antibodies specific to alpha-gal (alpha-gal IgE). Tests for alpha-gal IgE are available at several large commercial laboratories. Skin tests documenting reaction to certain allergens (such as pork or beef) may also be used to diagnose alpha-gal syndrome. *Treatment:* Alpha-gal syndrome reactions are managed with antihistamines, corticosteroids, and other medications. Many foods and products contain alpha-gal; providers should work with patients to understand which products they will need to avoid. Some evidence suggests that products may be safely reintroduced in patients after long periods of avoiding alpha-gal and tick bites.

- Most patients with alpha-gal syndrome must stop eating mammalian meat (e.g. beef, pork, lamb, venison, rabbit, etc.) Organ meats and those with high mammalian fat content typically contain high amounts of alpha-gal.
- Depending on the sensitivity and severity of their allergic reaction, patients need to avoid other products, such as cow’s milk, milk products, and gelatin, which may contain alpha-gal.
- Although rare, patients with severe alpha-gal syndrome may react to ingredients in certain vaccines or medications. There is no comprehensive list of alpha-gal-containing medications, but providers can look for products containing ingredients such as gelatin, glycerin, magnesium stearate, and bovine extract.
- Patients with alpha-gal syndrome should avoid tick bites. New tick bites may reactivate allergic reactions to alpha-gal.

Recommended AGS CME Training & Assessment: This module is a 20-question assessment of providers’ epidemiologic, clinical, and diagnostic management of AGS. Completion of the module will confer 0.25 hours of CME (ABIM MOC). The module may be found here:

https://www.medscape.org/viewarticle/988550?ecd=par_cdc_distr_mscpedu.

Tick	Distribution	Associated Illness	Infectious Agent
<i>Dermacentor variabilis</i> (American dog/wood tick)	Statewide	Rocky Mountain spotted fever	<i>Rickettsia rickettsii</i>
		Tularemia	<i>Francisella tularensis</i>
<i>Dermacentor andersoni</i> (Rocky Mountain wood tick)	NW Nebraska	Rocky Mountain spotted fever	<i>Rickettsia rickettsii</i>
		Tularemia	<i>Francisella tularensis</i>
<i>Amblyomma americanum</i> (Lone star tick)	Central, Eastern, and Southern Nebraska	Ehrlichiosis (formerly human monocytic ehrlichiosis)	<i>Ehrlichia chaffeensis</i>
		Southern Tick Associated Rash Illness (STARI)	Unknown etiology
		Tularemia	<i>Francisella tularensis</i>
		Heartland virus disease	Heartland Virus (Phlebovirus)
		Bourbon virus disease	Bourbon Virus (Thogotovirus)
		Alpha-gal Allergy	Alpha-gal sugar
<i>Ixodes scapularis</i> (deer tick or blacklegged tick)	Four counties in Eastern Nebraska	Lyme disease	<i>Borrelia burgdorferi</i>
		Anaplasmosis (formerly human granulocytic ehrlichiosis)	<i>Anaplasma phagocytophilum</i>

For more information, please visit relevant CDC pages as follows:

- RMSF: <https://www.cdc.gov/rmsf/>
- Tularemia: <https://www.cdc.gov/tularemia/>
- Ehrlichiosis: <https://www.cdc.gov/ehrlichiosis/>
- Anaplasmosis: <https://www.cdc.gov/anaplasmosis/index.html>
- Heartland Virus: <https://www.cdc.gov/heartland-virus/index.html>
- Bourbon Virus: <https://www.cdc.gov/ncezid/dvbd/bourbon/index.html>
- STARI: <https://www.cdc.gov/stari/>
- Alpha-gal: <https://www.cdc.gov/ticks/alpha-gal/index.html>
- Tickborne Diseases of the US: A Reference Manual for Health Care Providers, Sixth Edition (2022): <https://www.cdc.gov/ticks/tickbornediseases/TickborneDiseases-P.pdf>

Jeff Hamik, MS
Vectorborne Disease Epidemiologist
402-471-2937

Timothy Tesmer, MD
CMO Public Health
402-471-8566

Matthew Donahue, MD
State Epidemiologist
402-471-8566