

Tick-Borne Diseases

by Thomas Safranek, M.D.

Tick-borne illnesses of interest to Nebraska residents, healthcare providers and laboratorians include Rocky Mountain Spotted Fever, Lyme disease, ehrlichiosis, and tularemia. Only two tick species are believed to be associated with these diseases in Nebraska: *Dermacentor variabilis* and *Amblyomma americanum*. *Ixodes scapularis* (formerly *Ixodes dammini*) is the only known vector of *Borrelia burgdorferi* and *Ehrlichia phagocytophila*, the causative agents of Lyme disease and human granulocytic ehrlichiosis, respectively. This tick has never been detected in Nebraska.

Rocky Mountain Spotted Fever (RMSF)

Persons with RMSF have been reported in Nebraska for many years. The Office of Epidemiology receives an average

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of 2 to 5 cases of such reports annually.

Because it is an uncommon disease, health

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care providers have a tendency to overlook this diagnosis. RMSF should be a diagnostic consideration in any person with a fever and a history of exposure to an environment where ticks might be encountered. The skin rash which gives this illness its name, is not universally present at the time of presentation to the physician. There are numerous reports in the literature where health care providers have missed diagnoses of RMSF with unfortunate patient outcomes. The laboratory diagnosis is traditionally made by detecting a rise in antibody titer to *Rickettsia rickettsii* on acute and convalescent sera specimens. The organism can also be detected using fluorescent antibody methods applied to tissue (e.g., skin biopsy) specimens. The disease responds to tetracycline-like antibiotics and chloramphenicol. Treatment should be started empirically while awaiting diagnostic test results.

Lyme Disease

Our knowledge of Lyme disease continues to develop following its first description as "pseudojuvenile rheumatoid arthritis" in young boys in Lyme, Connecticut. Lyme disease is now the most

prevalent tick-borne disease in the United States and is caused by a spirochete called *Borrelia burgdorferi*. *B. burgdorferi* is transmitted by the tick *Ixodes scapularis* which has not been identified in Nebraska. This makes it doubtful that any one has ever acquired classic Lyme disease caused by *B. burgdorferi* from a Nebraska exposure.

Confusion about whether classic Lyme disease could be acquired in Nebraska occurred because of technical issues related to the diagnostic tests. There are two laboratory diagnostic approaches to confirm the diagnosis of Lyme disease: serologic tests looking for antibody to *B. burgdorferi*, and tissue culture or other antigen detection methods. There has never been a tissue culture or other antigenic confirmation of *B. burgdorferi* in a person who acquired Lyme disease in Nebraska. There have been Nebraskans whose serologic tests for Lyme disease have reported as positive. While some of these people reported a tick-borne exposure in regions of the country where classic Lyme disease is clearly established, many of these people had never left Nebraska. The positive Lyme disease serologies in this latter group of patients is attributed to the lack of specificity in the early versions of the test: the false positive rate was unacceptably high. These false-positive tests could have resulted from underlying medical conditions such as rheumatoid arthritis, or they may have reflected prior exposure to other spirochetal organisms sufficiently similar to *B. burgdorferi* to result in a cross reaction with the serologic test (e.g., leptospirosis, treponemal species, or to the presence of *Borrelia* species other than *B. burgdorferi*).

One notable example of such cross-reactivity is the recently recognized existence of a poorly characterized *Borrelia*-like organism felt to be transmitted by *Amblyomma americanum*, often referred to as the Texas lone-star tick. This tick, which is quite common in southeast Nebraska has been reported to harbor a *Borrelia* species different from *B. burgdorferi*. Researchers are currently attempting to characterize this organism and its life cycle, and to develop tissue culture and serologic tests. Infection with this organism, tentatively assigned the

name "*Borrelia lonestarii*", appears capable of causing a clinical syndrome similar to Lyme disease, including erythema migrans skin lesions. Though the full spectrum of its clinical manifestations is currently poorly defined, persons infected with this organism appear to have less severe long-term sequelae compared to those infected with *B. burgdorferi*. Additionally, infection appears to respond to antibiotics used to treat classic Lyme disease.

The currently licensed serologic tests for Lyme disease include an initial ELISA procedure followed by a Westernblot for confirmation. The assays have greatly improved sensitivity and specificity in untreated patients tested two to three weeks following exposure. The extent to which current serologic tests may cross-react with *Borrelia* species other than *B. burgdorferi* (such as *B. lonestarii*) is currently under investigation.

Ehrlichiosis

Ehrlichiosis is caused by an intracellular bacteria that grows within cytoplasmic phagosomes of white blood cells. Laboratorians should be familiar with the classic inclusion or morulae in neutrophils and lymphocytes which suggests the diagnosis of ehrlichiosis. In many cases, review of the peripheral blood smear provides the clue sequelae to the diagnosis, which is confirmed by serologic testing or by molecular detection of *Ehrlichia* DNA.

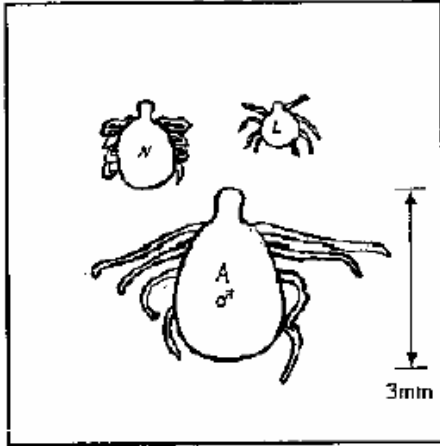
The symptoms of this disease include a maculo-papular rash as well as fever, chills, and leukopenia. The illness may progress with hypotension, coagulopathy, hemorrhage of internal organs and renal failure. Prior to 1986, ehrlichiosis was recognized primarily as a disease affecting horses or dogs which is caused by organisms related to but distinct from *E. chaffeensis*.

Tracking of tick-borne disease is an important function of the state health department and questions may arise regarding the speciation of a tick found on humans or animals. Dr. Wayne Kramer, the State Medical Entomologist emphasizes the importance of continued surveillance. Dr. Kramer encourages the submission of tick specimens to his office for identification. This office provides a valuable resource for

the identification of these ticks.

Summary

Because native *B. burgdorferi* infection is not felt to occur in Nebraska, and because so little is known about variant Lyme disease believed to be transmitted by the *A. americanum* tick and caused by "*B. lonestarii*", we currently recommend that a skin biopsy be obtained from any person with erythema migrans. Physicians and Tick-Borne Diseases laboratorians should contact either the State Entomologist (Dr. Wayne Kramer), the State Epidemiologist (Dr. Thomas Safranek, 402-471- 0550), or the NPHL Director (Dr. Steven H. Hinrichs, 402-559-8301) at the time of diagnosis, and make arrangements for the collection and processing of the skin biopsy. Similar arrangements should be made if other tissue thought to harbor *Borrelia* organisms, are collected/ biopsied (e.g., joint tissue, cerebrospinal fluid, etc). The CDC will test the specimens at no cost to the physician or patient in an attempt to identify a specific causative agent.



Size comparison of
Amblyomma americanum: Adult (A),
 Nymph (N) and Larval (L) forms.
 One of the most important
 issues relative to ticks in Nebraska is
 the small size of the immature stages of
Amblyomma americanum (lone-star
 ticks). This tick is found in southeastern
 Nebraska.

In the SE quarter of Nebraska,
 the lone-star tick can be locally
 abundant and it is common for people to
 come into contact with the immature
 stage (most commonly the nymphal
 stage) and not realize it is a tick
 because of the small size. Some
 individuals may call them deer ticks
 which is a term more accurately used in
 other parts of the country to refer to
Ixodes scapularis (the most important
 vector of Lyme disease in the U.S) but
 that tick is not found in Nebraska. Lonestar
 tick nymphs and adults are active
 from April through September. Lonestar
 tick adults are similar in
 morphology but slightly smaller than
 the most common tick in Nebraska
(*Dermacentor variabilis*)
A. americanum ticks do like to
 feed on deer, especially as nymphs and
 adults, and there may be some
 correlation between deer populations
 and tick populations in certain areas
 since deer are such abundant hosts.

TICK	DISTRIBUTION	ASSOCIATED ILLNESS	INFECTIOUS AGENT
<i>Dermacentor variabilis</i> (American dog tick or wood tick)	Statewide	Rocky Mountain Spotted Fever Human monocytic ehrlichiosis Tularemia	<i>Rickettsia rickettsii</i> <i>Ehrlichia chaffeensis</i> <i>Francisella tularensis</i>
<i>Amblyomma americanum</i> (Texas lone-star tick)	Southeast NE	Variant Lyme disease* Human monocytic ehrlichiosis	" <i>Borrelia lonestarii</i> " <i>Ehrlichia chaffeensis</i>
<i>Ixodes scapularis</i> (Deer tick)	Has not been in Nebraska	Lyme disease Human granulocytic ehrlichiosis	<i>Borrelia burgdorferi</i> <i>Ehrlichia phagocytophila</i>
*see text			