

MISSOURI
HOSPITALIST
SOCIETY

MISSOURI HOSPITALIST

Issue 51

April—June 2014

PUBLISHER:

Division of Hospital Medicine
University of Missouri
Columbia, Missouri

EDITOR:

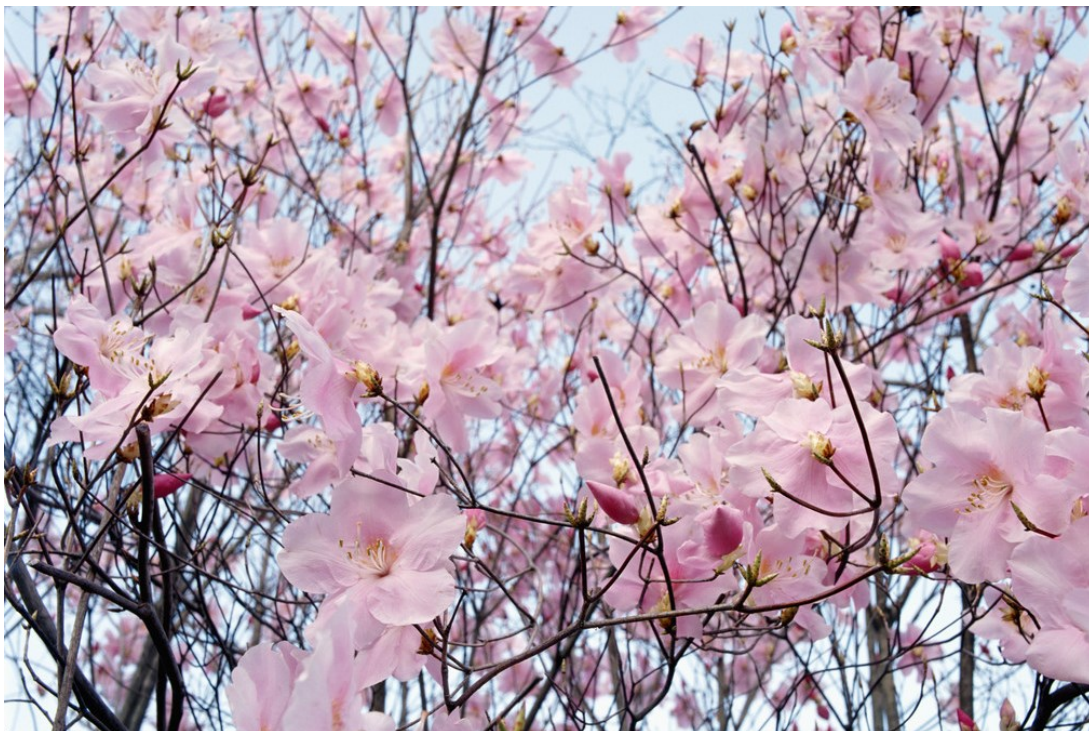
Ankur Jindal, MD

ASSOCIATE EDITORS:

S. Hasan Naqvi, MD
Natraj Katta, MD
Hariharan Regunath, MD
Raghav Gupta, MD

**DIVISIONAL
ADMINISTRATOR:**

Nicole L Garner



INSIDE this ISSUE:

Hospitalist Updates

Case Report

Hematology Update

Diagnostic Dilemma

Ask a Pathologist

ID Corner

Conference Calendar

Hospitalist Updates:

Tick Borne Illness in Missouri

William E. Roland, MD

Professor of Medicine, Division of Infectious Diseases, University of Missouri-Columbia
Associate Chief of Staff for Education, Harry S Truman Memorial Veterans Hospital, Columbia, MO

Missouri is a hotbed for tick-borne illness given its abundance of rural geography and wildlife, especially deer. The two most frequently encountered ticks in Missouri are the lone star tick, *Amblyomma americanum* and the American dog tick, *Dermacentor variabilis*. *Amblyomma* related diseases in Missouri include human monocytic ehrlichiosis, Rocky Mountain Spotted Fever (RMSF), Southern Tick-Associated Rash and Illness (STARI), Tularemia, and Heartland Virus. *Dermacentor* ticks are capable of transmitting RMSF and Tularemia.

Approximately 40% of all tularemia cases reported to CDC each year occur in Arkansas, Oklahoma, and Missouri.⁽¹⁾ Through 2000-2007, 190 cases of Tularemia were reported in Missouri, for an annual incidence of 4 cases per million population, accounting for about 20% of all cases annually nationwide. The infecting

agent, *Fransisella tularensis*, is highly contagious and is considered an agent of bioterrorism. The presentation of tularemia depends on the mode of acquisition. A tick bite usually leads to an ulceroglandular presentation, the most common presentation. The disease can also be contracted through contact with infected animal tissues, eating contaminated food or water, or inhalation of contaminated aerosols. Typically an ulcer appears at the point of the organism's entry with regional adenopathy developing; sometimes an ulcer is not found, though. Inhalation can lead to pneumonia and/or a typhoidal-like systemic illness. An oculoglandular presentation has been seen in microbiology lab workers handling live cultures. An oropharyngeal presentation manifests with neck adenopathy. The majority of patients give a history of fever. A pneumonic presentation usually shows a leukocytosis, but this is usually absent in other presentations. Glandular presentations are frequently misdiagnosed as other more common glandular diseases such as gram-positive lymphadenitis, cat scratch disease, and Epstein-Barr virus infection. Pneumonic presentations are usually diagnosed and treated initially as community-acquired pneumonia. The clinical diagnosis is confirmed by a 4-fold rise in antibody titer between acute and convalescent serum samples taken at least two weeks apart; culture; or by PCR which is not readily available. FDA-approved antimicrobials include tetracyclines and aminoglycosides. Tetracyclines should be given for at least 14 days. Ciprofloxacin for ≥ 10 days has shown a 90% success rate for treatment.(2, 3)

In 2011, Missouri practitioners identified 270 confirmed and probable cases of RMSF. This count translates to a statewide incidence rate of 4.5 per 100,000, making it Missouri's most common tick-borne disease. *Rickettsia rickettsii*, the infecting agent, is transmitted to the victim 6-10 hours after tick attachment, and the first symptoms usually begin 2-14 days after the tick bite. Patients with RMSF typically seek care in the first 2-4 days of illness; symptoms include sudden high fever, shaking chills, severe headache, muscle aches, and joint pain. Children sometimes suffer from nausea, vomiting, and a loss of appetite. The classic spotted rash of *R. rickettsii* infection is usually not apparent until the fifth or sixth day of illness and is not observed in all people. The rash has been mistaken for the rash of meningococcal septicemia. Additional diagnostic clues can include a low platelet count, low sodium levels, or elevated liver enzyme levels. Antibodies to *R. rickettsii* are detectable 7-10 days after illness onset. The gold-standard serologic test looks for a four-fold change in antibody titers using immunofluorescence assay (IFA) on paired samples. The first sample should be taken within the first week of illness and the second should be taken 2 to 4 weeks later. IgM antibodies are less specific than IgG antibodies and are more likely to generate false positives. IgM results alone should not be used for laboratory diagnosis. Antibody titers are frequently negative in the first 7-10 days of illness, thus serologic tests may be falsely negative during this time period. The infecting organism can also be detected by PCR of a biopsy of the rash. PCR is generally unreliable for acute blood samples. The organism can also be seen in tissues samples via immunohistochemical staining. First-line RMSF treatment for adults and children of any age is doxycycline. Treatment should continue for at least 3 days after defervescence and until the patient clinically improves. The minimum duration of therapy is 5-7 days. Fatalities from RMSF are often attributed to delays in diagnosis and inappropriate treatment.(3, 4)

In 2009, Missouri identified 167 cases of ehrlichiosis. The incidence of ehrlichiosis in men was about twice that of women, with 3.7 reported illnesses per 100,000 men compared with 2 cases per 100,000 in women. In 1 to 14 days after the infecting agent, *Ehrlichia chaffeensis*, is transmitted to the host, symptoms of fever and headache usually develop. Chills, malaise, muscle pains, gastrointestinal symptoms and central nervous system manifestations may also be seen. Rash may be present in a

minority of infected adult patients. Prolonged (>2weeks) fever has been described from the patient not seeking care, the practitioner not recognizing the disease, or both. Common lab abnormalities include leukopenia with lymphopenia, thrombocytopenia, and elevated liver function tests. With proper antibiotic therapy a profound lymphocytosis has been described. Antibodies to *E. chaffeensis* are detectable 7–10 days after illness onset. The gold-standard serologic test looks for a four-fold change in IgG-specific antibody titers using IFA on paired samples. The first sample should be taken within the first week of illness and the second should be taken 2 to 4 weeks later. *E. chaffeensis* DNA can be detected by PCR on whole blood. This method is most sensitive within the first week of illness and may decrease in sensitivity after administration of antibiotics. During the acute stage of illness, morulae, or cytoplasmic inclusion bodies, may be detected in about 20% of patients, most commonly in their monocytes. Doxycycline is the preferred therapy and should be given for at least 3 days after the fever subsides and until there is evidence of clinical improvement. The minimum course of treatment is 5–7 days. Rifampin has been used successfully in pregnancy with no apparent ill effects to the newborns.(3-7)

The Lone Star tick (*Amblyomma americanum*) is the vector of Lyme-like illness, also known as STARI or Masters Disease. The causative agent is not known at this time. An erythema migrans (EM)-like lesion is seen in these patients, usually without any accompanying symptoms. When compared to Lyme disease patients, STARI patients have fewer and smaller EM lesions which are more circular and more likely to have central clearing. It is not known whether antibiotic treatment is necessary or beneficial for patients with STARI. Nevertheless, because STARI resembles early Lyme disease, physicians will often treat patients with oral antibiotics.(8, 9)

There have been 2 patients to date from Missouri who have been thought to be infected with the Heartland Virus. They presented with fever, fatigue, diarrhea, thrombocytopenia, and leukopenia, and both had been bitten by ticks 5 to 7 days before the onset of illness. *E. chaffeensis* was suspected as the causal agent but was not found on serologic analysis, PCR assay, or cell culture. Electron microscopy revealed viruses consistent with members of the Bunyaviridae family. Next-generation sequencing and phylogenetic analysis identified the viruses as novel members of the phlebovirus genus. The virus has been recently detected in nymphal *A. americanum* ticks from Missouri. The disease is most closely related to Severe Fever with Thrombocytopenia Syndrome Virus infection, transmitted by *Haemaphysalis longicornis* ticks in China and Japan, where it has a 2-15% fatality rate. There is currently no readily available diagnostic test nor specific therapy for Heartland Virus infection.(10, 11)

Other rarely seen tick-borne diseases in Missouri include Q fever from *Coxiella burnetti* and Babesiosis. I have yet to recognize a case of Lyme disease acquired in Missouri.

Prevention of tick-borne disease can easily be done using repellent containing at least 20% DEET or permethrin-treated clothing; checking oneself for ticks daily and showering soon after being outdoors; and treating dogs for ticks. Embedded ticks should be removed with fine-tipped tweezers grasping the tick as close to the skin's surface as possible. The tick should be pulled 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 clean tweezers. If one is unable to remove the mouth parts easily, leave them alone and let the skin heal. After removing the tick, thoroughly clean the bite area and hands with rubbing alcohol, an iodine scrub, or soap and water.

Antibiotic treatment following a tick bite is not recommended as a means to prevent ehrlichiosis, babesiosis or RMSF. There is no evidence this practice is effective, and it may simply delay onset of disease. Instead, persons who experience a tick bite should be alert for symptoms suggestive of tick-borne illness and consult a physician if fever, rash, or other symptoms of concern develop. Tularemia prophylaxis is recommended only in cases of laboratory exposure to infectious materials. Doxycycline is generally recommended for prophylaxis in adults. Ciprofloxacin is not FDA-approved for prophylaxis of tularemia but has demonstrated efficacy in various studies, and may be an alternative for patients unable to take doxycycline.(3)

References:

1. Centers for Disease C, Prevention. Tularemia - Missouri, 2000-2007. MMWR Morbidity and mortality weekly report. 2009;58(27):744-8.
2. Weber IB, Turabelidze G, Patrick S, Griffith KS, Kugeler KJ, Mead PS. Clinical recognition and management of tularemia in Missouri: a retrospective records review of 121 cases. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2012;55(10):1283-90.
3. Services USDoHaS. Tickborne Diseases of the United States 2013 . Available from: <http://www.cdc.gov/lyme/resources/TickborneDiseases.pdf>.
4. Services MDoHaS. Data & Statistical Reports . Available from: <http://health.mo.gov/living/healthcondiseases/communicable/communicabledisease/reports.php>.
5. Roland WE, McDonald G, Caldwell CW, Everett ED. Ehrlichiosis--a cause of prolonged fever. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 1995;20(4):821-5.
6. Buitrago MI, Ijdo JW, Rinaudo P, Simon H, Copel J, Gadbar J, et al. Human granulocytic ehrlichiosis during pregnancy treated successfully with rifampin. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 1998;27(1):213-5.
7. Caldwell CW, Everett ED, McDonald G, Yesus YW, Roland WE. Lymphocytosis of gamma/delta T cells in human ehrlichiosis. *American journal of clinical pathology*. 1995;103(6):761-6.
8. Masters EJ, Grigery CN, Masters RW. STARI, or Masters disease: Lone Star tick-vectorred Lyme-like illness. *Infectious disease clinics of North America*. 2008;22(2):361-76, viii.
9. Wormser GP, Masters E, Nowakowski J, McKenna D, Holmgren D, Ma K, et al. Prospective clinical evaluation of patients from Missouri and New York with erythema migrans-like skin lesions. *Clinical infectious diseases : an official publication of the Infectious Diseases Society of America*. 2005;41(7):958-65.
10. McMullan LK, Folk SM, Kelly AJ, MacNeil A, Goldsmith CS, Metcalfe MG, et al. A new phlebovirus associated with severe febrile illness in Missouri. *The New England journal of medicine*. 2012;367(9):834-41.
11. Savage HM, Godsey MS, Jr., Lambert A, Panella NA, Burkhalter KL, Harmon JR, et al. First detection of heartland virus (Bunyaviridae: Phlebovirus) from field collected arthropods. *The American journal of tropical medicine and hygiene*. 2013;89(3):445-52.