

Health Update:

UPDATE to Emergency Room and Primary Care Providers' Reference Sheet on Ehrlichiosis and Tick-Borne Spotted Fever Illnesses

July 25, 2011

This document will be updated as new information becomes available. The current version can always be viewed at <http://www.health.mo.gov>

The Missouri Department of Health & Senior Services (DHSS) is now using 4 types of documents to provide important information to medical and public health professionals, and to other interested persons:

Health Alerts convey information of the highest level of importance which warrants immediate action or attention from Missouri health providers, emergency responders, public health agencies, and/or the public.

Health Advisories provide important information for a specific incident or situation, including that impacting neighboring states; may not require immediate action.

Health Guidances contain comprehensive information pertaining to a particular disease or condition, and include recommendations, guidelines, etc. endorsed by DHSS.

Health Updates provide new or updated information on an incident or situation; can also provide information to update a previously sent Health Alert, Health Advisory, or Health Guidance; unlikely to require immediate action.

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July 25, 2011

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SUBJECT: UPDATE to Emergency Room and Primary Care Providers' Reference Sheet on Ehrlichiosis and Tick-Borne Spotted Fever Illnesses

Summary

The Missouri Department of Health and Senior Services (DHSS) alerts health care providers that reports of ehrlichiosis illnesses through July 12, 2011 are 21% higher than for the same period, on average, for the years 2006 through 2010. Ehrlichiosis is an acute infection similar in initial presentation to many viral and bacterial febrile illnesses, including Rocky Mountain spotted fever (RMSF). Peak transmission of tick-borne *Ehrlichia* species can continue into early August. Active transmission in Missouri typically is observed from late April through early October. As of July 12, 2011, reports of RMSF are not elevated in Missouri compared with activity observed over the previous five years.

Ehrlichiosis and RMSF are tick-borne rickettsial diseases (TBRD) transmitted primarily through the bites of the lone star and American dog tick, respectively. The rickettsial disease agents most frequently reported in Missouri are *Ehrlichia chaffeensis* (ehrlichiosis); *Ehrlichia ewingii* (ehrlichiosis); and *Rickettsia rickettsii* (RMSF).

Ehrlichiosis and RMSF can cause severe illness and death in otherwise healthy adults and children. Diagnosis of these illnesses must be made on the basis of clinical signs and symptoms, and can later be confirmed using specialized laboratory tests.

Delay in diagnosis and treatment is associated with more severe illness and death. Case-fatality rates for immunocompromised patients are characteristically higher than case-fatality rates reported for the general population. Care providers should include ehrlichiosis and spotted fevers in the differential diagnosis of summertime febrile patients with known or potential tick exposure, and/or who do not respond to antibiotic therapy.

Clinical presentation, diagnostic assessment, and antibiotic therapy for Missouri's TBRDs are summarized in the attached physicians' Reference Sheet. For detailed information, refer to: *Diagnosis and Management of Tick-borne Rickettsial Diseases: Rocky Mountain Spotted Fever, Ehrlichioses, and Anaplasmosis, United States – A Practical Guide for Physicians and Other Health-Care and Public Health Professionals* at <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm>.

See the last page of the Reference Sheet for public health disease reporting guidance, and additional clinical references, on ehrlichiosis and RMSF.

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Emergency Room and Primary Care Providers' Reference Sheet on
Ehrlichiosis and Tick-Borne Spotted Fevers
Missouri Department of Health and Senior Services Updated July 2011

Tick-Borne Rickettsial Disease (TBRD) Agents Covered In This Reference Sheet

Ehrlichia chaffeensis (ehrlichiosis)
Ehrlichia ewingii (ehrlichiosis)
Anaplasma phagocytophilum (human
anaplasmosis)

Rickettsia rickettsii (traditional Rocky
Mountain spotted fever [RMSF])
Rickettsia parkeri (a newly recognized
febrile, eschar-associated illness)

Clinical Presentation

- Ehrlichiosis and spotted fever illnesses can be difficult to distinguish from viral febrile infections.
- Most patients present during the first 2 to 4 days of illness when serologic detection is unlikely.
- Onset is frequently rapid; the majority of patients experience high fever, shaking chills, severe headache, and generalized myalgias or arthralgias.
- Some patients, especially children, suffer early from nausea, vomiting, and anorexia.
- The diagnosis of ehrlichiosis and RMSF must be made based on clinical signs and symptoms, and can later be confirmed using specialized laboratory tests.
- The majority of reported cases of ehrlichiosis and traditional RMSF require hospitalization.
 - + Manifestations of ehrlichiosis due to *E. ewingii* generally are less severe than infection with *E. chaffeensis*.
 - + Newly described rickettsial illness due to ***R. parkeri*** has manifestations similar to RMSF, but is a milder illness. Because it is usually associated with an eschar, it can also resemble rickettsialpox.
 - + Anaplasmosis in Missouri patients is linked to travel in the upper Midwest or New England states.

Rash – Presentation Varies with Infecting Agent

- Ehrlichiosis:
 - + Rash is described in up to two-thirds of children infected with *E. chaffeensis*¹, but is less common in adults.
 - + Can be transient; typically late in the course of disease.
 - + Varies in character from petechial or maculopapular to diffuse erythema.
- RMSF
 - + The classic spotted or generalized petechial rash of *R. rickettsii* is absent in about 10% of patients.
 - + Rash is non-itchy and usually not apparent until day 5 or 6 of illness.
 - + Rash on the palms and soles usually does not appear until late in the illness.
- *R. parkeri* eschar(s) or eruptions²
 - + Infected tick bites, 0.5 - 1.5 cm wide, with a central area of ulcerated or scabbed skin surrounded by a halo of erythema (see photos at <http://cid.oxfordjournals.org/content/47/9/1188.long>).
 - + Also have been observed as a maculopapular or papulovesicular eruption on the trunk and extremities, occasionally involving the palms and soles.
 - + Obtain skin biopsy or swab for PCR analysis – for submission instructions and a link to the submission form, go to http://health.mo.gov/lab/virology/pdf/rickettsial_instructions.pdf, or call (573)751-3334.

Routine Laboratory Tests

- Ehrlichiosis: Important findings
 - + Low platelet count (thrombocytopenia), low white blood cell count (leukopenia), and elevated levels of hepatic transaminases.
 - + In CSF: mild lymphocytic pleocytosis (<250 cells/mm³), elevated protein levels, and absence of low glucose levels (compared with other bacterial meningitides).
- RMSF: Findings in RMSF patients include normal white cell count with left shift, anemia, thrombocytopenia in severe cases, and hyponatremia. Increase in serum LDH and creatine kinase can also be observed due to diffuse tissue injury.

Tick Exposure Assessment

- Perform a detailed history for occupational, recreational, and residential exposure to ticks.
- Incubation period is five to ten days following a tick bite; tick attachment is often not recalled.

Serologic Diagnostic Tests

- Assessment is complicated by presence of antibodies, even in healthy populations, in endemic areas; persistence of some antibodies for years after the previous infection; and cross-reactivity in conventional serological assays.

- .Antibodies (IgM *and* IgG) via IFA are not yet detectable when most patients present.
 - + IgG is sometimes detectable before IgM.
 - + Increased IFA serology sensitivity with illness of seven to ten days.
 - + IFA estimated at 94-100% sensitive at >14 days of illness.
 - + Serological diagnosis can be considered confirmed only by a four-fold change of IgG-specific antibody titer by IFA between paired serum samples (second sample taken 2-4 weeks later).
- Never delay treatment decisions while waiting for laboratory confirmation of a diagnosis.

PCR Detection of Pathogen DNA

- PCR on an appropriate blood specimen, or on skin tissue, can identify DNA from the infecting bacteria; but the result may not be timely.
- Whole blood is useful for detecting *Ehrlichia* species by PCR because of the pathogen's tropism for circulating white blood cells.
- PCR is more sensitive in a biopsy or swab sample of the spotted rash or eschar than in an acute blood sample. (Spotted fever group rickettsial disease agents exhibit a tropism for epithelial cells.)

Diagnosis Confirmation

- Paired acute and convalescent serology and/or PCR assay to retrospectively confirm a diagnosis can be obtained at no charge through the Missouri State Public Health Laboratory.
- Specimen submission instructions and a link to the submission form are available at http://health.mo.gov/lab/virology/pdf/rickettsial_instructions.pdf, or call (573) 751-3334.

Treatment

- Treatment decisions are empirical – based on epidemiologic and clinical clues.
- Doxycycline is the drug of choice for TBRD infections in adults *and* children of any age
 - + TBRDs can be life-threatening.
 - + Available data suggest that courses of doxycycline <14 days do not cause significant discoloration of permanent teeth.³
- Refer to <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm> for dosing and management of patients with clinical manifestations of TBRD.
- **Include ehrlichiosis and spotted fevers in the differential diagnosis of summertime febrile patients with known or potential tick exposure, and/or who do not respond to antibiotic therapy.**

Clinical Consequences/Sequelae

- Severe and life-threatening damage can occur in various organs in the body, to the skin, or to the nervous system during the initial phase of the infection when the bacteria are actively spreading.
- Permanent or long-term sequelae have been reported in the medical literature in people who were severely ill with ehrlichiosis and tick-borne spotted fevers (e.g., people hospitalized with the illness).

Public Health Disease Reporting

- Ehrlichiosis and RMSF (also known as a "spotted fever rickettsiosis") are reportable conditions in Missouri.
- Fax positive laboratory reports and case report forms to your local public health agency (LPHA), or to (573) 526-0235. Cases can also be reported by phone to your LPHA, or to the Missouri Department of Health and Senior Services at (573) 751-6113.

References

1. CDC. Diagnosis and management of tickborne rickettsial diseases: Rocky Mountain spotted fever, ehrlichioses, and anaplasmosis — United States: a practical guide for physicians and other health-care and public health professionals. *MMWR* 2006;55(No. RR-4).
<http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5504a1.htm>
2. *Rickettsia parkeri* rickettsiosis and its clinical distinction from Rocky Mountain spotted fever. Paddock CD, et al. *Clinical Infectious Diseases*, 2008;47:1188-96.
<http://cid.oxfordjournals.org/content/47/9/1188.long>.
3. Absence of Tooth Staining With Doxycycline Treatment in Young Children. Volovitz B., et al. *Clinical Pediatrics*, 2007;46:121-6.
<http://cpj.sagepub.com/content/46/2/121.abstract> (subscription required).