

**Health
Advisory:**
**Illness Associated With
Infection by a Novel
Phlebovirus in Two
Missouri Residents**

Health Advisory
June 11, 2012

**FROM: MARGARET T. DONNELLY
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**SUBJECT: 2009 Illness Associated With Infection by a Novel
Phlebovirus in Two Missouri Residents**

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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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Phleboviruses are members of the large and diverse *Bunyaviridae* family, with human infections often linked to biting arthropods, including sand flies, mosquitoes, and ticks. In 2009, a previously unknown phlebovirus was identified in Missouri and linked to illnesses in two state residents. The two patients were hospitalized with non-specific febrile illnesses accompanied by leukopenia and thrombocytopenia; both have recovered. Sequencing of viral isolates from these patients indicated the presence of a new phlebovirus.

In collaboration with the two medical care facilities where the patients presented and the Centers for Disease Control and Prevention (CDC), the Missouri Department of Health and Senior Services (DHSS) is conducting a public health investigation to learn more about the epidemiological characteristics of this novel pathogen, including possible routes of transmission, and the spectrum of clinical presentation.

Background

In 2009, acute blood specimens from two hospitalized Missouri residents were sent to CDC, as part of an ongoing collaboration, for advanced testing for suspected ehrlichiosis (caused by infection with the tick-borne pathogens *Ehrlichia chaffeensis* and *E. ewingii*). Both patients reported multiple tick exposures in the days prior to their illness. Presenting signs and symptoms for these individuals were similar, and consisted of fever, fatigue, anorexia, diarrhea, leukopenia, thrombocytopenia, and slightly elevated transaminases.

The two patients developed more significant thrombocytopenia, as well as moderately elevated transaminases, during hospitalization. Both received treatment with doxycycline for suspected ehrlichiosis, but no significant improvement was noted. Following 10 to 12 days of hospitalization, both patients were released home. One patient completely recovered within a month of his hospitalization. The other patient has returned to his normal activities, but reports fatigue and headaches two years later.

Viral sequences obtained from these patients' specimens showed genetic similarity to a phlebovirus identified in 2011 in China. Human infections with this new Chinese virus can reportedly result in severe fever and thrombocytopenia syndrome (SFTS)¹. The illnesses in the two Missouri patients were somewhat similar to the SFTS patients, but they were not identical: the Missouri patients lacked the overt bleeding, cerebral hemorrhage, and multi-organ failure described in SFTS patients in China.

Given the fact that the phlebovirus discovered in the two Missouri patients has never been described before, and the small number of cases, caution should be used at this time when making inferences about the clinical spectrum of the infection and its possible sequelae.

Human pathogens of the genus *Phlebovirus* are predominantly transmitted by arthropod vectors. The SFTS virus is believed to be transmitted by ticks; Rift Valley fever virus is transmitted by mosquitoes; and Toscana virus, sand fly virus, Sicilian virus, Punta Toro virus, and others are transmitted by sandflies.¹⁻³ To better understand the spatial and temporal distribution of potential vectors of the novel Missouri phlebovirus, CDC and DHSS are collecting ticks, mosquitoes, and sand flies in Missouri to screen for the presence of the new virus.

The DHSS/CDC Epidemiological and Clinical Study

The DHSS/CDC epidemiological and clinical study is a cooperative project between these agencies and the two Missouri medical care facilities where the phlebovirus patients were seen in 2009. Study activities began in May 2012, and continue throughout the vector transmission season. Study personnel at the two facilities have been trained to collect information on specific clinical signs and symptoms, pre-existing conditions, laboratory results (including complete blood counts), and basic metabolic parameters. The objectives of the study are to:

1. Gather data to further clarify the role of the novel phlebovirus as a human pathogen;
2. Examine possible routes of transmission;
3. Better define the epidemiology and clinical characteristics of the disease; and
4. Prospectively obtain clinical specimens from additional cases for diagnostic assay development.

NOTE: The study methods have been agreed to by the investigators, and establish strict procedures designed to protect potential study participants' rights to informed consent, ensure participants' privacy and confidentiality, and minimize the risk of physical or psychological harm resulting from study activities. In accordance with ethical principles dictated by federal and state laws and regulations, only personnel from the two participating health care facilities who have been trained in the study procedures and protocols are permitted to enroll patients in the study at this time.

DHSS Comments and Recommendations

- ***There is no evidence to suggest the novel phlebovirus is a common pathogen.***
 - ✓ Clinicians should adhere to their normal assessment of patient history, signs and symptoms, and physical and laboratory findings to guide their approach in developing a differential diagnosis and treatment plan for any suspected infectious disease.
 - ✓ Health care providers are urged to consider one or more of Missouri's endemic tick-borne rickettsial diseases (e.g., ehrlichiosis, spotted fever rickettsiosis) as a possible diagnosis when evaluating patients with symptoms of fever, headache, myalgia, and findings of leukopenia, thrombocytopenia, mild hyponatremia, or elevated hepatic transaminase levels.
- ***Diagnostics assays for the novel phlebovirus are still under development and are not yet available to medical practitioners or researchers.***

- ***Antiviral therapy for infection with the novel phlebovirus is unknown.***
- ***Transmissibility of this novel phlebovirus is unknown – health care providers should always strictly observe standard precautions, the prevention of needlestick injuries, and appropriate management of clinical specimens.***
- ***Providers are asked to contact their local public health agency or DHSS to report unusual increases in unexplained severe febrile illnesses with thrombocytopenia and leukopenia.***

Note: In addition to the current DHSS/CDC study described here, a previous study was undertaken that more fully describes the two Missouri patients' clinical illnesses, as well as the isolation, electron microscopy, and sequencing methods used to identify the phlebovirus. This study has been submitted for publication.

Questions from the Medical and Health Community should be directed to:

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Background Information

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