County of Riverside
Department of Public Health

Disease Control Branch
Phone: (951) 358-5107
Fax: (951) 358-5102

Cameron Kaiser, M.D.
Interim Public Health Officer

Susan D. Harrington, M.S., R.D.
Director, Department of Public Health

Alert and Guidance for Physicians with Patients Presenting with Concerns or Symptoms of Hantavirus Pulmonary Syndrome after Visit to Yosemite National Park

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Situation Update

The California Department of Public Health (CDPH) is collaborating with the U.S. Centers for Disease Control and Prevention (CDC) and the National Park Service (NPS) to investigate an outbreak of Hantavirus Pulmonary Syndrome (HPS) in recent visitors to Yosemite National Park (YOSE) (http://www.cdph.ca.gov/Pages/NR12-040.aspx; http://www.cdph.ca.gov/Pages/NR12-049.aspx).

As of September 10, 2012, acute infection with hantavirus has been identified in eight patients, six Californians, one from Pennsylvania and one from West Virginia. Three cases were fatal. On August 27, the National Park Service sent a letter or e-mail to over 1700 guests who had stayed in the "signature" tent cabins between June 10 and August 24, alerting them to the hantavirus concerns and recommending that they seek medical attention if they experience illness suggestive of HPS. Because a large proportion of these visitors were from California and some of them may present to medical attention after hearing about the HPS outbreak, we want to provide the following information to guide your clinical evaluation, diagnosis, and management of these patients.

Background

Hantavirus Pulmonary Syndrome in the U.S. is caused by Sin Nombre virus, which is carried primarily by deer mice (*Peromyscus maniculatus*) and shed in their urine and droppings. The fatality rate is approximately 36%. People are exposed through inhalation of aerosolized deer mice excreta, usually within confined, poorly ventilated spaces. In California, 63 cases of HPS have been reported since 1993 and most of the patients were exposed in the Sierra Mountains.

Clinical Presentation

The incubation period for HPS is commonly 2-3 weeks, but can occasionally be as long as 5 weeks. HPS typically begins with a non-specific prodrome that lasts 3-5 days. Early symptoms include fever, headache, chills, arthralgias, back pain, and abdominal pain. Non-productive cough, shortness of breath, nausea, vomiting, diarrhea, and lightheadedness are reported by approximately half of all patients. These non-specific symptoms make HPS difficult to differentiate from other more common causes of viral illness during the prodrome. Hematologic abnormalities commonly observed during the HPS prodrome include progressive thrombocytopenia, leukocytosis, and immature leukocytes (myelocytes, metamyelocytes) in the peripheral circulation.

Following the prodrome, the cardinal clinical feature of HPS is a rapid onset of respiratory distress and hemodynamic compromise. Within 24 hours, patients experience hypotension, progressive pulmonary edema, and hypoxia, often requiring intubation and supplemental oxygen. Patients may progress to acute respiratory

distress syndrome (ARDS). Chest radiographs show progression from minimal changes of interstitial pulmonary edema to bilateral infiltrates consistent with ARDS. Patients with fatal infections appear to have severe myocardial depression which can progress to sinus bradycardia with subsequent electromechanical dissociation, ventricular tachycardia or fibrillation.

Treatment

There is no effective treatment for HPS and management consists solely of providing cardiopulmonary support. Of note, extracorporeal membrane oxygenation (ECMO) support has been reported to improve survival of patients with severe HPS (Wernly JA, et al. Eur J Cardiothorac Surg 2011;40(6):1334-40).

Laboratory Diagnosis

The chief diagnostic test for HPS is serology using an enzyme immunoassay (EIA). As most HPS patients seroconvert at or prior to onset of symptoms, the EIA is highly sensitive in patients displaying clinically compatible symptoms. Serologic testing for HPS is available through some commercial diagnostic laboratories; however, it is critical that the assay employs antigen of Sin Nombre virus, the cause of HPS in the western U.S., as non-specific cross-reactivity is commonly observed for assays that use other hantavirus antigens. The CDPH Viral and Rickettsial Diseases Laboratory provides confirmatory testing for patients with strong clinical or laboratory indications of HPS, and request for such testing can be made through the County of Riverside Department of Public Health.

Infection control

There is no evidence of person-to-person transmission of Sin Nombre virus in North America**.** This includes healthcare settings where studies of antibody levels have not documented asymptomatic transmission. Nonetheless, the usual Standard Precautions are recommended when managing a possible case of Hantavirus infection. These include hand hygiene, masking a coughing patient, and wearing a mask in the presence of a coughing patient. Surfaces should be cleaned with a disinfectant, and gloves and gowns may be worn if a splash or mucus membrane exposure is possible.

Public Health Recommendations

1. If a patient presents with concerns or non-specific symptoms well after 6 weeks from their stay in Yosemite, the patient most likely does not have hantavirus infection and testing for hantavirus infection is not indicated.
2. If a patient presents with non-specific symptoms within 6 weeks of their stay in Yosemite and hantavirus infection is **not** suspected, the patient should be followed as clinically indicated, but testing for hantavirus infection is not indicated.
3. If a patient presents with fever and mild symptoms suspicious for early hantavirus infection within 6 weeks of their stay in Yosemite, then a complete blood count (CBC) and chemistry panel, including LHD, should be done at baseline and hantavirus serology should be requested. The patient should be followed closely for development of tachypnea and other symptoms of HPS, and serial CBC may show progressive thrombocytopenia, leukocytosis, and hemoconcentration, which are strongly suggestive of progressing HPS.
4. If a patient presents with fever, shortness of breath, and other symptoms suggestive of HPS within 6 weeks of their stay in Yosemite, or if the patient in #3 above progresses to having symptoms and laboratory tests suggestive of HPS, the patient should be transferred to a hospital emergency department for full evaluation and cardiopulmonary monitoring and support if needed. Hantavirus serology should be requested, and the local public health department should be notified.
5. Hantavirus infections are reportable to public health. Confirmed and suspect cases should be reported to Disease Control at (951) 358-5107 or page, at 1 (888) 430-5195 for non business hours.

Additional information on hantavirus and HPS is available at the CDC webpage:

http://www.cdc.gov/hantavirus/