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Hantavirus Infections

Overview^{1, 2, 3, 5, 6, 7, 9}

Infection with a hantavirus can progress to Hantavirus Pulmonary Syndrome (HPS), a rare but severe, sometimes fatal, respiratory disease in humans. Hantaviruses belong to the *Bunyaviridae* family of viruses. There are 5 genera within the family: bunyavirus, phlebovirus,airovirus, tospovirus, and hantavirus. The viruses causing HPS in this country are Sin Nombre, Black Creek Canal, Bayou, and New York-1.

Rodents are the only known reservoir of hantaviruses, and individual virus species appear to be associated with a single major rodent species. In the United States, deer mice (along with cotton rats and rice rats in the southeastern states and the white-footed mouse in the Northeast) are the reservoir of the virus. The deer mouse, which is very common in North America, is the major host species of the Sin Nombre virus, which is responsible for the majority of HPS cases in the United States and Canada.

Transmission of the virus to humans occurs from the aerosolization of saliva, urine, or feces of infected mice or rats. To date, human-to-human transmission of a hantavirus has only been reported in cases of the Andes virus in Chile and Argentina. Due to the small number of HPS cases, the incubation period is not positively known. However, on the basis of limited information, it appears that symptoms may develop between 1 and 5 weeks after exposure to fresh urine, droppings, or saliva of infected rodents. Early symptoms include fatigue, fever, and muscle aches, especially in the large muscle groups (thighs, hips, back, and sometimes shoulders). These symptoms are universal. There may also be headache, dizziness, chills, and abdominal problems, such as nausea, vomiting, diarrhea, and abdominal pain. Roughly half of all HPS patients experience these symptoms. Four to 10 days after the initial phase of illness, the late symptoms of HPS appear. These include coughing and shortness of breath. **NOTE:** Hantavirus infection, non-HPS is a febrile illness with non-specific viral symptoms including fever, chills, myalgia, headache, and gastrointestinal symptoms, but no cardio-pulmonary symptoms.

There is no specific treatment, cure, or vaccine for hantavirus infection. However, we do know that if HPS patients are recognized early and receive medical care in an intensive care unit, they may do better. In intensive care, patients are intubated and given oxygen therapy to help them through the period of severe respiratory distress. Case fatality rates for HPS have been reported as high as 35 to 50%, and survivors may require weeks to months to fully recover.

Hemorrhagic Fever with renal Syndrome (HFRS) is a group of clinically similar illnesses caused by hantaviruses from the family *Bunyaviridae*. HFRS includes diseases such as Korean hemorrhagic fever, epidemic hemorrhagic fever, and nephropathis epidemica. The viruses that cause HFRS include Hantaan, Dobrava, Saaremaa, Seoul, and Puumala. Symptoms of HFRS usually develop within 1 to 2 weeks after exposure to infectious material, but in rare cases, they may take up to 8 weeks to develop. Initial symptoms begin suddenly and include intense headaches, back and abdominal pain, fever, chills, nausea, and blurred vision. Individuals may have flushing of the face, inflammation or redness of the eyes, or a rash. Later symptoms can include low blood pressure, acute shock, vascular leakage, and acute kidney failure, which can

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cause severe fluid overload. The severity of the disease varies depending upon the virus causing the infection. Supportive therapy is the mainstay of care for patients with hantavirus infections. Care includes careful management of the patient's fluid (hydration) and electrolyte (e.g., sodium, potassium, chloride) levels, maintenance of correct oxygen and blood pressure levels, and appropriate treatment of any secondary infections. Dialysis may be required to correct severe fluid overload. Intravenous (IV) ribavirin, an antiviral drug, has been shown to decrease illness and death associated with HFRS if used very early in the disease. IV ribavirin is ineffective for HPS.⁹

For a complete description of hantavirus infections, refer to the following references:

- *Control of Communicable Diseases Manual (CCDM)*, American Public Health Association, 20th ed. 2015.
- American Academy of Pediatrics. *Red Book: 2012 Report of the Committee on Infectious Diseases*. 29th ed. 2012.
- *Principles and Practice of Infectious Diseases*, 7th ed., Pennsylvania: Churchill Livingstone Elsevier, 2010.

2015 Case Definition – Hantavirus infections⁴ - (6/15)

Subtype(s): [Hantavirus Pulmonary Syndrome \(HPS\)](#)
[Hantavirus Infection, non-HPS](#)
[Hemorrhagic Fever with Renal Syndrome \(HFRS\)[§]](#)

Hantavirus Pulmonary Syndrome (HPS)

Clinical Description

HPS is an acute febrile illness (i.e., temperature greater than 101 F [greater than 38.3 C]) with a prodrome consisting of fever, chills, myalgia, headache, and gastrointestinal symptoms, and one or more of the following clinical features: Bilateral diffuse interstitial edema, or

- Clinical diagnosis of acute respiratory distress syndrome (ARDS), **or**
- Radiographic evidence of noncardiogenic pulmonary edema, **or**
- An unexplained respiratory illness resulting in death, and includes an autopsy examination demonstrating noncardiogenic pulmonary edema without an identifiable cause, **or**
- Healthcare record with a diagnosis of hantavirus pulmonary syndrome, **or**
- Death certificate lists hantavirus pulmonary syndrome as a cause of death **or** a significant condition contributing to death.

Laboratory Criteria for Diagnosis

- Detection of hantavirus-specific immunoglobulin M or rising titers of hantavirus-specific immunoglobulin G, **or**
- Detection of hantavirus-specific ribonucleic acid in clinical specimens, **or**
- Detection of hantavirus antigen by immunohistochemistry in lung biopsy or autopsy tissues

Case Classification

Confirmed

A clinically compatible case of HPS with laboratory evidence. *(Continued on next page)*

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Comment(s)

Laboratory testing should be performed or confirmed at a reference laboratory. Because the clinical illness is nonspecific and ARDS is common, a screening case definition can be used to determine which patients to test. In general, a predisposing medical condition (e.g., chronic pulmonary disease, malignancy, trauma, burn, and surgery) is a more likely cause of ARDS than HPS, and patients who have these underlying conditions and ARDS need not be tested for hantavirus.

Hantavirus infection, Non-Pulmonary Syndrome (Non-HPS)

Clinical Description

Non-HPS Hantavirus infection is a febrile illness with non-specific viral symptoms including fever, chills, myalgia, headache, and gastrointestinal symptoms, but no cardio-pulmonary symptoms. Typical clinical laboratory findings include hemoconcentration, left shift in the white blood cell count, neutrophilic leukocytosis, thrombocytopenia, and circulating immunoblasts.

NOTE: Patients that develop cardio-pulmonary symptoms should be classified as having HPS.

Laboratory Criteria for Diagnosis

- Detection of hantavirus-specific immunoglobulin M or rising titers of hantavirus-specific immunoglobulin G, **or**
- Detection of hantavirus-specific ribonucleic acid in clinical specimens, **or**
- Detection of hantavirus antigen by immunohistochemistry in lung biopsy or autopsy tissues

Case Classification

Confirmed

A clinically compatible case of hantavirus infection, Non-HPS with laboratory evidence.

Comment(s)

In June 2014, the Council of State and Territorial Epidemiologists (CSTE) recommended Non-HPS Hantavirus infection to be nationally notifiable. Laboratory testing should be performed or confirmed at a reference laboratory.

Hemorrhagic Fever with Renal Syndrome (HFRS)[§]

Background

HFRS is a group of clinically similar illnesses caused by hantaviruses from the family *Bunyaviridae*. HFRS includes diseases such as Korean hemorrhagic fever, epidemic hemorrhagic fever, and nephropathic epidemics. The viruses that cause HFRS include Hantaan, Dobrava, Saaremaa, Seoul, and Puumala. HFRS is found throughout the world. Hantaan virus is widely distributed in eastern Asia, particularly in China, Russia, and Korea. Puumala virus is found in Scandinavia, Western Europe, and Western Russia. Dobrava virus is found primarily in the Balkans, and Seoul virus is found worldwide. Saaremaa is found in central Europe and Scandinavia.

(Continued on next page)

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Clinical Description

Initial symptoms begin suddenly and include intense headaches, back and abdominal pain, fever, chills, nausea, and blurred vision. Individuals may have flushing of the face, inflammation or redness of the eyes, or a rash. Later symptoms can include low blood pressure, acute shock, vascular leakage, and acute kidney failure, which can cause severe fluid overload. The severity of the disease varies depending upon the virus causing the infection. Hantaan and Dobrava virus infections usually cause severe symptoms, while Seoul, Saaremaa, and Puumala virus infections are usually more moderate. Complete recovery can take weeks or months.

Laboratory Criteria for Diagnosis

Several laboratory tests are used to confirm a diagnosis of HFRS in patients with a clinical history compatible with the disease. Such patients are determined to have HFRS if they have:

- Serologic test results positive for hantavirus infection, **or**
- Evidence of hantavirus antigen in tissue by immunohistochemical staining, **or**
- Microscope examination or evidence of hantavirus RNA sequences in blood or tissue.

Confirmed

A clinically compatible case of HFRS with laboratory evidence.

Comment(s)

§ = All hantavirus infections are to be reported to CDC. A national case definition for HFRS is currently unavailable. The HFRS definition provided above is a Missouri case definition.

Information Needed for Investigation

Verify the diagnosis. Obtain demographic, clinical, laboratory information, and other epidemiological information necessary to complete the [Disease Case Report \(CD-1\)](#) and the from the attending physician, hospital, and/or laboratory and patient or a knowledgeable family member.

Establish the extent of illness. Determine if household or other close contacts are, or have been ill by contacting the health care provider, patient, or family member. Identify symptomatic household members, associates, or co-workers and strongly urge them to contact their physician for a medical evaluation.

Identify the source of infection. Determine the occupation of the case since this information may help narrow the search for the route of exposure. Information to obtain:

- Has the case visited or recently cleaned a vacation home or other seasonally opened dwelling (e.g., cabin, shed, or outbuildings, including barns, garages and storage facilities, that have been closed during the winter)?
- Has the case recently performed cleaning in and around their home? Has the case's home or nearby buildings had a rodent infestation?
- Has the case had a work-related exposure? (e.g., Laboratory workers with exposures to rodent excreta, fresh necropsy material, and animal bedding are presumed to be associated with risk. Construction, utility and pest control workers can be exposed when they work in crawl spaces, under houses, or in vacant buildings that may have a rodent population.)

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- Has the case recently gone on a camping or hiking trip? (e.g., Campers and hikers can be exposed when they use infested trail shelters or camp in rodent habitats.)
- Has the case recently travelled to a state with endemic hantavirus? (See the following link for states with reported hantavirus: <https://www.cdc.gov/hantavirus/data-research/cases/index.html>.)
- Have there been other cases linked by time, place or person?

Sometimes the source is not identified. **NOTE:** Any activity that puts you in contact with rodent droppings, urine, saliva, or nesting materials can place you at risk for infection. Hantavirus is spread when virus-containing particles from rodent urine, droppings, or saliva are stirred into the air. It is important to avoid actions that raise dust, such as sweeping or vacuuming. Infection occurs when you breathe in virus particles. If a rodent with the virus bites someone, the virus may be spread to that person, but this type of transmission is rare. Researchers believe that people may be able to get the virus if they touch something that has been contaminated with rodent urine, droppings, or saliva, and then touch their nose or mouth. Researchers also suspect people can become sick if they eat food contaminated by urine, droppings, or saliva from an infected rodent.

Provide information on Hantavirus infections to persons at risk for disease and the general public. Efforts should be made to promote hantavirus infection awareness and educate the public on sources of infection. 1) Keep mice and rats out of your home. 2) Minimize contact with rodents in your workplace or campsite. 3) Clean up mouse and rat urine, droppings, and nesting materials with a disinfectant or a mixture of bleach and water. Additional information on hantavirus infection prevention can be found on CDC's website at:

- <https://www.cdc.gov/hantavirus/about/index.html> and
- <https://www.cdc.gov/hantavirus/prevention/index.html>

Hantavirus Infection Surveillance. Review ShowMe WorldCare to determine whether there have been other cases in the same geographic area. When cases are related by person, place, or time, efforts should be made to identify a common source. Information obtained through the case investigation is used to identify a possible source of infection and to characterize persons or geographic areas in which additional efforts may be needed to raise awareness and reduce disease incidence.

Notification

- Immediately contact the [District Communicable Disease Coordinator](#), the [Senior Epidemiology Specialist](#) for the District, or the Missouri Department of Health and Senior Services (MDHSS) - BCDCP, phone (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/Emergency Response Center (ERC) at (800) 392-0272 (24/7) upon notification of a suspected case of hantavirus pulmonary syndrome.
- If a case(s) is associated with a child care center, BCDCP or the LPHA will contact the BEHS, phone (573) 751-6095, Fax (573) 526-7377 and the Section for Child Care Regulation, phone (573) 751-2450, Fax (573) 526-5345.

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- If a case(s) is a food handler, BCDP or the LPHA will contact the Bureau of Environmental Health Services (BEHS), phone (573) 751-6095, Fax (573) 526-7377.
- If a case(s) is associated with a long-term care facility, BCDP or the LPHA will contact the Section for Long Term Care Regulation, phone (573) 526-8524, Fax (573) 751-8493.
- If a case is associated with a hospital, hospital-based long-term care facility, or ambulatory surgical center BCDP or the LPHA will contact the Bureau of Health Services Regulation phone (573) 751-6303, Fax (573) 526-3621.

Control Measures

Rodent control is the primary strategy for preventing hantavirus infections and to minimize aerosolization and contact with the virus in rodent saliva and excreta. This is achieved by eliminating any food sources, sealing even the smallest entries into homes, and successfully trapping rodents in and around the home. Additional prevention information is available at: <https://www.cdc.gov/hantavirus/prevention/index.html>. **NOTE:** Chemoprophylaxis or vaccines for hantaviruses are currently not available.

Laboratory transmission of hantavirus from rodents to humans via the aerosol route is well documented. Exposures to rodent excreta, fresh necropsy material, and animal bedding are presumed to be associated with risk. Interim biosafety guidelines for preventing laboratory-associated infections with agents that cause hantavirus pulmonary syndrome can be found at: <https://www.cdc.gov/mmwr/PDF/rr/rr4307.pdf>.

Laboratory Procedures

The Centers for Disease Control and Prevention (CDC), National Center for Emerging and Zoonotic Infectious Diseases (NCEZID), Division of High-Consequence Pathogens and Pathology (DHCPP), Viral Special Pathogens Branch (VSPB) performs a variety of diagnostic techniques for hantavirus. See the CDC [Protocol for Specimen Submission](#) for hantavirus specimens. Also, “Instructions for submitting Diagnostic Specimens to CDC’s Viral Special Pathogens Branch” and “Specimen Submission Form” are available at: <https://www.cdc.gov/infectious-diseases-labs/php/submission-form/>.

IMPORTANT: CDC testing of Missouri residents is performed by means of **prior consultation** with a Missouri Department of Health and Senior Services (MDHSS) epidemiologist. Submitters should contact the MDHSS, Bureau of Communicable Disease Control and Prevention (CDCP), phone (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/ERC at (800) 392-0272 (24/7) before sending any specimens to CDC.

IMPORTANT: The following forms need to be completed for each patient:

- [CDC Specimen Submission Form](#).

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Reporting Requirements

HPS is a Category 2 (A) disease and shall be reported to the [local public health agency](#) or to MDHSS within one (1) day of first knowledge or suspicion by telephone, facsimile or other rapid communication. The MDHSS may be contacted by phone at (573) 751-6113, Fax (573) 526-0235, or for afterhours notification contact the MDHSS/ERC at (800) 392-0272 (24/7).

As a Nationally Notifiable Condition, **confirmed** HPS cases are a **STANDARD** report to the Centers of Disease Control and Prevention (CDC). **STANDARD** reporting requires the MDHSS to report to CDC by electronic transmission via WebSurv within the next normal reporting cycle.

1. For confirmed and probable cases, complete a “[Disease Case Report](#)” (CD-1) and send the completed form to the [DHSS District Health Office](#). Attach all laboratory results to the submitted specimens.
2. Entry of the completed CD-1 into the MOHSIS database negates the need for the paper CD-1 to be forwarded to the District Health Office.
3. If specimens are to be sent to CDC for testing, complete the "[Specimen Submission Form](#)". *NOTE: CDC testing of Missouri residents is performed by means of prior consultation with a MDHSS epidemiologist.*
4. MDHSS will report to CDC following the above reporting criteria (see boxes).
5. All outbreaks or “suspected” outbreaks must be reported as soon as possible (by phone, fax or e-mail) to the District Communicable Disease Coordinator. This can be accomplished by completing the [Missouri Outbreak Report Form \(MORE\)](#).
6. Within 90 days from the conclusion of an outbreak, submit the final outbreak report to the District Communicable Disease Coordinator.

References

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7. Canadian Centre for Occupational Health & Safety, Hamilton, Ontario Canada. *Hantavirus In: Home; OSH Answers; Biological Hazards; Diseases, Disorders & Injuries*. <http://www.ccohs.ca/oshanswers/diseases/hantavir.html> (6/15).
8. U.S. National Library of Medicine, Bethesda, MD, U.S. Department of Health and Human Services, National Institutes of Health. *Hantavirus Infections*. In: MedlinePlus. <http://www.nlm.nih.gov/medlineplus/hantavirusinfections.html> (6/15).