

Hantavirus Pulmonary Syndrome

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

1. To characterize the epidemiology and clinical aspects of this emerging disease.
2. To monitor disease trends and recognize outbreaks.
3. To target prevention and control messages.

B. Legal Reporting Requirements

1. Health care providers: notifiable to local health jurisdiction within 24 hours.
2. Health care facilities: notifiable to local health jurisdiction within 24 hours.
3. Laboratories: Hantavirus detection is notifiable to local health jurisdiction within 24 hours. Specimen submission is on request only but confirmation of positive results is recommended (see Section 4).
4. Local health jurisdictions: notifiable to the Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days.

C. Local Health Jurisdiction Investigation Responsibilities

1. Facilitate the transport of specimens to Washington State Public Health Laboratories for confirmatory testing.
2. Report all *confirmed* cases to CDES (see definition below). Use the hantavirus pulmonary syndrome report form (<http://www.doh.wa.gov/notify/forms/hantavirus.pdf>) and enter the data into the Public Health Issues Management System (PHIMS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Multiple hantaviruses have been identified in the Americas. Sin Nombre virus is the predominant hantavirus in North America and is responsible for all of the cases identified in Washington.

B. Description of Illness

Hantavirus pulmonary syndrome (HPS) is an acute viral disease characterized by a relatively short (3–5 days) prodrome of fever, myalgias (muscle aches), headache, and gastrointestinal complaints followed by the abrupt onset of acute respiratory distress syndrome (ARDS) and hypotension. The illness progresses rapidly to respiratory failure with bilateral pulmonary infiltrates, pulmonary edema, and shock. Circulating immunoblasts (immature myelocytes), elevated hematocrit, and thrombocytopenia are almost always present; a rapid drop in platelets marks onset of the cardiopulmonary phase. About a third of all cases in the United States have died. In survivors, recovery from acute illness is rapid, but full convalescence may require weeks or months.

Restoration of normal lung function generally occurs, but pulmonary function abnormalities may persist in some individuals.

C. Hantavirus Pulmonary Syndrome (HPS) in Washington State

Through 2009 there have been 39 reported cases of HPS among residents of Washington State, 13 (35%) of which were fatal. Additionally there were two cases in foreign nationals working in the state, one of which was fatal. In all, 41 cases with 14 (36%) associated deaths have occurred in Washington State. Between one and five cases occur annually. Cases occur in both western and eastern parts of the state. The median age of cases in Washington State is 35 years (range 14–75 years). The death rate and median age of cases in Washington are similar to the national rates.

D. Reservoirs

The deer mouse (*Peromyscus maniculatus*) is the major reservoir of Sin Nombre virus in the western United States. Deer mice live in all parts of Washington, but mainly in rural areas. They usually carry the virus without showing any signs of being sick. The deer mouse is about six inches long from the nose to the tip of its tail. It is grayish to light brown on top, with a white belly, large ears and eyes, and a furry tail that is white on the underside.



Photo source: CDC website
<http://www.cdc.gov/ncidod/diseases/hanta/hps/>

Rodent serosurveys were conducted in Washington from 1993 to 2001 by various state and federal agencies. During this time period, 14% of over 1,100 deer mice tested in Washington had antibodies against Sin Nombre virus, similar to prevalence in other western states. These data, as well as data from other states, also demonstrated that the percentage of infected mice may fluctuate widely from year to year.

E. Modes of Transmission

Exposure occurs by inhalation of virus that is excreted in mouse urine, feces or saliva and aerosolized during cleaning of buildings with rodent nests or other rodent contamination. Exposures have occurred in rodent-infested cabins, homes, barns, vehicles, outbuildings or less commonly when handling wild rodents without protective equipment. Nationally, rare transmission has been documented from a bite of a deer mouse.

F. Incubation Period

One to six weeks (7–45 days).

G. Period of Communicability

Person-to-person spread of hantaviruses in the United States has not occurred. However, person-to-person transmission of the related Andes virus was documented in Argentina during an outbreak of a similar syndrome.

H. Treatment

There is no antiviral treatment. Supportive care including intubation and ventilation and fluid and pharmacologic support of blood pressure is typically required.

3. CASE DEFINITION

A. Clinical Case Definition

An illness characterized by one or more of the following clinical syndromes:

- A febrile illness (i.e., temperature greater than 101.0° F [greater than 38.3° C]) corroborated by bilateral diffuse interstitial edema or a clinical diagnosis of acute respiratory distress syndrome (ARDS) or radiographic evidence of non-cardiogenic pulmonary edema, or unexplained respiratory illness resulting in death, and occurring in a previously healthy person; **OR**
- An unexplained respiratory illness resulting in death, with an autopsy examination demonstrating noncardiogenic pulmonary edema without an identifiable cause.

B. Laboratory Criteria for Diagnosis

1. Detection of hantavirus-specific immunoglobulin M (IgM) or rising titers of hantavirus-specific immunoglobulin G (IgG), **OR**
2. Detection of hantavirus-specific ribonucleic acid (RNA) sequence by polymerase chain reaction (PCR) in clinical specimens, **OR**
3. Detection of hantavirus antigen by immunohistochemistry (IHC).

Note: Laboratory testing should be performed or confirmed at a reference laboratory such as the Washington State Public Health Laboratories. Because the clinical illness is nonspecific and ARDS is common, a screening case definition should be used to determine which patients to test. In general, a predisposing medical condition (e.g., malignancy, chronic pulmonary disease, trauma, burn, or surgery) is a more likely cause of ARDS than hantavirus pulmonary syndrome. Patients with these underlying conditions and ARDS need not be tested for hantavirus.

C. Case Definition

Confirmed: a clinically compatible case that is laboratory confirmed.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Positive commercial laboratory results should be confirmed at a reference laboratory such as the Washington State Public Health Laboratories.

Serology: Diagnosis is most commonly made by detection of virus-specific IgM in serum using an enzyme immunoassay (EIA). Most patients have IgM antibodies at time of hospitalization. A test for IgG is used in conjunction with the IgM-capture test. Acute- and convalescent-phase sera should reflect a four-fold rise in IgG antibody titer. An acute-phase serum drawn as an initial diagnostic specimen may not yet have IgG present. IgG antibody is long-lasting once it develops, and sera of patients retrospectively identified appear to have retained antibody for many years.

Reverse transcriptase-polymerase chain reaction (RT-PCR) can be used to detect hantavirus RNA in fresh frozen lung tissue, blood clots, or nucleated blood cells.

Immunohistochemistry (IHC) testing of formalin-fixed tissues or paraffin-embedded tissues with specific monoclonal and polyclonal antibodies can be used to detect hantavirus antigens. IHC can be useful in fatal cases.

To date, no isolates of Sin Nombre virus-like viruses have been recovered from humans, and, therefore, virus isolation is not a consideration for diagnostic purposes.

There is no test for exposure to the virus. In addition, there is no test to determine if the urine, droppings or nesting material are infectious. Testing mice is not recommended.

Persons concerned about exposure to rodent urine, droppings or nesting material should monitor themselves and seek medical care if they develop symptoms.

Clinical signs such as decreasing platelets or the presence of immature cells (myelocytes or metamyelocytes) in the white blood count are suggestive of hantavirus infection but are not diagnostic.

B. Services Available at the Washington State Public Health Laboratories (PHL)

1. Enzyme immunoassay (EIA) for virus-specific IgM and IgG antibody in serum.
2. RT-PCR and IHC are available through the CDC. All specimens being submitted to CDC *must* be sent through the PHL.

Note that PHL require all clinical specimens have two patient identifiers, a name **and** a second identifier (e.g., date of birth) both on the specimen label and on the submission form. Due to laboratory accreditation standards, specimens will be rejected for testing if not properly identified. Also include specimen source and collection date.

C. Criteria for Testing HPS Specimens at PHL

1. Patients with suspected hantavirus pulmonary syndrome (fever, hypotension, hypoxia, bilateral interstitial pulmonary infiltrates, acute respiratory distress syndrome, thrombocytopenia, hemoconcentration without an identifiable cause).
2. Any person with laboratory evidence of hantavirus pulmonary syndrome from a commercial laboratory to confirm the positive test.
3. Deaths due to unexplained respiratory illness with autopsy demonstrating non-cardiogenic pulmonary edema without identifiable cause.

D. Specimen Collection

Serum

1. Submit at least 1 cc (2.5 cc preferred) of serum (separated serum, not whole blood) for EIA at PHL. Serum can be drawn upon hospital admission. If possible, also obtain as late a serum as available before death or hospital discharge, or a convalescent serum drawn approximately 21 days after the first specimen.
2. Separated serum specimens should be refrigerated and transported cold. Avoid repeated freeze-thaw cycles.
3. Specimens should be submitted by the clinical laboratory with a completed PHL Serology form: <http://www.doh.wa.gov/EHSPHL/PHL/Forms/SerVirHIV.pdf>

Tissue, bronchoalveolar lavage, blood clots, or nucleated blood cells

For information on sending specimens other than serum to CDC for RT-PCR or IHC, consult CDES and visit:

<http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/phys/specimen/specguide.htm>.

5. ROUTINE CASE INVESTIGATION

Interview the case and others who may be able to provide pertinent clinical information

A. Evaluate the Diagnosis

If the case tests positive for hantavirus at a laboratory other than a reference laboratory, facilitate transport of the specimen (i.e., serum or tissue) to Public Health Laboratories for further testing. If a patient tests IgG positive and IgM negative for hantavirus at a commercial laboratory, this indicates possible past exposure and does not need any further laboratory testing.

B. Identify Potential Sources of Infection

Obtain a history about possible exposure to fresh rodent urine, droppings, or nesting material. Exposures generally occur when urine, droppings, or nesting material are stirred up, aerosolized, and inhaled. A rodent bite can also transmit the virus; however inhaling the virus is a much more common transmission route to humans.

C. Identify Potentially Exposed Persons

It is very unusual to have multiple cases with the same exposure. However, other persons potentially exposed to the same source as the case should be educated about symptoms of hantavirus infection and told to seek medical attention if they develop such symptoms.

D. Environmental Evaluation

Notify local environmental health program of locally acquired cases. It may be appropriate to examine the environment where the case was exposed to make suggestions about rodent removal. However, since the deer mice are found throughout Washington and are identified as the reservoir for the Sin Nombre virus, testing rodents is generally not done.

6. CONTROLLING FURTHER SPREAD**A. Infection Control Recommendations / Case Management**

1. Hospitalized patients should be cared for using standard precautions.
2. Educate the case and/or others sharing the environment about avoiding future exposures (see Section 8B).

B. Contact Management

Other persons who may have been exposed to the same source as the case should be educated regarding the signs and symptoms of hantavirus pulmonary syndrome and told to seek medical attention if symptoms develop. However, it is rare to have two cases sharing an exposure. Person-to-person spread of hantaviruses has not occurred in the United States.

7. MANAGING SPECIAL SITUATIONS

Not applicable

8. ROUTINE PREVENTION

A. Immunization Recommendations: None

B. Prevention Recommendations

1. **Keep rodents out of your home and workplace.** Always take precautions when cleaning, sealing and trapping in rodent-infested areas.
2. **Seal up** cracks and gaps in buildings that are larger than 1/4 inch including window and door sills, under sinks around the pipes, in foundations, attics, and any rodent entry hole.
3. **Trap indoor rats and mice** with snap traps.
4. **Remove rodent food sources.** Keep food (including pet food) in rodent proof containers.
5. **Clean up rodent infested areas:**
 - Wear rubber, latex, vinyl or nitrile gloves.
 - Do not stir up dust by vacuuming, sweeping, or any other dust-generating means.
 - Thoroughly wet contaminated areas including trapped mice, droppings, nests with a bleach solution or household disinfectant. **Hypochlorite (bleach) solution:** Mix 1½ cups of household bleach in 1 gallon of water. Use only freshly mixed solution.
 - Once everything is soaked for 10 minutes, remove all of the nest material, mice or droppings with damp towel and then mop or sponge the area with bleach solution or household disinfectant.
 - Spray dead rodents with disinfectant and then double-bag along with all cleaning materials. Bury, burn, or throw out rodent in an appropriate waste disposal system.
 - Disinfect gloves with disinfectant or soap and water before taking them off.
 - After taking off the disinfected gloves, thoroughly wash hands with soap and water (or use a waterless alcohol-based hand rub when soap is not available).

Please visit the CDC HPS prevention website for more information

(<http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/prevent.htm>)

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UPDATES

March 2009: In Section 2C, the number of reported cases and deaths in Washington was updated. In Section 4D, the link for lab form was updated.

January 2010: In Section 2C case numbers were updated and in Section 3A the clinical case definition was revised to reflect the new 2010 CSTE case definition.

January 2011: The Legal Reporting Requirements section has been revised to reflect the 2011 Notifiable Conditions Rule revision. Sections 3B and 4A were modified to reflect that confirmatory testing should be performed at WA PHL or another PHL.