Hantavirus

(including, but not limited to: Andes virus, Bayou virus, Black Creek Canal virus, Dobrava-Belgrade virus, Hantaan virus, Seoul virus, Sin nombre virus)

Signs and Symptoms	• Prodrome (3-5 days) of fever, fatigue, muscle aches, headache and gastroenteritis • Hantavirus pulmonary syndrome (HPS) progresses rapidly to respiratory failure and hypotension (acute respiratory distress syndrome: ARDS) • Hemorrhagic Fever with Renal Syndrome (HFRS) progresses to renal failure • Laboratory (HPS): bilateral lung infiltrates, circulating immunoblasts (myelocytes), elevated hematocrit, thrombocytopenia (most <150,000)
Incubation	1-8 weeks
Case classification	**Clinical criteria** 1. Non-HPS Hantavirus: fever, chills, myalgia, headache, and gastrointestinal symptoms; typically hemoconcentration, left shift in the white blood cell count, neutrophilic leukocytes, thrombocytopenia, and circulating immunoblasts 2. HPS: fever >101F (38.3C), chills, myalgia, headache, and gastrointestinal symptoms and one or more of: Bilateral diffuse interstitial edema, **or** Clinical diagnosis of ARDS, **or** Radiographic evidence of noncardiogenic pulmonary edema, **or** Unexplained respiratory illness resulting in death and on autopsy noncardiogenic pulmonary edema without identifiable cause, **or** Healthcare record with a diagnosis of hantavirus pulmonary syndrome, **or** Death certificate lists HPS
	Confirmed: Clinically consistent with: hantavirus-specific immunoglobulin M (IgM) or rising titers of hantavirus-specific immunoglobulin G (IgG), **or** hantavirus-specific ribonucleic acid (RNA) in clinical specimens, **or** hantavirus antigen by immunohistochemistry (IHC).
Differential diagnosis	ARDS due to burn, trauma, malignancy, post-surgery, sepsis; chronic pulmonary disease; other causes of renal failure; other infectious etiologies such as leptospirosis, Legionnaire's disease, mycoplasma, Q fever, chlamydia, plague, tularemia, COVID-19, coccidioidomycosis, and histoplasmosis.
Treatment	Supportive care including supporting blood pressure. Case fatality rate of HPS is 35%; HFRS ranges from <1-15% depending on causative virus.
Duration	Convalescence weeks to months; may be persisting pulmonary function abnormality; no person-to-person transmission of North American hantaviruses
Exposure	Rodent excretions (urine, feces, saliva), particularly when cleaning buildings
Laboratory testing	Local Health Jurisdiction (LHJ) and Communicable Disease Epidemiology (CDE) arrange testing for individual cases • Washington State Public Health Laboratories should confirm positive serologic results and can forward specimens to CDC for PCR and immunohistochemistry • **Best specimens**: serum (at least 1.5 ml) acute and convalescent (21+ days) and promptly shipped fresh frozen lung tissue or whole blood for PCR; formalin-fixed or paraffin-embedded tissues for immunohistochemistry *Specimen shipping (Section 4):* • Keep serology specimens **cold,** specimens for PCR frozen, ship according to PHL requirements, include two identifiers on specimen and form https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu
Public health actions **URGENT**	Immediately report to CDE any cases with likely exposure in a public or occupational setting (e.g., campground work site) • Interview case or proxy about possible exposures to deer mice and their excretions • Educate the person about measures to avoid exposure • Notify others potentially exposed about symptoms and how to avoid exposure *Infection Control:* standard precautions

Hantavirus

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

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

B. Legal Reporting Requirements

1. Health care providers and Health care facilities: notifiable to **local health jurisdiction** within 24 hours.
2. Laboratories: notifiable to **local health jurisdiction** within 24 hours; submission required – specimen associated with positive result, within 2 business days.
3. Local health jurisdictions: notifiable to Washington State Department of Health (DOH) Communicable Disease Epidemiology (CDE) 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 CDE. Use the hantavirus infection report form (https://www.doh.wa.gov/Portals/1/Documents/5100/210-028-ReportForm-Hantavirus.pdf) and enter the data into the Washington Disease Reporting System (WDRS).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Hantaviruses are a family of RNA viruses spread by rodents; they can cause varied disease syndromes in people worldwide. Hantaviruses in the Americas are called "New World" hantaviruses – these are the cause of hantavirus pulmonary syndrome (HPS). The two major causative agents of HPS are Sin Nombre virus in North America, and Andes virus in South America. The majority of cases of HPS worldwide are reported from South America, primarily Brazil.

"Old World" hantaviruses are those that cause hemorrhagic fever with renal syndrome (HFRS); cases of HFRS are most commonly reported from China, but HFRS occurs worldwide. Causative agents of HFRS include Hantaan virus, Seoul virus, Puumala virus, and Dobrava virus, and Saaremaa virus.

Sin Nombre virus is responsible for all cases identified to-date in Washington. Most cases report exposure in Washington State. In late 2016 and early 2017, a multistate outbreak of Seoul virus infections occurred in the US, associated with Norway rats; no cases were reported in WA.

B. Description of Illness

Hantavirus pulmonary syndrome (HPS) is an acute viral disease with a relatively short (3–5 days) prodrome of fever, fatigue, myalgias (muscle aches), headache, and gastrointestinal complaints such as nausea, vomiting, diarrhea, or abdominal pain 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. Just over a third of all cases in the United States (35%) have died. In survivors, recovery from acute illness is rapid, but full convalescence may require weeks to months. Restoration of normal lung function generally occurs, but pulmonary function abnormalities may persist in some individuals.

Symptoms of hemorrhagic fever with renal syndrome (HFRS) begin with abrupt onset of headaches, back and abdominal pain, fever, nausea, blurred vision, conjunctivitis, or rash. Later symptoms can include hypotension, acute shock, vascular leakage, and acute renal failure. The severity of the disease varies depending on the virus causing infection; Hantaan and Dobrava virus infections are more severe while Seoul, Saaremaa, and Puumala infections are more moderate. Complete recovery can take weeks or months. Case fatality ranges from <1-15% depending on the virus.

C. Hantavirus Pulmonary Syndrome (HPS) in Washington State

Through 2022 there have been 58 reported cases of HPS among Washington residents, 20 (34%) of which were fatal. Between zero and five cases are reported annually. Cases have occurred throughout most counties, though the majority (approximately 70% of cases) report exposure in eastern Washington. It is extremely rare to see multiple cases with a single common exposure. However, during 2012 there was an outbreak associated with visits to Yosemite National Park in California. A total of 10 cases were identified; 9 stayed in the Signature Tent Cabins and the other had hiked nearby.
https://wwwnc.cdc.gov/eid/article/20/3/13-1581_article

D. Reservoirs

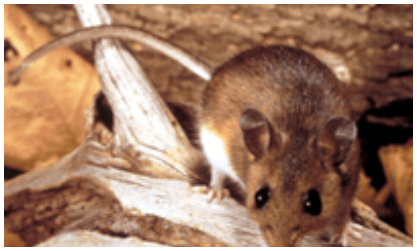

Photo source: CDC website
https://phil.cdc.gov/Details.aspx?pid=8358

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. They prefer an omnivorous diet of seeds, nuts, fruits, and insects in the wild, but they will enter structures, including homes, for shelter or additional food sources, particularly in rural and suburban areas. 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. Deer mice usually carry the virus without showing any signs of being sick.

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.

The Norway rat (*Rattus norvegicus*) is the major reservoir for Seoul virus; these rats are often bred and kept as pets but also exist in wild rat populations around the world. During late 2016, CDC reported an outbreak of Seoul virus associated with pet Norway rats:
https://www.cdc.gov/mmwr/volumes/67/wr/mm6704a5.htm
https://www.cdc.gov/mmwr/volumes/66/wr/mm6640a4.htm

E. Modes of Transmission

Transmission is via inhalation of virus that is excreted in rodent urine, feces or saliva and aerosolized during cleaning of buildings with rodent nests or other rodent contamination, movement of contaminated items, or less commonly routine activities (e.g., sleeping, light cleaning) in a space with a heavy infestation of deer mice. 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 eight weeks.

G. Period of Communicability

Person-to-person spread of hantaviruses has not occurred in this country. However, it has been documented in Argentina during an outbreak due to Andes virus.

H. Treatment

There is no specific antiviral treatment for HPS. If there is a high degree of suspicion for HPS, patients should be immediately transferred to an emergency department or ICU for close monitoring and care. Supportive care including intubation and ventilation with fluids and pharmacologic support of blood pressure are typically required.

HFRS may require dialysis. Intravenous ribavirin has been shown to decrease illness and death associated with HFRS if used very early in the disease.

3. CASE DEFINITION

A. Clinical Case Definition (Non-HPS and HPS)

1. Non-HPS Hantavirus infection is a febrile illness with non-specific viral symptoms including fever, chills, myalgia, headache, and gastrointestinal symptoms. Typical clinical laboratory findings include hemoconcentration, left shift in the white blood cell count, neutrophilic leukocytes, thrombocytopenia, and circulating immunoblasts.
2. Hantavirus Pulmonary Syndrome (HPS) is an acute febrile illness (i.e., temperature greater than 101.0 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

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) in clinical specimens, **OR**
3. Detection of hantavirus antigen by immunohistochemistry (IHC) in lung biopsy or autopsy tissues.

Note: Laboratory testing should be performed or confirmed at a public health reference laboratory. 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 HPS. Patients with these underlying conditions and ARDS need not be tested for hantavirus.

C. Case Definition (2015)

Confirmed: a clinically compatible case of HPS or non-HPS Hantavirus infection that is laboratory confirmed.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Positive commercial lab results should be confirmed at a public health reference lab 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/ELISA). Most patients have IgM antibodies at time of hospitalization. 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 retain antibody for many years. All specimens should be submitted for confirmatory testing at a public health reference lab if acute hantavirus disease is suspected. Because IgG can persist, when only IgG is positive and there is no suspicion for acute disease (case has no acute onset of symptoms consistent with hantavirus infection), confirmatory testing is not necessary, and a report can be ruled out.

Reverse transcriptase-polymerase chain reaction (RT-PCR) can be used to detect hantavirus RNA in fresh frozen lung tissue, whole blood, 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, so virus isolation is not a diagnostic consideration. There is no test for recent exposure to the virus. Decreased platelets (<150,000) or presence of immature cells (myelocytes, metamyelocytes) in the white blood count are suggestive but not diagnostic of hantavirus infection.

Testing mice is not recommended to rule in or out exposure; deer mice populations can be infected with a low prevalence and prevalence can vary over small geographic distances. There is no test to determine if the urine, droppings or nesting material are infectious. All deer mouse infestations should be treated as if they are potentially contaminated and infectious. Persons concerned about exposure to such materials should monitor themselves and seek medical care if they develop symptoms.

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

Serology (IgM and IgG) is available at PHL: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu

Additionally, serology, RT-PCR, and IHC are available through the CDC with approval. All specimens being submitted to CDC *must* be sent through the PHL. Please call Communicable Disease Epidemiology (CDE) for approval and consultation on appropriate specimens prior to submission.

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 through Public Health

1. Patients with suspected hantavirus pulmonary syndrome based on clinical (e.g., fever, hypotension, hypoxia, bilateral interstitial pulmonary infiltrates, acute respiratory distress syndrome, thrombocytopenia, hemoconcentration without an identifiable cause) and exposure history. Testing should routinely be performed at commercial laboratories first, unless HPS is strongly suspected based on clinical and exposure history.
2. Evidence of recent hantavirus infection based on a positive test from a commercial laboratory (ie. IgM or PCR positive).
3. Death due to unexplained respiratory illness with autopsy demonstrating non-cardiogenic pulmonary edema without identifiable cause.

Any person with a consistent exposure history (e.g. cleaning a rodent infested building, known rodent contact), and illness clinically compatible with non-HPS hantavirus should have a specimen sent commercially for hantavirus serologic testing. Positive specimens should be forwarded to PHL for confirmation when acute disease is suspected.

D. Specimen Collection

Serum

Submit at least 0.6 mL (1 mL preferred) of serum. 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. Separated serum specimens should be refrigerated and transported cold with regular ice

packs. Avoid repeated freeze-thaw cycles, but if specimen is already frozen, then ship on dry ice. Submit specimens according to PHL requirements: https://doh.wa.gov/public-health-provider-resources/public-health-laboratories/lab-test-menu

For information on specimens other than serum (tissue, bronchoalveolar lavage, blood clot, etc.), consult CDE.

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

A. Evaluate the Diagnosis

Obtain and review laboratory reports and medical records. If the case tests positive for hantavirus at a commercial laboratory and acute disease is suspected, facilitate transport of the specimen (i.e., serum or tissue) to Public Health Laboratories for further testing.

B. Manage the Case

Hospitalized patients should be cared for using standard precautions. Person-to-person spread of hantaviruses has not occurred in the U.S. Educate the case about avoiding future exposures (see Section 6B).

C. Identify Potential Sources of Infection

Obtain a history about possible exposure to rodents or their urine, droppings, or nesting material. Exposures generally occur when urine, droppings, or nesting material are stirred up, aerosolized, and inhaled. Common exposures include cleaning garages, attics, or cabins where rodent infestations are present. A rodent bite can also transmit the virus; however, inhaling the virus is a much more common transmission route to humans. If pet rats are a possible exposure source, contact CDE about follow-up and options for testing.

D. Identify Other Potentially Exposed Persons

Identify other persons who may have been in or around the presumed case's exposure location, e.g., other household residents, campground staff or residents, or facility employees. Posting a sign in public areas (e.g., campgrounds) may be appropriate.

E. Management of Others Exposed

Other persons who may have been exposed to the same source as the case should be educated regarding avoiding future exposures and the signs of hantavirus pulmonary syndrome. They should be advised to seek medical attention if symptoms develop within 8 weeks of the last possible exposure. However, it is rare to have multiple cases sharing a common exposure.

F. 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 and clean-up. However, since deer mice are found throughout Washington and are the known reservoir for the Sin Nombre virus, mouse testing is not routinely done. If pet rats are a possible exposure source, Seoul virus testing is available; contact CDE for further information.

6. ROUTINE PREVENTION

A. Immunization Recommendations: None

B. Prevention Recommendations

1. **Keep rodents out of your home, vehicles, and workplace:**

- **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. Fill small holes with steel wool secured with caulk or spray foam. Use lath screen, metal, cement, hardware cloth, or metal sheeting to fix large holes.
- **Trap indoor rats and mice** with snap traps.
- **Remove rodent food sources.** Keep food (including pet food) in rodent proof containers, clean up spilled food, put pet food away after use, and keep garbage in thick plastic or metal containers with tight lids.
- **Maintain outside areas.** Keep brush, grass, weeds, and shrubbery within 100 feet of your home well-trimmed, keep grains and animal feeds in tight sealing containers, move woodpiles 100 feet from your home and raise wood at least one foot off the ground.

2. **Practice healthy pet guidelines:** https://www.cdc.gov/healthy-pets/about/small-mammals.html
3. **Clean up rodent infested areas:** https://doh.wa.gov/community-and-environment/pests/rodents
    - 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 cool water. Use only freshly mixed solution.
    - Once everything is soaked for 5 minutes, remove all of the nest material, mice or droppings with damp paper towel; throw all debris and paper towels in the garbage.
    - 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. Throw out rodent in a secure garbage with a lid.
    - 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.

    The CDC has additional details, including guidance on cleaning vehicles: https://www.cdc.gov/hantavirus/prevention/?CDC_AAref_Val=https://www.cdc.gov/hantavirus/hps/prevention.html or https://www.cdc.gov/healthy-pets/rodent-control/clean-up.html or a WA DOH poster is available here: https://doh.wa.gov/sites/default/files/2024-02/420569-SafelyCleaningAfterRodents-Hantavirus-Poster-English.pdf

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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.

December 2012: Incidence and mortality data were updated (Section 2) The Routine Case Investigation and Controlling Further Spread sections were combined (Section 5).

January 2015: The case definition was updated, and now includes non-HPS Hantavirus infection.

March 2017: Updated to include information on Seoul virus and HFRS, front page added.

December 2019: General updates, criteria for testing HPS specimens at CDC updated to reflect current practice.

December 2022: For 2023 WAC revision combined provider and facility reporting requirement (Section 1B1-2), updated laboratory submission (Section 1B3)

April 2023: General updates, added availability of serology at PHL to Section 4B

December 2023: For 2024 WAC revision updated laboratory submission.

June 2024: CDC links updated.