Hantavirus Pulmonary Syndrome (HPS) 

PROTOCOL CHECKLIST

- ☐ Enter available information into Merlin upon receipt of initial report
- ☐ Review background on disease, case definition, and laboratory testing
- ☐ Contact provider
- ☐ Interview patient
  - ☐ Review disease facts
    - ☐ Modes of transmission
    - ☐ Incubation period
    - ☐ Symptoms/types of infection
  - ☐ Ask about exposure to risk factors
    - ☐ Contact with rodents
    - ☐ Recent travel to areas where there may have been exposure to rodents/droppings
  - ☐ Determine if patient was hospitalized for illness/symptoms consistent with HPS
    - ☐ Document pertinent clinical symptoms and laboratory findings
  - ☐ Identify possibly exposed contacts/family members who may be at risk (rare)
  - ☐ Provide education on prevention
    - ☐ Keep rodents out of home and workplace
    - ☐ Seal up cracks and gaps in buildings that may provide rodent entry
    - ☐ Trap indoor rats and mice
    - ☐ Remove rodent food sources
    - ☐ Clean up rodent infested areas
  - ☐ Address patient family's questions or concerns
- ☐ Follow-up on special situations, including exposed contacts or cases in sensitive situations
- ☐ Enter additional data obtained from interview into Merlin

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 provide targeted prevention and control messages.

B. Legal reporting requirements

Laboratories and practitioners are required to report Hantavirus Pulmonary Syndrome (HPS) immediately (24/7) by telephone to their county health department (CHD). Criteria for reporting include clinically compatible illness, health record contains a diagnosis of HPS, or death certificate lists HPS as cause of death or significant condition.

C. County health department investigation responsibilities

1. Facilitate the transport of specimens to Florida Department of Health (FDOH) Bureau of Public Health Laboratories (BPHL) for confirmatory testing.

2. Report all suspected or confirmed cases to FDOH Bureau of Epidemiology at (850) 245-4401. Use the Centers for Disease Control and Prevention (CDC) hantavirus pulmonary syndrome report form and enter the data into Merlin (reporting code = 07869).

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic agent

Hantaviruses have a worldwide distribution and are in the family *Bunyaviridae*. Multiple New World hantaviruses causing pulmonary syndrome have been identified in the Americas. Sin Nombre virus is the most important hantavirus in North America. Other hantaviruses responsible for sporadic infections of HPS in the United States include Bayou and Black Creek Canal viruses in the southeastern U.S. and New York, and Monongahela viruses in the eastern U.S. Numerous hantavirus variants are known to cause HPS in South America, the most predominant being the Andes virus. Old World hantaviruses are most common in Asia and Europe, although they have been identified worldwide including in the United States. Old World hantaviruses are associated with a clinical presentation of hemorrhagic fever with renal syndrome (HFRS). Only HPS cases are considered reportable, although other hantavirus infections may be of public health interest.

B. Description of illness

Hantavirus Pulmonary Syndrome is an acute viral infection characterized by a relatively short (three to five days) prodrome of fever, myalgias (muscle aches), chills, headache,

dizziness, and gastrointestinal complaints. Cough and shortness of breath may develop approximately seven days post disease onset and is generally followed by the abrupt onset of progressive pulmonary edema, hypoxia and hypotension. The illness progresses rapidly to respiratory failure with bilateral pulmonary infiltrates and pleural effusion, usually requiring mechanical ventilation. Clinical signs suggestive of a diagnosis other than HPS include rashes, hemorrhage of conjunctiva or other areas, throat or conjunctival erythema or petechiae, peripheral or periorbital edema and multi-organ failure. Circulating immunoblasts and atypical lymphocytes, neutrophilia with left-shift and circulating myelocytes, and thrombocytopenia are almost always present; a rapid drop in platelets marks onset of the pulmonary edema phase. The combination of atypical lymphocytes, a significant left shift (bandemia) and thrombocytopenia in conjunction with pulmonary edema is strongly suggestive of a hantavirus infection. About one third of all diagnosed cases in the U.S. 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. Some infected individuals may demonstrate febrile illness with no (or relatively mild) hypotension and pulmonary disease. Children less than 15 years of age tend to have less severe illness than adults. The majority of U.S. hantavirus cases involve residents of rural areas.

C. Reservoirs

Rodents usually carry the virus without showing any signs of being sick. The deer mouse *(Peromyscus maniculatus)* is the major reservoir of Sin Nombre virus in the western U.S. The mouse is found throughout the U.S. but is uncommon in the southeast. Potential reservoirs in Florida include the cotton rat (*Sigmodon hispidus*), which prefers overgrown areas with shrubs and tall grasses, and the rice rat (*Oryzomys palustris*), which is semi-aquatic and prefers living in marshy areas. The cotton rat has been associated with Black Creek Canal virus and rice rats residing in the U.S. have been associated with Bayou virus. Neither the cotton rat nor the rice rat commonly reside in human residential structures. A serosurvey of 1,500 small mammals in Miami-Dade County found approximately 11% of cotton rats seropositive for hantavirus. Rodent serosurveys in western states have shown that approximately 14% of deer mice have antibodies against Sin Nombre virus, although the percentage of infected mice may fluctuate widely from year to year. Other rodent species are associated with additional hantaviruses that have yet to be implicated in human disease. Therefore, it is best to consider all wild mice and rats infected when considering potential exposures.

In 1993, a single case of HPS was identified in Florida in a Miami-Dade County resident. Black Creek Canal virus was isolated from cotton rats in the area. Hantaviruses have a worldwide distribution and have been identified in international travelers to Florida.

D. Modes of transmission

Exposure occurs by inhalation of virus that is excreted in mouse urine, feces or saliva and aerosolized during cleaning or disturbing rodent nests or other areas with rodent contamination. Exposures are most common in confined areas such as rodent-infested cabins, homes, barns, vehicles, outbuildings, crawl spaces or less commonly when handling wild rodents without protective equipment. Nationally, rare transmission has been documented from a deer mouse bite. Ingestion or direct contact with mucous membranes such as the mouth or nose is believed to be other potential routes of exposure. Person-to-

person transmission has not been reported except for occasional infections involving the South American Andes virus.

E. Incubation period

Approximately one to six weeks (7 to 42 days) with most illnesses occurring two to four weeks following exposure.

F. Period of communicability

Person-to-person spread of hantaviruses in the U.S. has not occurred. However, person-to-person transmission of the related Andes virus in South America has occasionally been reported in close contacts of infected persons.

G. Treatment

There is no antiviral treatment for HPS. Hospitalization and supportive care including intubation, ventilation and fluid and pharmacologic support to manage hypoxia and hypotension are indicated.

H. Hantavirus Pulmonary Syndrome in Florida

Through 2012, there has only been one confirmed case of HPS reported in Florida.*

*Imported HPS cases from South America have been identified in Florida and a case of HFRS involving a German visitor was reported in 2012.

3. CASE DEFINITION

A. Clinical description

Hantavirus pulmonary syndrome, commonly referred to as hantavirus disease, is a febrile illness characterized by bilateral interstitial pulmonary infiltrates and respiratory compromise usually requiring supplemental oxygen and clinically resembling acute respiratory disease syndrome (ARDS). The typical prodrome consists of fever, chills, myalgia, headache and gastrointestinal symptoms. Typical clinical laboratory findings include hemoconcentration, left shift in the white blood cell count, neutrophilic leukocytosis, thrombocytopenia and circulating immunoblasts.

B. Clinical case definition

- An illness characterized by one or more of the following clinical features: A febrile illness (temperature >101.0°F [>38.3°C]) in a previously healthy person with bilateral diffuse interstitial edema or clinical diagnosis of ARDS, or radiographic evidence of noncardiogenic pulmonary edema;
- An unexplained respiratory illness resulting in death.

C. Laboratory criteria for diagnosis

- Detection of hantavirus-specific IgM or rising titers of hantavirus-specific IgG,
  Or
- Detection of hantavirus-specific RNA sequence by polymerase chain reaction (PCR) in clinical specimens,
  Or
- Detection of hantavirus antigen by immunohistochemistry (IHC) in lung biopsy or autopsy tissues.

D. Case classification

Confirmed: A clinically compatible case that is laboratory confirmed.

E. Comment

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. Risk factors are contact with rodents in the six weeks prior to onset.

Any available specimens must be sent to the BPHL for confirmatory testing. Requests for clinical specimens to be sent to the CDC for diagnostic testing must be cleared through the Bureau of Epidemiology (DCBE) and assigned a tracking number; specimens must be routed through the BPHL. This condition has been identified as a potential bioterrorism agent by the CDC.

Reporting: Immediate; criteria for reporting include clinically compatible illness, health record contains a diagnosis of HPS, or death certificate lists hantavirus pulmonary syndrome as cause of death or significant condition.

4. LABORATORY TESTING

A. Laboratory diagnosis

Serology: The most commonly used commercial laboratory testing involves a hantavirus screening enzyme immunoassay (EIA) followed by reflex Sin Nombre EIA testing for samples that are IgM positive for hantavirus. False positive hantavirus IgM EIA results are common, so Sin Nombre specific EIA testing should always be performed for samples testing positive for hantavirus IgM. Sin Nombre EIA can also be used to detect other hantaviruses associated with HPS and HRFS. Most patients have IgM antibodies at the time of hospitalization. A test for IgG is used in conjunction with the IgM-capture test. Acute- and convalescent-phase sera should reflect seroconversion or a fourfold 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. Therefore, negative IgM and positive IgG hantavirus EIA results are suggestive of past exposure and not acute illness.

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, 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.

B. Services available at the FDOH Bureau of Public Health Laboratories

1. Any available specimens must be sent to the BPHL for confirmatory testing with EIA for Sin Nombre virus-specific IgM antibody in serum.

2. RT-PCR and IHC are available through the CDC. Requests for clinical specimens to be sent to the CDC for diagnostic testing must be cleared through the DCBE and assigned a tracking number; specimens must be routed through the BPHL. The causative viruses have been identified as potential bioterrorism agents by the CDC (Category C).

C. Criteria for testing Hantavirus Pulmonary Syndrome specimens at the Bureau of Public Health Laboratories

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. Risk factors are contact with rodents or an environment thought or known to be contaminated with rodent urine, feces or saliva in the six weeks prior to onset.

D. Specimen collection

Serum:

1. Submit at least 1 cc (2.5 cc preferred) of serum (separated serum, not whole blood) for EIA at BPHL. Serum can be drawn upon hospital admission. If possible, also obtain as late of 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 on ice packs or frozen in a plastic tube and sent on dry ice. Avoid repeated freeze-thaw cycles. Specimens should be submitted by the clinical laboratory with a completed BPHL Clinical Lab Submission Form:

DH1847-Clinical Lab Submission Form.pdf

3. Packaging and shipping


Packaging_Flowchart_0422051.pdf


Packaging_Flowchart_notes_0422051.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 DCBE and BPHL first and reference the following website: http://www.cdc.gov/hantavirus/health-care-workers/specimen-submission/index.html for further information.

5. CASE INVESTIGATION

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

A. Evaluate the diagnosis

If the patient tests positive for Sin Nombre virus at a laboratory other than a reference laboratory, facilitate transport of the specimen (i.e., serum or tissue) to BPHL 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 in the six weeks prior to symptom onset. Exposures generally occur when urine, droppings, or nesting material are stirred up, aerosolized, and inhaled. A bite from the rodent 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 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 to seek medical attention if they develop such symptoms.

E. Environmental evaluation

In the event of a locally acquired case, it may be appropriate to examine the environment where the case was exposed to make suggestions about rodent removal. The DCBE can provide further guidance if needed. See also: http://www.cdc.gov/hantavirus/hps/prevention.html

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 uncommon to have two cases sharing an exposure. Person-to-person spread of hantaviruses has not occurred in the United States; however, if the case had exposure in Argentina, Brazil or Chile, (potential Andes virus exposure) close contacts should be identified.

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 doorsills, 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 and nesting sites. Keep food (including pet food) in rodent proof containers. Clean up debris close to homes and keep grass and shrubs close to the home trimmed and well maintained.

5. Clean up rodent infested areas:
   - Cross-ventilate the infested area for at least 30 minutes prior to cleaning by opening doors and window. Leave the area while cross-ventilating.
   - Wear rubber, latex, vinyl or nitrile (synthetic latex) gloves.
   - Do not stir up dust by vacuuming, sweeping, or any other dust-generating means.
   - Thoroughly wet contaminated areas including trapped dead rodents, droppings, urine and nests with a bleach solution or household disinfectant. **Hypochlorite (bleach) solution:** Mix 1.5 cups of household bleach in 1 gallon of water. Use only freshly mixed solution, do not mix with other chemicals, use in a well-ventilated area and

wear eye protection to prevent splashes to the eye. Potentially contaminated carpets and upholstery can be steam cleaned.

- Once everything is soaked for 10 minutes, remove all of the nest material, rodents, urine or droppings with damp towel and then mop or sponge the area with bleach solution or household disinfectant.
- Spray material with disinfectant and double-bag it, along with all cleaning materials and dispose 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 and hands are not visibly soiled).

For further information, please visit the CDC HPS prevention website available at http://www.cdc.gov/hantavirus/hps/prevention.html

REFERENCE

A. CDC, Preventing Hantavirus Pulmonary Syndrome webpage: http://www.cdc.gov/hantavirus/hps/prevention.html

B. FL Department of Health, Bureau of Public Health Laboratories: http://www.doh.state.fl.us/lab/index.html