NATIONAL INSTITUTE FOR COMMUNICABLE DISEASES
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Centre for Emerging Zoonotic and Parasitic Diseases and
Outbreak Response Unit, Division of Public Health Surveillance and Response

Hantavirus Pulmonary Syndrome (HPS) Frequently Asked Questions

1. What is HPS?

Hantavirus Pulmonary Syndrome (HPS; also called hantavirus cardiopulmonary syndrome, HCPS) is a severe and sometimes fatal respiratory disease caused by hantaviruses (family *Hantaviridae*, genus *Orthohantavirus*). Hantaviruses cause two main clinical presentations: 1) Hemorrhagic fever renal syndrome (HFRS) and 2) HPS, which differ by the causative virus species, geographic distribution, and clinical features. Several hantavirus species cause HPS, including Sin Nombre virus, Rio Mamoré virus, Andes virus, Laguna Negra virus, Juquitiba virus, Araraquara virus, Choclo virus, and New York virus. These HPS-causing viruses are found in the Americas and are associated with cricetid rodent hosts (i.e., specific species of rats and mice belonging to the *Cricetidae* family of rodents) in endemic areas of South and North America. With the deer mouse as its primary host, the Sin Nombre virus is the most significant hantavirus in Southwest North America and a major cause of serious medical conditions in humans. The Rio Mamoré virus is the most well-known strain in northern South America, and its primary host is the pygmy rice rat. However, the entire region is contaminated with several localised variants rather than a single dominating virus. Long-tailed pygmy rice rats are the primary carriers of the Andes virus, which is the primary cause of hantavirus pulmonary disease in southern South America.

2. Who can get HPS and how are hantaviruses that cause HPS transmitted?

Anyone exposed to infected rodents or their secretions/excreta in endemic areas of the Americas can develop HPS. Individuals at higher risk include farmers, forestry workers, construction workers, and people who clean or occupy rodent-infested buildings. In endemic countries, transmission mainly occurs through inhalation of aerosolised virus particles from rodent urine,

droppings, or nesting materials. Less commonly, infection may occur through rodent bites or direct contact with rodent-contaminated surfaces. Human-to-human transmission of hantaviruses that cause HPS is very uncommon. There is no evidence of person-to-person transmission for the majority of HPS-causing viruses, and rodent exposure — rather than human contact — causes infection. Andes virus (reported from parts of South America) is the only hantavirus with well-documented human-to-human transmission. Transmission of the Andes virus has been inefficient and required close contact in household and health facility settings, unlike highly transmissible respiratory viruses such as SARS-CoV-2 and influenza viruses. Evidence from Andes virus outbreaks (particularly in Argentina and Chile) indicates transmission can occur through close, prolonged contact with an infected person, especially involving household contacts, sexual partners, and caregivers. Likely routes of exposure include respiratory secretions (e.g., droplets from coughing), direct contact with saliva, and possibly other body fluids during the early symptomatic phase.

3. Where does HPS occur?

HPS cases have been reported from parts of North and South America. Argentina, Chile, Brazil, Bolivia and Paraguay are the core endemic countries, especially southern regions (e.g., Andes virus zone and have the strongest evidence of ongoing human diseases of HPS. Other countries in South America have reported HPS cases or infected rodents, but transmission data are less consistent. In parts of Europe and Asia, different hantaviruses (i.e. Hantaan virus, Puumula virus, and Dobrava-Belgrade virus) are associated with HFRS linked to specific rodent and some mouse/rat hosts. China has one of the highest burdens of HFRS, mainly due to the striped field mouse (Hantaan virus) and the Norway rat (Seoul virus). Unlike HPS, which mostly affects the lungs and causes rapid respiratory failure, HFRS primarily affects the kidneys, resulting in fever, vascular leakage, thrombocytopenia, and variable degrees of acute renal injury. Seoul virus, another hantavirus, is more widespread in Asia, parts of Europe, North America and South America. In Africa, hantavirus infections are rarely reported, but rodent reservoirs exist, and surveillance is limited, resulting in human diseases likely being under-recognised. The main confirmed African hantaviruses are Sangassou, Tanganya, Azagny, and Mouyassué, are caused mainly by the African wood mice species and other possible reservoirs, such as Mastomys and Cricetomys species.

4. What are the signs and symptoms of HPS?

Early symptoms include fever, fatigue, muscle aches, headache, dizziness, chills, nausea, vomiting, diarrhea, and abdominal pain in the first 3 to 5 days. As the disease progresses, patients may develop coughing and shortness of breath due to fluid accumulation in the lungs (pulmonary oedema) and a drop in blood pressure resulting in shock. The cardio-pulmonary phase can progress very quickly (within hours), and the case fatality rate (CFR) for HPS is high, between 30 – 50 %. The CFR varies by virus, region, and access to intensive care, and patient factors (i.e., the influence of co-morbidities). Common differential diagnoses (i.e., other diseases presenting with similar signs and symptoms) of suspected cases of HPS include (but are not limited to) influenza (i.e., flu), COVID-19, respiratory syncytial virus infection, Legionnaire's disease, mycoplasma pneumonia, or severe community-acquired pneumonia.

5. How is HPS diagnosed and notified?

HPS is diagnosed based on clinical presentation, exposure history, and laboratory testing. Diagnostic tests include serology (IgM/IgG antibodies), PCR for viral RNA, and immunohistochemistry in specialised laboratories. In South Africa, laboratory testing for suspected cases of HPS is conducted at the National Institute for Communicable Diseases.

The Notifiable Medical Conditions (NMC) Surveillance System in South Africa covers hantavirus infection. Classification: Hantavirus disease, which includes HPS and HFRS, is classified as a Category 1 medical condition that requires notification. Therefore, Category 1 conditions necessitate: Prompt notification (within 24 hours or sooner). Reporting through: Clinicians (suspected or verified cases) or laboratories (positive test findings) and prompt investigation and public health response. Hantavirus is included as an NMC because it is zoonotic (rodent-borne), rare but highly impactful, and capable of causing severe, swiftly deadly disease (HPS/HFRS). Exposure clusters can be avoided with early detection.

In South Africa, human hantavirus cases are extremely uncommon. There are rodent reservoirs, such as multimammate mice. Diagnostic confirmation is crucial because the majority of cases of febrile illness are more frequently caused by other infections.

6. How is HPS treated?

There is no specific antiviral treatment for HPS. Management is supportive and may include hospitalisation, oxygen therapy, mechanical ventilation, and intensive care. Early recognition and treatment may improve outcomes.

7. How can HPS be prevented?

In endemic countries, prevention focuses on reducing exposure to rodents. This includes sealing homes to prevent rodent entry, proper food storage, safe cleaning of rodent-infested areas (using disinfectants and avoiding sweeping), and using protective equipment when necessary. Since most hantaviruses that cause HPS are not readily transmissible from person-to-person, no other precautions are recommended, and for patients with HPS, isolation precautions may not be required. In the case of the Andes virus, patients diagnosed with HPS should be isolated with droplet precautions and careful handling of respiratory secretions. For HPS associated with the Andes virus, contacts of cases should be identified and monitored for 42 days (i.e., the maximum incubation period of the virus). There is no WHO-approved or globally licensed vaccine for HPS and HFRS. Inactivated vaccines have been used regionally only and in limited settings in China and Korea against Hantaan and Seoul viruses (HFRS)

8. Where can I find more information?

More information can be obtained from national public health institutes and the World Health Organization (WHO).

Guidelines and other useful resources are available on the NICD website.

9. Queries?

Laboratory queries:

Dr Jacqueline Weyer 011 386 6376/jacquelinew@nicd.ac.za, and/or

Dr Naazneen Moolla 0113866338/naazneenm@nicd.ac.za

Please copy all requests to cezd@nicd.ac.za

Clinical queries (healthcare workers only):

NICD Doctor on Call 0800 212 552

Outbreak-related queries:

Outbreak Response Unit outbreak@nicd.ac.za

Media/Press queries:

NICD Communications Manager media@nicd.ac.za