Hantavirus Infection: Review of Clinical Management

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ABSTRACT

Hantavirus infection is a rodent-borne zoonotic disease that can present as Hemorrhagic Fever with Renal Syndrome (HFRS) or Hantavirus Cardiopulmonary Syndrome (HCPS). Both diseases are associated with substantial morbidity and mortality. The rise of new Hantavirus species and recurrent outbreaks worldwide has renewed interest in the epidemiology, pathogenesis, diagnosis, and management of this viral infection.

A narrative literature review was conducted using published articles, review papers, epidemiological reports, and clinical studies on Hantavirus up to 2026. Relevant evidence regarding epidemiology, pathogenesis, clinical manifestations, diagnostic approaches, treatment, complications, and prevention was analyzed and synthesized.

Hantaviruses primarily infect endothelial cells, leading to increased vascular permeability, thrombocytopenia, and capillary leakage through immune-mediated mechanisms. HFRS affects the kidneys, and HCPS is characterized by severe cardiopulmonary symptoms, although overlap between the two syndromes has increasingly been observed. Diagnosis is based on clinical suspicion supported by epidemiological exposure history, serological testing, and virological confirmation from reverse transcription polymerase chain reaction (RT-PCR). Current management remains largely supportive, including hemodynamic stabilization, respiratory support, and renal replacement therapy when indicated. Ribavirin may provide benefit in selected HFRS cases when given early, but evidence remains inconclusive, especially for HCPS. Favipiravir has demonstrated promising antiviral activity in vitro and in animal studies, yet clinical data in humans are still lacking. Preventive measures focus primarily on minimizing exposure to infected rodents and contaminated environments, while vaccine development remains ongoing. Hantavirus infection continues to represent an important global public health concern due to its potential for severe disease and high mortality. Improved understanding of disease pathogenesis, advances in diagnostic methods, and ongoing research into antiviral therapies and vaccines are essential to improve patient outcomes and strengthen future prevention strategies.

Keywords: *Hantavirus, hemorrhagic fever with renal syndrome, hantavirus cardiopulmonary syndrome.*

INTRODUCTION

Significant progress has been made in understanding Hantavirus infection in recent years, yet the magnitude of its outbreaks has not been a main focus until the recent emergence of an ongoing multi-country Andes Hantavirus outbreak linked to the Atlantic Ocean cruise ship MV Hondius. The outbreak was first reported to the World Health Organization (WHO) on May 2, 2026. Person-to-person transmission of the virus was considered unlikely, but the spread of ANDV in an HCPS outbreak in Argentina in 1996 changed this view.[1,2]

Multiple newly identified Hantavirus species with uncertain pathogenic potential have recently been detected in insectivore hosts, expanding the known geographical distribution of Hantaviruses. Recently, several novel species were identified in Africa. In humans, Hantavirus infection may lead to two different major clinical syndromes: Hemorrhagic Fever with Renal Syndrome (HFRS), primarily caused by Old World Hantaviruses, and Hantavirus Cardiopulmonary Syndrome (HCPS), associated with New World Hantaviruses.[2,3]

In 1978, about 25 years after HFRS was first recognized, Hantaan virus (HTNV) was identified as its causative agent, along with its rodent host, the striped field mouse (Apodemus agrarius), making it the first of the Old-World Hantaviruses to be recognized. As a result of this discovery, other Hantaviruses associated with HFRS were later identified in Asia, Europe, and the United States. HTNV and related viruses were later detected in Apodemus agrarius and Apodemus peninsulae in Russia, China, and South Korea, while Dobrava virus (DOBV) and related strains were found in Apodemus flavicollis, Apodemus agrarius, and Apodemus ponticus in Europe.[3]

During the 1980s, urban HFRS cases in Asia were linked to Seoul virus (SEOV), which is carried by rats. Around the same period, nephropathia epidemica (NE), a milder form of HFRS, was found to be caused by Puumala virus (PUUV) harbored by the bank vole, Myodes glareolus. These discoveries revealed that HFRS is a major global disease.[3,4]

The causative agent of HCPS, Sin Nombre virus (SNV), was identified only weeks after the outbreak of an acute pulmonary distress disease in America due to advances in molecular biology techniques. Initial suspicion of Hantavirus etiology was based on weak serologic cross-reactivity with Old-World Hantavirus antigens. More strains are then recognized, from the common deer mouse as host, as part of the New-World Hantaviruses.[3]

EPIDEMIOLOGY

Pathogenic Hantaviruses are primarily carried by specific rodent hosts and can cause severe human disease with mortality rates reaching approximately 12% in HFRS and up to 40% in HCPS. Humans are most commonly infected by breathing in aerosolized materials contaminated with the urine, feces, or saliva of infected rodents. More than 28 pathogenic Hantavirus species have been recognized worldwide, causing diseases that range from acute renal dysfunction to severe pulmonary edema and hemorrhagic symptoms. While only about 1,000 cases of HCPS have been documented worldwide, the annual incidence of HFRS is estimated to range from 150,000 to 200,000 cases, with many infections likely remaining underdiagnosed and underreported.[2,5]

Hantaviruses do not naturally infect humans as part of their normal host range, but person-to-person transmission remains a possibility that needs to be further researched. Transmission of Hantavirus infection is strongly influenced by the degree of human exposure to infected rodent populations. Individuals whose occupations or daily activities involve frequent interaction with rodents, including forestry professionals, farmers, military members, mammalogists, and animal trappers, are at the greatest risk of infection. Exposure commonly occurs during activities such as harvesting crops or handling hay, chopping wood in dusty storage areas, and cleaning enclosed environments, including barns, sheds, and basements.[6]

The epidemiological patterns of Hantavirus disease closely correspond to the geographic distribution of rodents. HFRS is predominantly reported throughout Europe and Asia, whereas HCPS has been identified exclusively in the

Americas. China is the most endemic region, accounting for approximately 70-90% of global HFRS cases. Nevertheless, the true burden of infection is likely underestimated because asymptomatic cases and mild non-specific illnesses probably occur more frequently than clinically recognized disease.[2–4]

According to the most recent epidemiological data in Asia, severe cases of HFRS are caused by the HTNV and the Amur/Soochong virus. The mortality rate of those infections reaches 15%. Infections with the SEOV result in moderate illness and a case fatality rate of 1% to 2%. Among the 40.000 - 60.000 reported cases in Asia, 99% are from China.[7,8] In Indonesia, the most recent data show there were 256 suspected cases of Hantavirus with 23 confirmed cases of HFRS from 2024 - 2026, resulting in 3 deaths, making the case fatality rate about 13%. The viral strain associated with HFRS in Indonesia is SEOV.[9]

Europe reports more than 9,000 HFRS cases annually, most of which are caused by PUUV. Distributed across central and northern Europe, Russia, and the Balkans within the habitat of Myodes glareolus, PUUV generally causes a mild form of HFRS known as NE. The majority of cases occur in Finland, Sweden, and European Russia.[10–12] More severe HFRS cases in Europe are mainly associated with DOBV, particularly in the Balkan region. In contrast, SAAV (DOBV-Aa), carried by Apodemus agrarius, is linked to milder disease and has not been associated with fatal cases. Tula virus has been linked to human infections in parts of Europe, although its pathogenic role remains uncertain.[3,10,11]

ETIOPATHOGENESIS AND PATHOPHYSIOLOGY

Hantaviruses are enveloped RNA viruses. It has a spherical shape, with a diameter ranging from 80 to 120 nanometers. They are part of the Bunyaviridae family. Its genome has three negative-sense, single-stranded RNAs. Three genomic segments, which are small (S), medium (M), and large (L), are responsible for encoding the nucleoprotein (N), the envelope glycoproteins Gn and Gc, and the viral RNA-dependent RNA polymerase known as the L protein.[2]

HFRS typically presents with renal impairment and hemorrhagic manifestations, whereas HCPS is characterized by pulmonary and cardiovascular involvement.[2]

PATHOGENESIS

Hantavirus infection primarily targets endothelial cells and macrophages in the lungs and kidneys. Following inhalation, viral surface glycoproteins (Gn and Gc) bind to β-integrin receptors on endothelial and dendritic cells, facilitating virus spread through the lymphatic system. Infected rodents typically remain asymptomatic while continuously shedding the virus throughout their lives, complicating the understanding of Hantavirus pathogenesis in humans. Viral replication occurs relatively slowly, with viremia usually developing 5-10 days after infection, suggesting a persistent infection rather than an acute lytic progression observed in other viral hemorrhagic fevers.[2,13–15]

The main pathological features of HFRS and HCPS include increased vascular permeability, thrombocytopenia, endothelial dysfunction, and capillary leakage. Although Hantaviruses replicate within vascular endothelial cells, tissue injury is thought to result from immune-mediated mechanisms rather than direct viral cytotoxicity. Studies of infected renal tissue have demonstrated viral antigens accompanied by inflammatory cell infiltration and tubular damage, supporting the role of both viral replication and host immune responses in tissue injury.[2,13,14]

Unlike several other hemorrhagic fever viruses that suppress the maturation of dendritic cells, Hantaviruses stimulate dendritic cell activation and trigger a strong T-cell response, particularly involving activated CD8+ T cells. It also causes delayed type I interferon responses and excessive release of pro-inflammatory cytokines, including interleukin-6, tumor necrosis factor-α, and interferon-γ. In addition, host genetic factors, particularly certain HLA haplotypes, have been associated with increased susceptibility and more severe clinical outcomes.[2,13,14]

Excessive production of pro-inflammatory cytokines, combined with insufficient regulatory immune responses, contributes to endothelial injury and disease severity.

Hantavirus pathogenesis is therefore considered a multifactorial process involving immune dysregulation, platelet dysfunction, and impairment of endothelial barrier integrity. In addition, host genetic factors, particularly certain HLA haplotypes, have been associated with increased susceptibility and more severe clinical outcomes.[2,13,14]

PATHOPHYSIOLOGY

Hemorrhagic Fever with Renal Syndrome (HFRS)

The clinical manifestations of HFRS span a broad spectrum of severity, ranging from asymptomatic or mild infection to moderate to severe disease, depending largely on the infecting Hantavirus species. Infections caused by HTNV, Amur/Soochong virus, and DOVB are generally associated with mortality rates of 5 -15%. PUUV and SAAV commonly cause milder disease with mortality rates below 1%, although severe cases may still occur. Subclinical seroconversion is also commonly observed.[4,15,16]

Following an incubation period of about 2 to 4 weeks, HFRS classically progresses through five clinical stages: febrile, hypotensive, oliguric, polyuric, and convalescent phases, as seen in **Figure 1** below. The differences among these stages are most easily observed in severe diseases caused by HTNV or DOBV infections. The febrile phase usually begins with high fever, chills, headache, abdominal or back pain, nausea, vomiting, and occasionally visual disturbances. Hemorrhagic manifestations, including petechiae and conjunctival hemorrhage, may appear toward the end of this stage. During the hypotensive phase, some patients develop circulatory collapse or shock, accompanied by thrombocytopenia, leukocytosis, and varying degrees of bleeding manifestations ranging from mild petechiae to severe internal hemorrhage. Renal involvement is most prominent during the oliguric phase, characterized by oliguria or anuria, proteinuria, hematuria, azotemia, and elevated serum creatinine levels. Severe cases may require hemodialysis. This oliguric phase usually lasts 3 - 7 days. Recovery of renal function marks the polyuric phase, during which urinary output increases markedly, followed by the convalescent period, which could last several months before complete clinical recovery. The convalescent stage is characterized by improvement in clinical and laboratory markers for up to 6 months.[2,4,7,14]

Milder forms of HFRS, particularly NE caused by PUUV, often present with less distinct clinical phases and reduced severity of hemorrhagic and renal manifestations. Shock and severe bleeding are uncommon, while hypotension and transient renal dysfunction occur more frequently. Because these cases may resemble non-specific febrile illnesses with abdominal symptoms, they are often underdiagnosed. SEOV infection shares many clinical similarities with HTNV-associated disease but is more frequently associated with hepatic involvement, including hepatitis.[2,15,16]

Hantavirus Cardiopulmonary Syndrome (HCPS)

Compared to HFRS, HCPS is a more aggressive disease, generally associated with a more aggressive clinical course and higher mortality. The case fatality rates of HCPS range from 30% to 50%. The disease usually goes through three stages: prodromal, cardiopulmonary, and convalescent.[2,14,17]

Early manifestations are usually non-specific and resemble an influenza-like illness, including fever, chills, myalgia, headache, and gastrointestinal symptoms including abdominal pain. This initial stage is often followed by rapid clinical deterioration characterized by cough, dyspnea, tachycardia, hypotension, and pulmonary edema. Progressive bilateral pulmonary infiltrates and pleural effusions may develop, frequently leading to acute respiratory failure requiring mechanical ventilation. Severe cases can further progress to cardiogenic shock, lactic acidosis, and marked hemoconcentration, with death occasionally occurring within hours after hospitalization. Patients who survive the acute cardiopulmonary phase typically enter a recovery period marked by gradual resolution of pulmonary edema and polyuria. Although prolonged fatigue and exercise intolerance are common during convalescence, long-term sequelae are uncommon, and recovery is usually complete.[2,14,17]

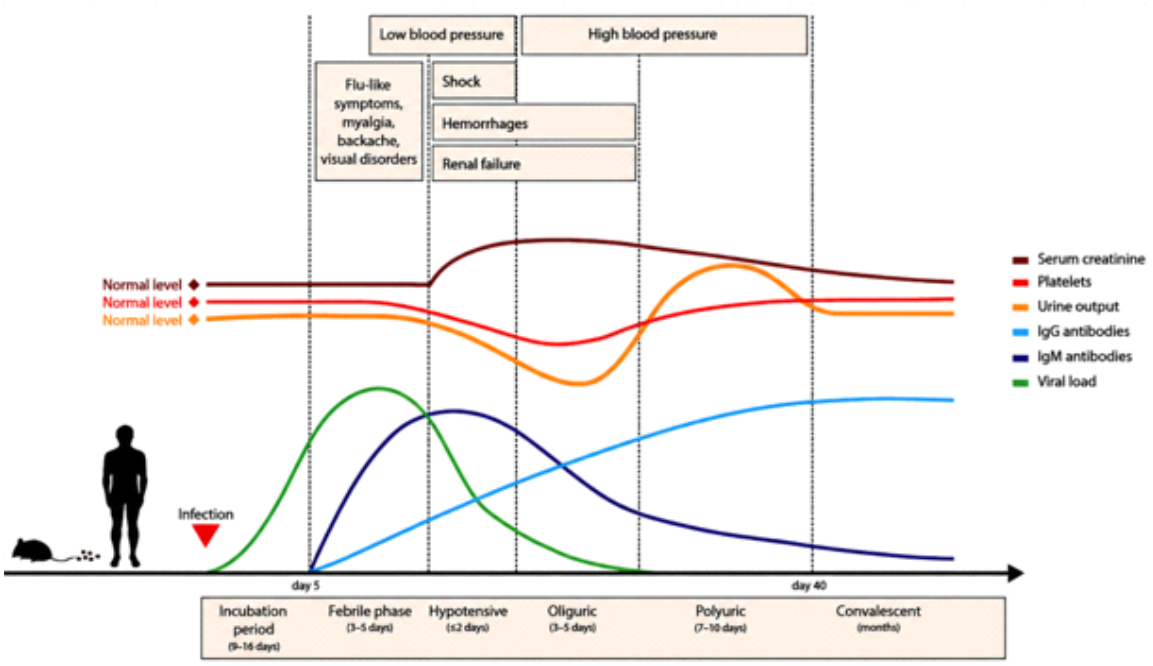

Figure 1. Clinical progress of hemorrhagic fever with renal syndrome (HFRS) in humans. Cited from: Avšič-Županc T, Saksida A, Korva M. Hantavirus infections. Clinical Microbiology and Infection. 2019 Apr 1;21:e6–16. doi:10.1111/1469-0691.12291.[2]

Traditionally, HFRS has been primarily associated with renal involvement, while pulmonary manifestations are considered the main feature of HCPS. However, growing clinical evidence indicates that the two syndromes overlap, as pulmonary complications may also occur in HFRS, whereas renal and hemorrhagic manifestations have increasingly been reported in HCPS cases.[2]

DIAGNOSIS

The diagnosis of HFRS and HCPS relies on a combination of clinical presentation, epidemiological data, and laboratory investigations. Hantavirus infection should be suspected in individuals who have lived in or traveled to areas where Hantaviruses are endemic within the previous 5 - 50 days. Common clinical manifestations to watch for include acute high fever lasting over 48 hours, headache, abdominal or back pain, and laboratory abnormalities such as leukocytosis, thrombocytopenia, elevated serum creatinine, proteinuria, and hematuria, with a urine dipstick usually conducted to identify the last two. However, early manifestations are often non-specific, making diagnosis based solely on clinical findings particularly challenging, especially in mild cases.[2,18] **Table 1** below outlines the comparison of clinical features between HFRS and HCPS.

Serological testing is very important in the diagnostic process, as most patients develop detectable IgM and IgG antibodies in their serum at symptom onset. Antibodies against the Hantavirus nucleocapsid protein are predictable, with IgM antibodies detectable at the onset of the febrile phase and IgG antibodies appearing by the end of the febrile phase. IgM is detectable from days 3 to 5, peaking in the second week, and can persist up to 6 months, while IgG is detectable on days 7 to 10 and persists for years.19 Commonly used diagnostic methods include indirect IgM and IgG ELISA, IgM-capture ELISA, and indirect immunofluorescence assays, with IgM-capture ELISA usually demonstrating superior specificity. Enzyme-linked immunosorbent assay (EIA) is considered the reference serological method for diagnosis. Rapid immunochromatographic IgM assays based on nucleocapsid antigens have also been developed for HFRS caused by PUUV, HTNV, and DOBV, either individually or in combination,

Table 1. Difference in clinical features between HFRS and HCPS.

Features	HFRS (Old World Hantaviruses)	HCPS (New World Hantaviruses)
Primary causative viruses	HTNV, SEOV, PUUV, and DOBV	SNV, ANDV, ARAV, and LANV
Geographic focus	Asia (China, Korea, and Russia), Europe, and Scandinavia	Americas (USA, Brazil, Argentina, and Chile)
Primary target organ	Kidney	Lung (non-cardiogenic ARDS) and heart (myocardial depression)
Clinical phases	Five phases:	Three phases:
	Febrile	Prodromal
	Hypotensive	Cardiopulmonary
	Oliguric	Recovery
	Diuretic	
	Convalescent	
Thrombocytopenia	Yes, early onset, moderate	Yes; early, severe; key warning sign
Hemorrhagic manifestations	Common and prominent	Uncommon
	Petechiae, GI, retroperitoneal	
Acute kidney injury	Central feature: dialysis required in 20 - 40%	Mild, common, but rarely severe
Respiratory failure	Rare	Defined
	Mild pulmonary edema in severe cases	Rapid progression to ARDS, often requiring ECMO
Cardiogenic shock	Uncommon, hypotension	Distinctive mixed pattern:
		Low CO + elevated PCWP
Person-to-person transmission	Not documented	ANDV only through droplet/contact
Specific antiviral therapy	IV ribavirin reduces mortality when given within 5 days	No proven antiviral Favipiravir currently investigated
Key ICU intervention	Continuous RRT (CVVHDF); electrolyte management	ECMO (VA-ECMO for cardiogenic shock); conservative fluids
Case Fatality Rate	<0.5% (PUUV) to 5 - 15% (severe HTNV/DOBV)	25 - 40% (SNV/ANDV) Up to 72% (CASV)
Long-term sequelae	Residual proteinuria/reduced GFR in ~30%; hypertension	Generally, full recovery Cognitive symptoms in some survivors

Cited from: As AK, John J. Hantavirus: A Comprehensive Contemporary Review of Virology, Global Epidemiology, Clinical Variants, Diagnosis, Treatment, and Intensive Care Management. Indian J. Crit. Care Med. 2026 May 25;30(5):430–42. doi:10.5005/jp-journals-10071-25215.19

demonstrating diagnostic performance exceeding 90% when compared with EIA-based IgM testing. Similar immunochromatographic assays designed for PUUV have been applied to SNV and ANDV infections. For the diagnosis of acute infection and epidemiological seroprevalence studies, IgG EIA is commonly performed together with IgM EIA. In contrast, neutralizing antibody assays are usually reserved for investigations of natural immunity.[18]

Rapid immunochromatographic antibody tests have also been developed to facilitate point-of-care detection. Molecular confirmation may be achieved through reverse transcription polymerase chain reaction (RT-PCR) performed on blood or serum samples, allowing detection of viral RNA during the viremic phase. In a 2026 review, RT-PCR is found to be the most sensitive during the febrile phase (days 1 -7) and is the gold standard for confirmation of virology. Sensitivity of RT-PCR peaks at day 5 and declines after. Both conventional and quantitative RT-PCR techniques are utilized, and higher viral loads have been associated with a more severe disease. Importantly, viral RNA may be detectable before seroconversion, supporting the value of molecular testing in early infection.[2,20–22]

MANAGEMENT

Currently, there is no approved antiviral therapy for HFRS or HCPS. The management of these conditions is prioritized to be supportive. Patients presenting with severe disease usually require intensive care monitoring, with treatment focused on maintaining hemodynamic stability, adequate oxygenation, and careful fluid and electrolyte management. In HFRS, close monitoring of renal function and urine output is important to prevent fluid overload, particularly in patients with oliguria, pulmonary edema, and other signs of capillary leakage. If a patient is shown to have severe renal impairment, dialysis might be needed. Platelet transfusions may also be considered in cases of significant thrombocytopenia or hemorrhage. In HCPS, respiratory and cardiovascular support, including supplemental oxygen, mechanical ventilation, vasopressor therapy, and cautious fluid administration, are critical components of care.[2,18]

Among potential antiviral agents, Ribavirin has demonstrated anti-hantaviral activity in both in vitro and animal studies. Clinical studies in China have suggested that early administration of intravenous ribavirin, within the first five days of symptom onset, may reduce mortality and lessen the severity of renal complications in HFRS.[23] A study by Rusnak shows that early administration of Ribavirin decreases the incidence of oliguria and renal insufficiency.[24] Although the study reported a reduction in mortality among patients with HFRS treated with intravenous ribavirin, the available data are insufficient to establish its routine use. At the same time, evidence supporting its efficacy in HCPS remains limited, as several clinical studies have failed to demonstrate significant therapeutic benefit. In North America, a small randomized, placebo-controlled trial evaluating intravenous ribavirin in HCPS did not demonstrate improved survival.[25] In another study, treatment with high-dose intravenous methylprednisolone during the cardiopulmonary stage of HCPS was not associated with clinical benefit in a controlled study performed in Chile.[26] A recent meta-analysis gathered the available data on ribavirin use in Hantavirus infections and suggested that the use of ribavirin is significant in animal studies but not in human treatments.[27]

The most recent development in the search for a potential antiviral for Hantavirus infections is the administration of favirapavir, although its use has only been observed in vitro and in animal studies. Favipiravir (T-705), a broad-spectrum antiviral agent, has demonstrated promising activity against Hantaviruses that cause HCPS, particularly SNV and ANDV. In vitro studies showed that favipiravir effectively inhibited viral replication, resulting in reduced viral RNA levels and lower infectious viral titers. In a lethal hamster model of ANDV infection, daily oral administration of favipiravir significantly reduced viral RNA and antigen detection in tissues and increased survival. The treatment remained protective when given right before viremia, suggesting potential use as post-exposure prophylaxis. Similar reductions in viral RNA and antigen levels were observed in hamsters infected with an SNV strain.[28] A 2021 in vitro study on HTNV demonstrated that favipiravir and ribavirin act through distinct antiviral mechanisms and exhibit additive effects when used in combination. The combined use of suboptimal doses of both agents produced greater antiviral activity than either drug alone, suggesting that favipiravir may reduce the ribavirin dose required to achieve therapeutic efficacy.29 Clinical studies in humans are still needed to confirm its efficacy.

COMPLICATIONS

Most patients with Hantavirus infection recover completely, and long-term complications are uncommon. When present, persistent sequelae may include chronic renal impairment and hypertension. In pediatric patients, the disease generally resembles the adult presentation but is generally milder, although abdominal symptoms are reported more frequently.[2]

Renal function generally returns to normal, and chronic kidney disease is relatively uncommon, although persistent proteinuria or hematuria may occur in a minority of patients following NE. Cardiovascular complications have also been observed, particularly after PUUV infection, with an increased short-term risk of acute myocardial infarction, stroke, deep vein thrombosis, and pulmonary embolism during the

weeks following illness. In severe HFRS cases, cardiovascular mortality may remain elevated during the first year after infection. Hypertension has frequently been identified during long-term follow-up, although its direct association with Hantavirus infection remains uncertain. In addition, prolonged fatigue lasting several weeks is commonly reported, while severe permanent sequelae are otherwise rare.[2,26,30,31]

PREVENTION

The primary strategy for preventing hantavirus is avoiding exposure to infected rodents and contaminated areas. Individuals living near forested regions or performing cleaning activities in houses, barns, or sheds are at increased risk of infection. Preventive strategies, therefore, focus on rodent control measures, such as reducing access to food and shelter around human dwellings, eliminating rodent infestations indoors, and avoiding contact with areas contaminated by rodent excreta.[2]

Currently, no Hantavirus vaccine has been approved to be used globally. However, in the Republic of Korea, Hantavax has been used for years. This vaccine is produced from formalin-inactivated Hantaan virus-infected mouse brain tissue, and repeated booster doses are required to maintain immunity. China has also developed several formalin-inactivated vaccines derived from animal tissues, but these have not received approval outside Asia. In addition, experimental molecular vaccines, including recombinant vaccinia-vectored and plasmid DNA vaccines, have undergone human testing. DNA-based vaccines are considered promising because they can induce durable humoral and cellular immune responses and may allow the development of multivalent formulations. A DNA vaccine targeting the M segment of HTNV and Puumala virus has also entered Phase I clinical trials in the United States to evaluate its safety and immunogenicity.[2,32]

CONCLUSION

Hantavirus infection remains an important emerging zoonotic disease with significant global public health implications. Advances in clinical recognition, diagnostic methods, and research on rodent reservoirs have substantially improved understanding of the disease and contributed to increased detection worldwide. Environmental changes are also believed to influence the distribution and population dynamics of reservoir hosts, affecting Hantavirus epidemiology. Despite progress in Hantavirus research, these infections continue to pose a persistent health threat. Continued investigation into pathogenesis, improved diagnostics, effective antiviral therapies, and vaccine development remains important.

REFERENCES

1. Andes Virus Outbreak Working Group. Andes Hantavirus Outbreak on a Cruise Ship, 2026. New England Journal of Medicine. 0(0). doi:10.1056/NEJMc2606496
2. Avšič-Županc T, Saksida A, Korva M. Hantavirus infections. Clinical Microbiology and Infection. 2019 Apr 1;21:e6–16. doi:10.1111/1469-0691.12291
3. Jonsson CB, Figueiredo LTM, Vapalahti O. A global perspective on hantavirus ecology, epidemiology, and disease. Clin Microbiol Rev. 2010 Apr;23(2):412–41. doi:10.1128/CMR.00062-09
4. Kim YS, Ahn C, Han JS, Kim S, Lee JS, Lee PW. Hemorrhagic fever with renal syndrome caused by the Seoul virus. Nephron. 1995;71(4):419–27. doi:10.1159/000188762
5. Bi Z, Formenty PBH, Roth CE. Hantavirus infection: a review and global update. J Infect Dev Ctries. 2008 Feb 1;2(1):3–23. doi:10.3855/jidc.317
6. Klempa B. Hantaviruses and climate change. Clin Microbiol Infect. 2009 Jun;15(6):518–23. doi:10.1111/j.1469-0691.2009.02848.x
7. Lee HW. Epidemiology and pathogenesis of hemorrhagic fever with renal syndrome. In: Elliott RM, editor. The Bunyaviridae [Internet]. Boston, MA: Springer US; 1996 [cited 2026 May 29]. p. 253–67.
8. Hart CA, Bennett M. Hantavirus infections: epidemiology and pathogenesis. Microbes Infect. 1999 Dec;1(14):1229–37. doi:10.1016/s1286-4579(99)00238-5
9. Kementerian Kesehatan Republik Indonesia. Antisipasi peningkatan kasus, kemenkes perkuat kewaspadaan virus hanta [Internet]. 2026 [cited 2026 May 29]. Available from: https://kemkes.go.id/id/antisipasi-peningkatan-kasus-kemenkes-perkuat-kewaspadaan-virus-hanta
10. Heyman P, Vaheri A, Lundkvist A, Avsic-Zupanc T. Hantavirus infections in Europe: from virus carriers to a major public-health problem. Expert Rev Anti Infect Ther. 2009 Mar;7(2):205–17.

doi:10.1586/14787210.7.2.205
11. Heyman P, Ceianu CS, Christova I, Tordo N, Beersma M, João Alves M, et al. A five-year perspective on the situation of haemorrhagic fever with renal syndrome and status of the hantavirus reservoirs in Europe, 2005-2010. Euro Surveill. 2011 Sep 8;16(36):19961. doi:10.2807/ese.16.36.19961-en
12. Vapalahti O, Mustonen J, Lundkvist A, Henttonen H, Plyusnin A, Vaheri A. Hantavirus infections in Europe. Lancet Infect Dis. 2003 Oct;3(10):653–61. doi:10.1016/s1473-3099(03)00774-6
13. Vapalahti O, Lundkvist A, Vaheri A. Human immune response, host genetics, and severity of disease. Curr Top Microbiol Immunol. 2001;256:153–69. doi:10.1007/978-3-642-56753-7_9
14. Terajima M, Hayasaka D, Maeda K, Ennis FA. Immunopathogenesis of hantavirus pulmonary syndrome and hemorrhagic fever with renal syndrome: Do CD8+ T cells trigger capillary leakage in viral hemorrhagic fevers? Immunol Lett. 2007 Nov 15;113(2):117–20. doi:10.1016/j.imlet.2007.08.003
15. Ala-Houhala I, Koskinen M, Ahola T, et al. Increased glomerular permeability in patients with nephropathia epidemica caused by Puumala hantavirus. Nephrol Dial Transplant. 2002 Feb;17(2):246–52. doi:10.1093/ndt/17.2.246
16. Settergren B. Clinical aspects of nephropathia epidemica (Puumala virus infection) in Europe: a review. Scand J Infect Dis. 2000;32(2):125–32. doi:10.1080/003655400750045204
17. Enria DA, Briggiler AM, Pini N, Levis S. Clinical manifestations of New World hantaviruses. Curr Top Microbiol Immunol. 2001;256:117–34. doi:10.1007/978-3-642-56753-7_7
18. Vial PA, Ferrés M, Vial C, et al. Hantavirus in humans: a review of clinical aspects and management. The Lancet Infectious Diseases. 2023 Sep 1;23(9):e371–82. doi:10.1016/S1473-3099(23)00128-7
19. As AK, John J. Hantavirus: A comprehensive contemporary review of virology, global epidemiology, clinical variants, diagnosis, treatment, and intensive care management. Indian Journal of Critical Care Medicine. 2026 May 25;30(5):430–42. doi:10.5005/jp-journals-10071-25215
20. Aitichou M, Saleh SS, McElroy AK, Schmaljohn C, Ibrahim MS. Identification of Dobrava, Hantaan, Seoul, and Puumala viruses by one-step real-time RT-PCR. J Virol Methods. 2005 Mar;124(1–2):21–6. doi:10.1016/j.jviromet.2004.10.004
21. Hujakka H, Koistinen V, Kuronen I, et al. Diagnostic rapid tests for acute hantavirus infections: specific tests for Hantaan, Dobrava and Puumala viruses versus a hantavirus combination test. J Virol Methods. 2003 Mar;108(1):117–22. doi:10.1016/s0166-0934(02)00282-3
22. Kallio-Kokko H, Vapalahti O, Lundkvist A, Vaheri A. Evaluation of Puumala virus IgG and IgM enzyme immunoassays based on recombinant baculovirus-expressed nucleocapsid protein for early nephropathia epidemica diagnosis. Clin Diagn Virol. 1998 May 1;10(1):83–90. doi:10.1016/s0928-0197(97)10019-8
23. Huggins JW, Hsiang CM, Cosgriff TM, et al. Prospective, double-blind, concurrent, placebo-controlled clinical trial of intravenous ribavirin therapy of hemorrhagic fever with renal syndrome. J Infect Dis. 1991 Dec;164(6):1119–27. doi:10.1093/infdis/164.6.1119
24. Rusnak JM, Byrne WR, Chung KN, et al. Experience with intravenous ribavirin in the treatment of hemorrhagic fever with renal syndrome in Korea. Antiviral Res. 2009 Jan;81(1):68–76. doi:10.1016/j.antiviral.2008.09.007
25. Mertz G, Miedzinski L, Goade D, et al. Placebo-controlled, double-blind trial of intravenous ribavirin for the treatment of hantavirus cardiopulmonary syndrome in North America. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2004;39 9:1307–13. doi:10.1086/425007
26. Vial PA, Valdivieso F, Ferres M, et al. High-dose intravenous methylprednisolone for Hantavirus cardiopulmonary syndrome in Chile: A double-blind, randomized controlled clinical trial. Clin Infect Dis. 2013 Oct 1;57(7):943–51. doi:10.1093/cid/cit394
27. Moreli ML, Marques-Silva AC, Pimentel VA, da Costa VG. Effectiveness of the ribavirin in treatment of hantavirus infections in the Americas and Eurasia: a meta-analysis. VirusDis. 2014 Sep 1;25(3):385–9. doi:10.1007/s13337-014-0219-7
28. Safronetz D, Falzarano D, Scott DP, Furuta Y, Feldmann H, Gowen BB. Antiviral efficacy of Favipiravir against two prominent etiological agents of hantavirus pulmonary syndrome. Antimicrob Agents Chemother. 2013 Oct;57(10):4673–80. doi:10.1128/AAC.00886-13
29. Mayor J, Engler O, Rothenberger S. Antiviral efficacy of Ribavirin and Favipiravir against Hanta virus. Microorganisms. 2021 Jun 15;9(6):1306. doi:10.3390/microorganisms9061306
30. Karanfilovski V, Gjorgjievski N, Dzekova-Vidimliski P, et al. Beyond the kidneys: Pulmonary-renal involvement in Hantavirus infection - A 10-year experience. Indian Journal of Nephrology. 2026. doi:10.25259/ijn_639_2025
31. Latus J, Schwab M, Tacconelli E, et al. Clinical course and long-term outcome of Hantavirus-associated nephropathia epidemica, Germany. Emerging Infectious Diseases. 2015;21:76–83. doi:10.3201/eid2101.140861
32. Yi Y, Park H, Jung J. Effectiveness of inactivated hantavirus vaccine on the disease severity of hemorrhagic fever with renal syndrome. Kidney Res Clin Pract. 2018 Dec;37(4):366–72. doi:10.23876/j.krcp.18.0044.