REVIEW

Is Hantavirus a Threat to Global and Regional Public Health?

Ion MARUNTELU[1], Corina Andreea ROTARESCU[2], Alexandra Elena CONSTANTINESCU[3], Andreia Ioana CONSTANTINESCU[4], Ileana CONSTANTINESCU[5]

[1]Fundeni Center for Immunogenetics and Virology, Fundeni Clinical Institute, Bucharest, Romania.
[2]Fundeni Center for Immunogenetics and Virology, Fundeni Clinical Institute, Bucharest, Romania.
[3]Fundeni Center for Immunogenetics and Virology, Fundeni Clinical Institute, Bucharest, Romania; "Emil Palade" Center of Excellence for Young Researchers in Scientific Research (EP-CEYR), Romanian Academy of Scientists, Bucharest, Romania.
[4]Fundeni Center for Immunogenetics and Virology, Fundeni Clinical Institute, Bucharest, Romania; "Emil Palade" Center of Excellence for Young Researchers in Scientific Research (EP-CEYR), Romanian Academy of Scientists, Bucharest, Romania.
[5]Faculty of Medicine, "Carol Davila" University of Medicine and Pharmacy Bucharest, Bucharest, Romania; Fundeni Center for Immunogenetics and Virology, Fundeni Clinical Institute, Bucharest, Romania; "Emil Palade" Center of Excellence for Young Researchers in Scientific Research (EP-CEYR), Romanian Academy of Scientists, Bucharest, Romania; (email: ileana.constantinescu@imunogenetica.ro).

Abstract. Hantaviruses are RNA viruses with a tri-segmented genome and a lipid envelope, making them vulnerable to common disinfectants and environmental exposure. The pathogenesis of hantavirus infection in humans is primarily driven by a massive, immune-mediated dysregulation of the endothelial barrier, leading to massive pulmonary edema in Hantavirus Cardiopulmonary Syndrome or renal impairment and hemorrhage in Hemorrhagic Fever with Renal Syndrome. The reported hantavirus cases on the ship MV Hondius in May 2026 showed that hantaviruses can affect global tourism flows, requiring immediate response measures at ports and airports. This outbreak could be favoured by global warming and altered rainfall patterns, which have modified the geographical distribution of hantaviruses. The identified cases from Romania and other countries confirm that hantavirus is a major public health issue due to its impact on infected individuals and the widespread difficulties it presents.

Keywords: *Hantaviruses, RNA viruses, climate changes, cardiopulmonary syndrome, renal syndrome.*

DOI **10.56082/annalsarscimed.2026.1.18**

1. Introduction

The risk assessment of emerging infectious diseases places hantaviruses in a category of critical importance for global public health, driven by extremely high fatality rates, the absence of specific antiviral treatments, and the complex interaction between the ecological dynamics of animal reservoirs and human activities [1–3]. Hantaviruses are a group of rodent-borne RNA viruses capable of causing severe disease, ranging from hemorrhagic fever with renal syndrome (HFRS) in Europe and Asia to hantavirus cardiopulmonary syndrome (HCPS/HPS) in the Americas [1,4,5]. Although the global annual incidence fluctuates between 10,000 and over 100,000 cases, the sporadic nature of these infections is counterbalanced by their clinical severity, with death rates reaching up to 50% in certain regions of the Western Hemisphere [1,6].

The importance of this pathogen as a public health issue was recently reaffirmed by the large outbreak in May 2026, linked to the cruise ship MV Hondius, which demonstrated the potential for international spread of South American strains with documented human-to-human transmission [2,7,8]. This situation underscores the need for constant monitoring and rigorous international coordination under the International Health Regulations to manage the risks of spillover and transmissibility in closed or densely populated environments [2,9].

2. Viral Architecture and Pathogenicity Mechanisms

Hantaviruses belong to the Hantaviridae family, genus Orthohantavirus, and are characterized by a genome consisting of negative-sense, single-stranded RNA segmented into three distinct units: the L (Large) segment, the M (Medium) segment, and the S (Small) segment [10,11]. This tri-segmented structure is protected by a lipid envelope, making the virus vulnerable to common disinfectants and environmental exposure, yet allowing significant persistence in rodent excretions under low-temperature, high-humidity conditions [10].

The L segment encodes RNA-dependent RNA polymerase, essential for viral replication, while the M segment encodes a glycoprotein precursor that is subsequently cleaved into Gn and Gc [11,12]. These glycoproteins are responsible for cell receptor recognition and fusion with the host cell membrane. The S segment encodes the nucleocapsid (N) protein, which protects viral RNA. This molecular framework has co-evolved with specific rodent species for over 20 million years, allowing the virus to persist asymptomatic in its natural host while triggering a devastating immune response upon crossing the species barrier to humans [3,13,14].

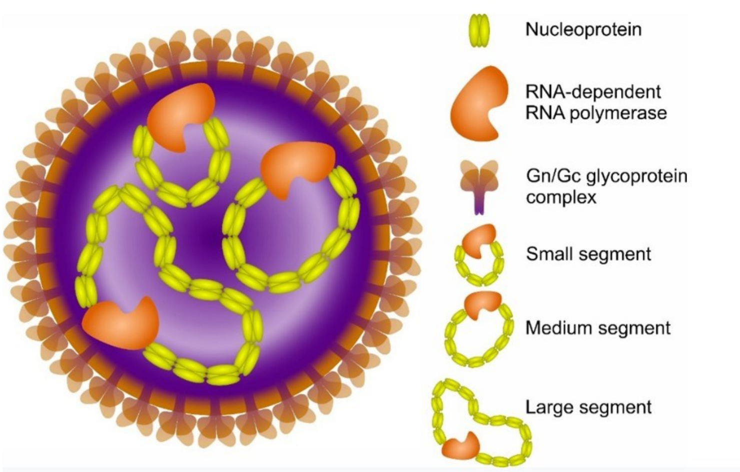

Fig. 1. https://www.ecdc.europa.eu/en/infectious-disease-topics/hantavirus-infection/factsheet-orthohantavirus-infections

The pathogenesis of hantavirus infection in humans is not primarily driven by the virus's direct cytopathic effect on cells, but by a massive immune-mediated dysregulation of the endothelial barrier [3]. The virus predominantly infects endothelial cells, triggering a cytokine release that increases vascular permeability [3,12]. This phenomenon, known as "capillary leak syndrome", leads to plasma extravasation into the interstitial space, resulting in massive pulmonary edema in HCPS or renal impairment and hemorrhage in HFRS [1,3,13]. The disease represents an extreme form of maladaptive immune response, in which clinical severity reflects the severity of endothelial dysregulation [3].

Table 1. Comparison between major hantaviral syndromes [1,3,5,6,13]

Feature	*Hantavirus Cardiopulmonary Syndrome (HCPS/HPS)*	*Hemorrhagic Fever with Renal Syndrome (HFRS)*
Geographic Region	North and South America	Europe, Asia, Africa
Case Fatality Rate	30% - 60%	< 1% - 15%
Main Target Organs	Lungs, Heart	Kidneys, Blood vessels
Key Symptoms	Rapid dyspnea, pulmonary edema, shock	Renal failure, proteinuria, hemorrhage
Representative Strains	Sin Nombre, Andes, Bayou	Hantaan, Puumala, Dobrava, Seoul
Human-to-Human Transmission	Documented for the Andes virus	Not documented

3. Global Epidemiology and Disease Burden in the 21st Century

An analysis of the geographical distribution reveals a global presence of hantaviruses with marked variations in incidence and severity. In the United States, surveillance initiated in 1993 recorded 890 confirmed cases by the end of 2023, the majority occurring in western regions. The "Four Corners' region, comprising New Mexico, Colorado, Arizona and Utah, remains the area with the highest activity, mainly because of the presence of the deer mouse (Peromyscus maniculatus), the primary reservoir for the Sin Nombre virus.

In Europe, Puumala virus (PUUV) causes a milder form of HFRS known as endemic nephropathy. The ECDC report for 2023 indicates that Finland and Germany reported more than 60% of the 1,885 European cases. China continues to bear the highest burden of HFRS in Asia, representing about 90% of global cases, although the incidence has decreased in recent years due to aggressive rodent control measures and vaccination programs.

Table 2. Demographic characteristics of patients with hantavirus in the United States (1993-2023) [14]

Category	*Subcategory*	*Percentage (%)*
Sex	Male	62%
	Female	38%
Race	White	75%
	American Indian/Alaska Native	19%
	Black / African American	1%
	Asian	<1%
Ethnicity	Hispanic / Latino	14%
	Non-Hispanic / Latino	66%
	Unknown	20%

The predominance of cases among men (62%) is often attributed to increased occupational exposure in sectors such as agriculture, forestry and construction, where contact with rodent habitats is more frequent. Furthermore, the high percentage of cases among Native American populations (19%) highlights vulnerabilities related to living conditions in rural areas, where rodents tend to enter the vicinity of human dwellings for food and shelter.

3.1. Transmission Dynamics and Human-to-Human Risks of the Andes Virus

The main mechanism of hantavirus transmission to humans is the inhalation of aerosols contaminated by urine, faeces or saliva from infected rodents. The aerosolization process occurs when dried excretions are disturbed during cleaning activities in enclosed or poorly ventilated spaces such as cellars, attics or barns. Although rarely, infections can also occur through rodent bites, the ingestion of contaminated food or direct mucosal contact with infected materials.

The Andes virus (ANDV), endemic to Argentina and Chile, has demonstrated the ability to transmit from person to person. Transmission generally occurs under conditions of close, prolonged contact, as documented among intimate partners, family members, or in hospital settings where standard precautions are not applied. Recent studies suggest that ANDV can be present in saliva and breast milk, which poses additional challenges for infection control in maternity wards and communities.

The outbreak reported in May 2026 on the ship MV Hondius served as an alarming case study of how hantavirus can become a threat to international health security. The ship, which departed from Ushuaia, Argentina, travelled an itinerary through Antarctica and South Georgia before a cluster of severe respiratory illnesses was identified [2,9].

The epidemiological investigation suggested a mixed hypothesis: first exposure to rodents during onshore activities, followed by limited human-to-human transmission within enclosed spaces on the ship. This incident forced the authorities in Spain, Cape Verde and the United Kingdom to impose strict quarantine measures for all 147 passengers and crew members, monitoring them for 45 days. The event demonstrated that hantavirus is no longer restricted to isolated rural areas, but can affect global tourism flows, calling for rapid action protocols in ports and airports.

3.2. Environmental Factors: Climate Change and Rodent Dynamics

A key dimension of hantavirus as a public health issue is its dependence on ecosystem balance. Human infections are often the result of ecological "pulse events" [10,15].

In Central Europe and the Balkans, the abundant seed production by trees (beech, oak), known as masting, provides a massive food source for rodents such as the bank vole (Myodes glareolus) [10]. This leads to a rodent population explosion in the autumn and winter, followed by an increase in human cases the following spring [10,16]. In northern regions, such as Finland, rodent density follows multi-year predator-prey cycles, with peak incidences occurring every 3–4 years [10].

Global warming and altered rainfall patterns modify the geographic distribution of hantaviruses through several mechanisms:

- Tropicalization of Temperate Regions: In Argentina, the climate is becoming more tropical, allowing reservoir rodents to migrate to regions that were previously too cold to sustain their populations [17,18].
- Extreme Hydrometeorological Events: Floods can force rodents to leave their natural habitats and seek refuge in human settlements. Conversely, extreme droughts can dry out vegetation, causing rodent excretions to become fine dust that is easily aerosolized and inhaled by humans [16,17].
- Urban Heat Islands: Higher temperatures in cities attract synanthropic rodents, such

as rats carrying the Seoul virus, increasing the risk of transmission in densely populated areas [12,17].

Research conducted by NASA and partner universities has used Landsat satellite imagery to predict hantavirus risk based on vegetation indices, demonstrating that environmental monitoring can serve as an early warning system for public health [15,16].
The development of a hantavirus vaccine is considered a global public health priority, but progress is slowed down by economic and logistical barriers [19,20]. Several candidates are under development:

- DNA Vaccines (pWRG/AND-M): Developed by the US Army (USAMRIID), this vaccine targets the M segment of the Andes virus. Although it induces a good immune response, it requires four doses administered via needle-free injection, which is difficult to implement during an active outbreak [19].
- mRNA Vaccines (mRNA-1018): mRNA platforms, validated during the COVID-19 pandemic, are being tested to provide faster and more robust protection against the Sin Nombre and Andes strains [19,21].
- MVA-Hanta Vaccine: An ongoing Phase 1 study (2025–2026) uses the modified vaccinia virus Ankara vector to assess safety and immunogenicity in healthy adults [22].
- Passive Immunisation (SAB-163): Involves the use of human polyclonal antibodies produced in trans-chromosomic cattle, providing an emergency solution for exposed medical personnel or close contacts of confirmed Andes virus cases [19].

The major difficulty remains Phase 3 clinical trials. Because hantavirus occurs in sporadic and unpredictable outbreaks, it is nearly impossible to organize a large-scale efficacy study that meets the rigorous standards of regulatory agencies (FDA, EMA) [19]. For this reason, experts advocate for the use of the "animal rule" or immune correlates for approval [19].
In the absence of a vaccine, hantavirus control relies on reducing human-rodent contact. Public health depends on educating citizens about hidden risks in rural and urban environment [1,12,23].
Recommendations for the Public and Cleaning Personnel: When cleaning areas contaminated with rodent excretions, dry sweeping or vacuuming should be avoided because these actions can aerosolize the virus and increase the risk of inhaling it [12,23]. Instead, contaminated surfaces should first be sprayed with a bleach solution (1 part bleach to 10 parts water) or another disinfectant, then cleaned with wet wiping ways while wearing gloves and a protective mask [23,24]. Additionally, rooms that have remained closed for long periods and show signs of rodent activity should be ventilated by opening windows and doors for at least 30 minutes before entering or cleaning the area [12,24,25].
In the context of a media crisis, such as the outbreak on the MV Hondius, pharmacists have a vital role in assessing actual risk and educating patients, helping them distinguish between common respiratory symptoms and hantavirus warning signs [26]. It is essential to avoid panic by insisting that human-to-human transmission is extremely rare and limited to specific conditions [26,27].

3.3. The Situation in Romania and South-Eastern Europe

Hantavirus represents an active but often underestimated public health issue in Romania. Although the interim minister of health stated in May 2026 that the virus "is not a cause for concern," data from the National Institute of Public Health show an endemic presence [28].
Between 2023 and 2026, approximately 15 confirmed cases were reported in Romania [28]. Studies conducted at the Fundeni Clinical Institute described cases of HFRS that initially presented with clinical manifestations of thrombotic microangiopathy (TMA), requiring a kidney

biopsy to clarify the diagnosis [29]. In the Balkan region, the Dobrava virus causes severe forms of HFRS, with a case fatality rate of up to 12% [29].

The Romanian healthcare system faces several specific challenges related to hantavirus infections. Because the clinical manifestations are often non-specific, hantavirus is frequently overlooked in the differential diagnosis of acute kidney injury or severe pneumonias with unknown etiology [16,29]. This issue is particularly relevant in Romania, where a substantial proportion of the population is engaged in agriculture and forestry, occupations associated with an increased risk of exposure to rodents carrying Puumala and Dobrava viruses [30,31]. In addition, limited awareness contributes to the underrecognition of the disease, as many moderate cases of epidemic nephropathia are managed as non-specific viral infections or transient renal disorders without being reported to the national surveillance system [16].

4. Hantavirus Diagnosis: The Difficulties of Prodromal Phases

The symptomatology of hantavirus infection is characterized by a biphasic progression, which makes early diagnosis extremely difficult. The incubation period ranges from 1 to 8 weeks, during which the patient remains asymptomatic, but the virus begins to replicate within endothelial cells.

Hantavirus diagnosis is often a diagnosis of exclusion within the first 72 hours of symptoms, as the virus is not always detectable in secretions during the initial stages [32].

Confirmation is based on a combination of laboratory and histopathological findings, including serology, RT-PCR, and immunohistochemistry. Serological testing identifies specific IgM antibodies, which indicate an acute infection, or demonstrates a fourfold increase in IgG antibody titers [1,4]. RT-PCR allows detection of viral RNA in blood or tissue samples during the acute phase of the disease [1]. In addition, histopathological examination using immunohistochemistry on tissue specimens, such as lung or kidney biopsies, can confirm the presence of hantaviral antigens [4,29].

Laboratory samples are considered high-level biohazards. Their transport requires a triple-packaging system, and testing of non-inactivated samples must be performed under maximum biosafety conditions (BSL-3 or BSL-4, depending on the strain) [1,31]. This technical requirement limits rapid diagnostic capacity in underdeveloped regions, where hantavirus infections can be mistaken for sepsis or other hemorrhagic fevers [1,33].

Conclusions

The integrated analysis of the provided data confirms that hantavirus is a major public health issue, not due to the total number of cases, but because of its devastating impact on infected individuals and the systemwide challenges it generates [1,3,6].

Hantavirus requires more attention from researchers and government officials. Investing in "One Health" surveillance systems, developing rapid bedside diagnostics, and accelerating vaccine research are mandatory steps to protect the population against a threat that, although rare, is of uncompromising severity [12,20,34]. Romania, as an endemic area for European strains, and other countries must strengthen their reporting protocols and raise awareness among medical personnel to reduce the burden of these silent but dangerous infections [28,29].

R E F E R E N C E S

[1] World Health Organization. Hantavirus [Internet]. Geneva: WHO; [cited 2026 May 22]. Available from: https://www.who.int/news-room/fact-sheets/detail/hantavirus.

[2] World Health Organization. Hantavirus cluster linked to cruise ship travel, Multi-country [Internet]. Geneva: WHO; 2026

[cited 2026 May 22]. Available from: https://www.who.int/emergencies/disease-outbreak-news/item/2026-DON599.

[3] Hantavirus: How climate change may be increasing disease risk [Internet]. Columbus (OH): CAS; [cited 2026 May 22]. Available from: https://www.cas.org/resources/cas-insights/hantavirus.

[4] Hantavirus cardiopulmonary syndrome - Symptoms, diagnosis and treatment [Internet]. London: BMJ Publishing Group; [cited 2026 May 22]. Available from: https://bestpractice.bmj.com/topics/en-us/928.

[5] Liu R, Ma H, Shu J, Zhang Q, Han M, Liu Z, et al. Vaccines and Therapeutics Against Hantaviruses. Front Microbiol 2020;10:2989. https://doi.org/10.3389/fmicb.2019.02989.

[6] Hantavirus: What you need to know [Internet]. London: BMJ; 2026 [cited 2026 May 22]. Available from: https://www.bmj.com/content/393/bmj.s877.

[7] Cases of Hantavirus by State (2026 Updates). Box-Kat 2026. https://www.box-kat.com/blogs/box-kat-blog/cases-of-hantavirus-by-state-what-you-need-to-know (accessed May 21, 2026).

[8] Andes hantavirus outbreak: ECDC continues working on the frontline to support EU Member States 2026. https://www.ecdc.europa.eu/en/news-events/andes-hantavirus-outbreak-ecdc-continues-working-frontline-support-eu-member-states (accessed May 21, 2026).

[9] European Centre for Disease Prevention and Control. Summary [Internet]. Stockholm: ECDC; 2026 [cited 2026 May 21]. Available from: https://www.ecdc.europa.eu/sites/default/files/documents/TAB-hantavirus-06052026.pdf.

[10] European Centre for Disease Prevention and Control. Factsheet on orthohantavirus infections [Internet]. Stockholm: ECDC; [cited 2026 May 22]. Available from: https://www.ecdc.europa.eu/en/infectious-disease-topics/hantavirus-infection/factsheet-orthohantavirus-infections.

[11] Bellomo C, Alonso DO, Ricardo T, Coelho R, Kehl S, Periolo N, et al. Emerging hantaviruses in Central Argentina: First case of Hantavirus Pulmonary Syndrome caused by Alto Paraguay virus, and a novel orthohantavirus in Scapteromys aquaticus rodent. PLoS Negl Trop Dis. 2021;15(11):e0009842. doi:10.1371/journal.pntd.0009842.

[12] Hantavirus: The Growing Public Health Threat Demanding Greater Global Awareness n.d. https://www.biopharmaboardroom.com/news/5/4683/hantavirus-the-growing-public-health-threat-demanding-greater-global-awareness.html (accessed May 21, 2026).

[13] Centers for Disease Control and Prevention. About Hantavirus [Internet]. Atlanta (GA): CDC; [cited 2026 May 22]. Available from: https://restoredcdc.org/www.cdc.gov/hantavirus/about/index.html.

[14] Centers for Disease Control and Prevention. Reported Cases of Hantavirus Disease [Internet]. Atlanta (GA): CDC; [cited 2026 May 22]. Available from: https://www.cdc.gov/hantavirus/data-research/cases/index.html.

[15] Scott M. Hantavirus Risk Maps | NASA Earthdata 2020. https://www.earthdata.nasa.gov/news/feature-articles/hantavirus-risk-maps (accessed May 21, 2026).

[16] Spencer F. Deadly rodent-borne hantavirus is an emerging disease with pandemic potential [Internet]. 2025 [cited 2026 May 22]. Available from: https://news.vt.edu/articles/2025/04/hantavirus-environmental-factors-influence-distribution-paanwaris-paansri-luis-escobar.html.

[17] Hantavirus pulmonary syndrome. Wikipedia [Internet]. [cited 2026 May 22].

Available from: https://en.wikipedia.org/wiki/Hantavirus_pulmonary_syndrome.

[18] Science News. Some South American rodent-borne viruses may spread as climate warms [Internet]. [cited 2026 May 22]. Available from: https://www.sciencenews.org/article/rodent-arenaviruses-hantavirus-climatearming may help rodent-borne viruses spread more widely 2026. https://www.sciencenews.org/article/rodent-arenaviruses-hantavirus-climate.

[19] We are still likely years away from a hantavirus vaccine n.d. https://www.rdworldonline.com/we-are-still-years-away-from-a-hantavirus-vaccine/ (accessed May 21, 2026).

[20] Protective CD8+ T-cell response against Hantaan virus infection induced by immunization with designed linear multi-epitope peptides in HLA-A2.1/Kb transgenic mice - PubMed n.d. https://pubmed.ncbi.nlm.nih.gov/33028368/ (accessed May 21, 2026).

[21] Research Roundup: Hantavirus vaccine research, mRNA flu vaccine trial, HIV biology discovery n.d. https://www.ghtcoalition.org/blog/research-roundup-5-11-26 (accessed May 21, 2026).

[22] ISRCTN Registry. ISRCTN17868912: A clinical trial to determine the safety and immune responses to a new vaccine against Hantavirus disease [Internet]. [cited 2026 May 22]. Available from: https://www.isrctn.com/ISRCTN17868912.

[23] Hantavirus [Internet]. London: National Travel Health Network and Centre; [cited 2026 May 22]. Available from: https://travelhealthpro.org.uk/disease/66/hantavirus.

[24] International SOS. Hantavirus briefing document [Internet]. 2026 [cited 2026 May 21]. Available from: https://cdn1.internationalsos.com/-/jssmedia/pandemic/Files/dand-p-pd-fs/intl-sos-hantavirus-briefing-document-may-2026.pdf.

[25] ANRS Emerging Infectious Diseases. Hantaviruses [Internet]. [cited 2026 May 22]. Available from: https://anrs.fr/en/scientific-research/diseases-and-pathogens/hantaviruses.

[26] Is Hantavirus Human-To-Human Transmissible? Contemporary Clinic 2026. https://www.contemporaryclinic.com/view/is-hantavirus-human-to-human-transmissible- (accessed May 21, 2026).

[27] Reddit. Can a professional weigh in here? r/epidemiology [Internet]. [cited 2026 May 22]. Available from: https://www.reddit.com/r/epidemiology/comments/1t6723r/can_a_professional_weigh_in_here.

[28] Hantavirus not a reason for concern for Romania, interim health minister says | Romania Insider n.d. https://www.romania-insider.com/hantavirus-not-reason-concern-romania-may-2026 (accessed May 21, 2026).

[29] Lupuşoru G, Andronesi AG, Lupuşoru M, Ailincăi I, Sfeatcu R, Văcăroiu I, et al. Hantavirus infections in the South-Eastern European countries: A study of two cases and literature review. Exp Ther Med 2023;26:430. https://doi.org/10.3892/etm.2023.12129.

[30] Human Hantavirus Infections in Hungary (2018-2025): Epidemiology, Molecular Detection Across Clinical Sample Types, and Phylogenetic Analysis - PubMed n.d. https://pubmed.ncbi.nlm.nih.gov/41902274/ (accessed May 21, 2026).

[31] Canada PHA of. Pathogen Safety Data Sheets: Infectious Substances – Hantavirus spp. 2011. https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment/hantavirus.html (accessed May 21, 2026).

[32] 2026 Multi-country Hantavirus Cluster Linked to Cruise Ship | HAN | CDC n.d.

https://www.cdc.gov/han/php/notices/han00528.html (accessed May 21, 2026).

[33] What Is Hantavirus? Understanding the Virus, Recent 2026 Concerns, and Actual Public Health Risks - Fact Crescendo Sri Lanka English | The leading fact-checking website n.d. https://srilanka.factcrescendo.com/english/hantavirus-mv-hondius-cruise-ship-cluster-global-spread-claim/ (accessed May 21, 2026).

[34] Hantavirus cluster linked to cruise ship travel, Multi-country n.d. https://www.who.int/emergencies/disease-outbreak-news/item/2026-DON600 (accessed May 21, 2026).