

Zoonotic Spillover: Global Diversity of Mammals And Distribution of Hantaviral Strains in Synanthropic Animals and The Perspective for Public Health

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SUMMARY

Introduction: Viral hemorrhagic fevers (VHF) refer to a group of diseases caused by different viral families. Rodents represent 42% of the world's mammalian biodiversity and are reservoir hosts for a wide range of disease agents. Hantaviruses are harbored in numerous mammalian reservoirs, including rodents. To prevent and mitigate possible outbreaks of zoonotic diseases, it is necessary to know the geographic distribution, intra-specific relationships, diversity and identity of the incriminated species.

Objectives: To describe the ecology, epidemiology, epizootiology and natural history of hemorrhagic infections caused by hantavirus serotypes and their respective reservoirs.

Methodology: Bibliographical consultations and online articles were carried out in the databases relating the highlighted subjects.

Results: Rodents from the subfamilies Murinae, Arvicolinae, Neotominae and Sigmodontinae are the main reservoirs of hantavirus disease. Orthohantaviruses are the most studied group, highlighting the Hantaan, Seoul, Puumala and Dobrava serotypes. Rodents of the genus *Oligoryzomys*, include several species and have parasite-host relationships reported for the genus *Hantavirus*. Other species of mammals, such as bats, squirrels and opossums, have already been described as possible reservoirs.

Conclusion: Hantavirus infections occur as a result of close interactions between humans and animals. One Health approaches highlight concerns through interdisciplinary collaboration and development of public health interventions when animals become vectors of infections, with the aim of achieving global results by recognizing the interconnection between wildlife, humans and the environment.

KEYWORDS: Rodents, mammals, disease ecology, emerging infectious diseases, epidemic outbreaks.

INTRODUCTION

Viral hemorrhagic fevers (VHF) refer to a group of diseases caused by 6 families, different from single-stranded RNA viruses, of zoonotic origin: Hantaviridae (hantavirus hemorrhagic fever with renal syndrome (HFRS) and pulmonary and cardiovascular syndrome by hantavirus (SPCVH)), Arenaviridae (junin (JUNV), Machupo (MACV), Guanarito (GTOV) and Sabiá (SBAV) hemorrhagic fevers in South America and Lassa virus (LASV) in Africa and Filoviridae, hantavirus (SPCVH) Marburg virus (MARB) and Ebola virus (EBOV), Flaviviridae (Omsk hemorrhagic fever (OHF), Kyasanur forest disease (KFD), dengue hemorrhagic fever (DHF)/dengue shock syndrome (DSS) and yellow fever (YF), Nairoviridae (Congo and Crimean hemorrhagic fever (CCHF)), Phenuiviridae (Rift Valley fever (RVF)), Paramyxoviruses (such as Nipah virus and Hendra virus). They are characterized by systemic involvement, with an acute febrile syndrome that can cause bleeding causing serious cases with risk of death¹.

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Some animal species can be accidental transmitters between hosts (rodents or bats) and humans, resulting in nosocomial transmission and the involvement of healthcare professionals and patients. Although humans are not the natural reservoir for any of the viruses that cause hemorrhagic fever.

Many specialized human viruses also originate from mammals or birds. In fact, a substantial proportion of mammalian viruses may be able to cross the species barrier and reach humans, although only about half of these are capable of being transmitted by humans and about half, again, of transmitting sufficiently well to cause large outbreaks².

In recent decades, despite extensive research and the enormous efforts of scientific research and modern medicine to eliminate and eradicate infectious diseases, a large number of previously unknown or underestimated pathogens have become fundamental threats to human health as they have shown their plasticity and adaptability to infections. In this context, emerging or re-emerging pathogens give rise to new diseases, including zoonotic diseases that constitute a major concern for the scientific community that studies infectious diseases at different spatial and temporal scales³.

Many viruses that spread through nature, affecting wildlife and consequently reaching humans, do not result in pandemics⁴ and when they find a human host, these viruses often result in thousands of infections and cases fatal. Mammals and birds alone are believed to host around 1.7 million undiscovered viruses, leading to many studies searching for the cause of the next pandemic that could hit our species⁵. Most viral outbreaks are closely related to wild animals, many of which are almost exclusive hosts and are geographically sheltered by arthropods (insects, especially mosquitoes), small rodents and chiropterans.

Attacks on the environment, climate and environmental changes, globalization and anthropogenic actions in the modern world have been offering a wide range of opportunities for repercussions and the emergence of zoonotic diseases, as well as adaptations of microorganisms to their reservoirs and consequently strengthening the new hosts. Currently, according to ICTV, there are around 11,273 species of viruses on the planet⁶ and three to four new species are still found every year. More than 224 viruses that cause human diseases are zoonotic in nature and 88% of these are present in these animal groups².

Despite its ubiquity and importance, coinfection is an underappreciated phenomenon in modern disease ecology. Viruses and other co-infectious agents can interact in ways that shape host-effector communities, influence infection dynamics, and induce evolutionary selection pressures. Previous reviews have focused their information on viruses rather than mammalian hosts. Thus, we provide a previously unaddressed perspective and report host-virus associations on a global taxonomic and geographic scale, with an emphasis on rodent host diversity and distribution. Knowing the diversity, distribution and associations of mammalian pathogens is essential for understanding the ecology of zoonotic diseases.

CHARACTERISTICS OF SYNANTHROPIC RODENTS

The taxonomy, ecology and geographic distribution of rodents in Brazil, covered in literature, presents the ecology of these animals suggesting that there are morphological, physiological and behavioral changes associated with adaptation to the habitats in which these rodents live. Therefore, it is important to clarify that the best way to characterize the geographic distribution of rodents is to associate them with the main ecological complexes of fauna and flora where these small animals live, taking into account their respective specificities.

There are around 6,718 species of mammals in the world, including 6,594 existing wild species, 17 domestic species⁷ available at: (www.mammaldiversity.org). The order Rodentia constitutes the most numerous order of placental mammals, corresponding to around 42% of the world's biodiversity of the Mammalia class, totaling 2,500 species distributed in 34 families⁸. Rodents populate all continents (except Antarctica) and are reservoir hosts for a wide variety of zoonotic pathogens, including rats, mice, squirrels, capybaras, porcupines, beavers distributed across the planet, which vary enormously in size and habitat preference, living in the most diverse environments that provide them with survival conditions, as they have a great capacity for ecological and physiological adaptations⁹.

Brazil has biomes with great faunal diversity, covering 778 species of Brazilian mammals. The most diverse orders are Rodentia (267 sp.), Chiroptera (183 sp.) and Primates (131 sp.). Rodents are distributed across nine families, and, in total, represent more than 34.5% of all mammals. Among the rodent families, Cricetidae is the most diverse, with 155 species⁹, which points to the need for studies on zoonotic pathogens in rodents, including synanthropic species found in the urban environment.

They can transmit a wide range of microbial pathogens, including viruses, bacteria and parasites, and act as definitive and intermediate hosts of zoonotic and vector-borne diseases, both by direct (bite, contact) and indirect (urine and feces) means, by vectors (ticks, fleas and mites) that infest rodents, or when they are preyed upon by other species. Rodents are known to carry more than 85 zoonotic pathogens and, together with their high diversity, represent a significant threat to human health¹⁰, many have a great capacity to adapt to the urban environment (synanthropism).

Among the rodent families, Cricetidae is the most diverse, with 155 species, occurring in Brazil. Although the order Rodentia does not present a high risk of extinction when considering other groups of mammals, many families present global patterns of different types of threat¹¹.

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The viruses associated with HFRS (Hemorrhage Fever with Renal Syndrome) are transmitted by rodents of the subfamily Murinae and Arvicolinae, which occur in the Eurasian territory. The viruses that cause HCPS (hantavirus cardiopulmonary syndrome) are transmitted by rodents of the subfamily Sigmodontinae and Neotominae, present on the American continent (Table 1).

ONE WORLD, ONE HEALTH AND ZOOBOTIC IMPACT

The “one health” concept defines a fundamental principle of biology: it recognizes that the health of people is connected to the health of animals and the environment¹².

Zoonoses, diseases transmitted between animals and humans, are of great importance in global public health, where around 60% of human infectious diseases originate in animals; being responsible for 75% of emerging infectious diseases in the world and at least 5 new human diseases emerge every year and 3 of them are of animal origin^{13,14}.

In 2008, according to the World Health Organization (WHO), the Food and Agriculture Organization of the United Nations (FAO) and the World Organization for Animal Health (OIE), the term emerging zoonosis is defined as a newly recognized pathogen or that has undergone recent evolution or has already occurred previously, but which shows an increase in its incidence or expansion in the geographic area in terms of the number of hosts or vectors. These institutions launched an initiative called “One World, One Health”, in which the term “One health” was suggested to demonstrate the inseparability of human, animal and environmental health^{15,16}.

Currently, several directions are established for these events; Spillover, according to Wells and Clark¹⁷, refers to the transmission between species of pathogens from wildlife to humans, and when this transmission occurs in reverse, from a pathogen from humans to wildlife it can be called of “spillback”¹⁸. According to Becker¹⁹ in relation to the transmission of pathogens between different species, the crossing of species barriers is an ecological phenomenon known as host jumping, pathogen spillover, interspecies transmission, zoonotic transfer, or zoonotic transmission. These forms of horizontal virus transmission present an independent direction between the different viral species and the different existing biological kingdoms.

Studies have focused on infections that occur as a result of close interactions between humans and animals²⁰. One Health approaches could address these concerns through interdisciplinary collaboration and consultation during the development of public health interventions when animals become vectors of infections. Similarly, the concept of “Planetary Health” has also emerged and driven by the human health sector, emphasizes health systems and links with political, economic and social contexts, and the conditions of the natural environments of planet Earth²¹.

Within the conception of animal disease and human disease, this concept ceased to exist, when currently the single health terminology has become a transdisciplinary and multisectoral approach, with the aim of achieving global results recognizing the interconnection between fauna (including man), flora and environment.

These discoveries and emerging infectious diseases are closely related to how humans interact with animal species and the environment. This relationship increases public responsibility for the conservation of Brazilian biodiversity. Because today it has become very clear that nature conservation is also a public health need.

In this article, we review the ecology, epidemiology, epizootiology, and natural history of hantavirus hemorrhagic infections and the characterization of their mammalian hosts and other synanthropic animals; we advocate integrative and multidisciplinary approaches in an attempt to understand the dynamics in populations of rodents, bats and other reservoirs and thus mitigate, through discussion and analysis, the prevention of outbreaks of potentially alarming diseases, addressing the main factors involved in the emergence and re-emergence of zoonoses, as well as future threats and the strategic importance of research and surveillance in Public Health.

METHODOLOGY

Bibliographical consultations and online articles from the last years were carried out, using the databases BIREME (Regional Library of Medicine), Highwire, PubMed (National Public Library), Scielo (Scientific Electronic Library Online), Lilacs (Latin American and Caribbean in Health Sciences), Web of Science, ScienceDirect, US National Library of Medicine (www.nlm.nih.gov) and related books on pertinent subjects using the search term “virus” in combination with “disease” and “mouse or rodent or murine.” The articles analyzed were published in the last 10 years, related to the words mentioned. At the end of the survey, 81 references were duly used, selected according to the proposed theme.

Our objective was to assemble a globally comprehensive list of wild mammals in which hantavirus-specific genetic material (RNA) has been identified, including animal species in host-virus associations confirmed by PCR methodology, excluding results criteria in which they were not related to hantaviruses.

Confirmation of the current virus names and their respective taxonomy were confirmed using the NCBI Taxonomy Browser database (<https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/>) and the ICTV (International Committee on Taxonomy of Viruses) (<https://www.ictv.global>), which is currently the safest source for updated taxonomic information on classifications suggesting the

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characterizations of these viral organisms.

RESULTADOS

A total of 81 references were consulted, addressing issues involving Zoonotic RNA viruses (Hantavirus) and the infections produced by this agent, focusing on the reservoirs and hosts of these viral agents.

Among the five viral genera for the Bunyaviridae family: Nairovirus, Orthobunyavirus, Phlebovirus, Tosopovirus and Hantavirus; orthohantaviruses are the most studied group. The serotypes Hantaan (HTNV), Seoul (SEOV), Puumala (PUUV), Sin Nombre (SNV) and Dobrava (DOBV) are related to hemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS) (Table 1).

In Brazil, the Araraquara virus (ARAV) appears to be the most lethal and virulent emerging strain for the disease. Rodents from the subfamilies Murinae, Arvicolinae, Neotominae and Sigmodontinae are the main reservoirs, housing the genera *Necromys*, *Oligoryzomys*, *Apodemus*, *Rattus* and *Akodon*, recognized and incriminated as causing HCPS (hantavirus cardiopulmonary syndrome) in Brazil and around the world. Other mammals, such as chiropterans of the genera *Eptesicus*, *Rhinolophus*, *Pipistrellus*, *Diphylla*, *Carollia*, *Desmodus*, *Molossus*, *Glossophaga*, *Anoura* among others, are also cited as serological reservoirs for the viral strains of Hantavirus in Africa, China and Brazil (Figure 1).

DISCUSSION

Hantaviruses are among the emerging pathogens that have received increasing attention in recent decades. These viruses are members and belong to the Order Bunyvirales, Family Hantaviridae, Subfamily Mammarenavirinae, genus Orthohantavirus and are classified in a separate genus called Hantavirus, currently consisting of four genera: Loanvirus, Mobatvirus, Orthohantavirus and Thottinivirus, with orthohantaviruses being the most widely studied group⁶.

Hantaviruses are enveloped, single-stranded, negative-sense ribonucleic acid (RNA) viruses, containing a small segment (Small or S), which varies from 1.7 to 2.1 kb, a medium segment (Medium or M), which varies from 3.7 to 5.6 kb, and a large one (Large or L), which varies between 6.5 and 6.6 kb. They are unexpectedly stable in air and can survive >10 days at room temperature and >18 days at 4°C and -20°C.

Hantaan (HTNV), Seoul (SEOV), Puumala (PUUV) and Dobrava (DOBV) virus serotypes mainly cause hemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS), a disease characterized by renal failure, bleeding and illness characterized by shock.

The Bunyaviridae family are classic arboviruses, as they are all transmitted through obligatory arbovirus intermediate vectors, such as mosquitoes, ticks, sandflies, among other arthropods. Viruses of the Hantavirus genus are the only ones in the Bunyaviridae family that are not transmitted by arthropods, but directly by small rodent mammals that are the natural reservoir²². In 2015, it was recently reported²³, isolation of 112 new ancestral viruses from much of the genetic diversity, including arenaviruses, filoviruses, hantaviruses, influenza viruses, lyssaviruses and paramyxoviruses, including hantaviruses in mosquitoes, which can have important consequences on the evolution of this viral group (Table 1).

Currently, records of Hantaviruses in more than 50 species of shrews from the order Eulipotyphla of the subfamilies Soricinae, Crocidurinae and Myosoricinae have been recorded. In bats of different genera²⁴⁻²⁸ they have also been described (Table 1). In non-human primates, the species *Macaca fascicularis* and *Pan troglodytes* infected by Puumala (PUUV) and Tula (TULV) viruses²⁹ have also been described, and finally neotropical primates of the species *Callithrix jacchus*, *C. geoffroyi*, *C. penicillata*, *Alouatta caraya*, *A. guariba*, *Sapajus apella*, *S. libidinosus*, *Saguinus midas* and *Saimiri sciureus*, were isolated in Brazil³⁰ (Table 1).

Inhalation of aerosols and contact with secretions or excretions, which can eliminate the virus through urine, saliva and feces, produced by infected rodents, is the source of dispersion of hantavirus, in contact between susceptible hosts to humans^{31,32}.

Historically, the virus was first isolated in the 1970s from a wild rodent captured on the banks of the Han River, inspiring the name Hantaan virus or Hantavirus³³. A historical account, described by Smadel³⁴ indicates that HFRS was brought to the West for the first time associated with an outbreak that occurred during the Korean War (1950-53) in North American troops in conflict with Korean troops, in the 1950s, where more than 3,200 soldiers were affected by the infection. Older reports record that the viral agent infected around 12,000 Japanese soldiers in the invasion of Manchuria in the 1930s.

The CDC³⁵ reported that in the United States, 538 human hantavirus infections were reported, with the highest numbers of cases in Colorado, Arizona and New Mexico. The mouse *Oligoryzomys fulvescens* (Fulvous pygmy rice rat) was incriminated as the virus reservoir. The first cases of HCPS, in Panama, were reported in 1999, with 106 human infections and a mortality rate of 26%³⁶.

The virus was only isolated in 1977; in 1993, there was an outbreak in the United States, involving the southwestern region of that country: Arizona, New Mexico, Colorado and Utah (Four Corners), among the rodents captured, it was discovered that

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Peromyscus maniculatus (deer mouse) was the main host of a previously unknown type of hantavirus. The new virus was called Muerto Canyon virus, later renamed Sin Nombre (SNV) and the new disease called Hantavirus Pulmonary Syndrome or HPS³⁷.

Reports described by the CDC³⁷, which occurred in the USA in 1993, showed that there was not just one hantavirus that caused HPS, but several strains that could present the same symptoms: a traveler from Louisiana was diagnosed with symptoms similar to the virus Sin Nombre (SNV), and discovered a new hantavirus, called Bayou virus (BAYV), associated with the *Oryzomys palustris* (Marsh rice rat) reservoir. At the end of this same year, a male patient in Florida presented symptoms of HPS, revealing another new hantavirus, called Black Creek Channel virus (BCCV), its carrier is *Sigmodon hispidus* (Hispid cotton rat). Later, another case occurred in New York, called New York-1 (NY-1) and the mouse *Peromyscus leucopus* (white-footed mouse), was incriminated as the carrier of the virus. In the following years, in South America, cases had already been confirmed in Argentina (1993), Chile (1995), Paraguay (1995), Bolivia (1997), Uruguay (1997) and Venezuela (1999), which recorded only three cases until the present moment (Table 1).

In Brazil, the first report of hantavirus occurred in the same year, when the Juititaba virus, transmitted by the rodent *Oligoryzomys nigripes* (black-footed pygmy rice rat), was detected by Silva³⁸, in the report of three brothers, all rural workers, fell ill and two of them died in the city of Juititaba (SP) (Southeastern Region of Brazil). Hantavirus cases in children represented 8.6% (n=100) of the total. This result is higher than that found in the USA, lower than that in Chile, which is around 15%, similar to that in Argentina, which is between 12%, considering cases up to 17 years of age^{39,40}. HPS is associated with high mortality rates 35% in the USA, 38% in Canada and in Brazil 41% have already been recorded⁴¹.

In South America, cases of HCPS have been identified in Argentina, Bolivia, Brazil, Chile, Paraguay, Uruguay, Venezuela and Peru, making it a pan-hemispheric disease. Around 4,000 cases of HCPS have been reported, associated with the following hantaviruses: Andes (ANDV), Anajatuba (ANJV), Araraquara (ARQV), Paranoá (PARV), Bermejo (BMJV), Castelo dos Sonhos (CASV), Juititaba (JUQV), Araucária (Juititaba-like), Laguna Negra (LANV), Lechiguanas (LECV), Maripa (MARV), Oran (ORNV), Rio Mamoré (RIOMV) and Tunari (TUNV)⁴².

Hantavirus is a virus supposedly emerging in Brazil and carried by more than 16 wild rodents that are endemic in the Atlantic Forest and Cerrado biomes⁴³. Given the geographic distribution of two viruses and the assumption that generalist species *Oligoryzomys nigripes* (JUQV), the main reservoir for human cases of HPS in the Atlantic Forest, and *Necromys lasiurus* (ARAV), the reservoir in Brazilian Cerrado and Caatinga environments⁴⁴, This genus *Necromys* has two species described in Brazil, they have a terrestrial habit and have two peaks of activity, one at twilight and one in the morning in the domain region (Figure 1). The main species and genera considered hosts of Hantavirus in Brazil: *Akodon* spp., *Calomys* spp., *Oligoryzomys* spp., and *Necromys lasiurus* (Figure 1).

Studies conducted in Brazil demonstrated that the Araraquara virus (ARAV) is one of the most virulent hantaviruses that can induce HCPS, with a lethality rate of 50%^{42,45}. For Muylaerte and collaborators⁴⁵, a considerable diversity of pathogenic hantavirus genotypes harbored by wild rodents common in the Atlantic Forest of South America.

Phylogenetic studies carried out by Argentine researchers⁴⁶ confirmed the geographical distribution of the most prominent genus, when it comes to Hantavirus: the species *Oligoryzomys longicaudatus* (Long-tailed Colilargo) (Argentina, Chile), *O. nigripes* (Argentina, Paraguay, Brazil), *O. chacoensis* (Chacoan pygmy rice rat) (Argentina, Bolivia, Paraguay), *O. fornesi* (Fornes' colilargo) (Argentina, Paraguay), *O. destructor* (destructive pygmy rice rat) (Argentina, Bolivia) and *O. microtis* (Small-eared Pygmy Rice Rat) (Bolivia, Brazil). *O. longicaudatus* is closely related to the *O. flavescens* (yellow pygmy rice rat) complex, which comprises four clades; *O. nigripes* is closely related to *O. stramineus* (straw-colored colilargo), and *O. vegetus* (sprightly pygmy rice rat), to *O. fulvescens* from Central America. *O. chacoensis*, *O. destructor*, *O. fornesi*, *O. longicaudatus*, *O. microtis*, *O. nigripes*, *O. stramineus*, *O. moojeni* (Moojen's pygmy rice rat), *O. rupestres* (Rice rock rat), *O. fulvescens* and *O. vegetus* are confirmed as valid species, while *O. flavescens*, *O. magellanicus* (Magellanic pygmy rice rat), *O. griseolus* (Grayish pygmy rice rat), *O. victus* (St. Vincent pygmy rice rat), *O. andinus* (Andean pygmy rice rat) and *O. arenalis* (Sandy pygmy rice rat) require exhaustive review. The sister species to all remaining entities in the genus was *O. microtis*, suggesting an Amazonian origin for the genus.

There are currently more than 80 genotypes of hantavirus circulating worldwide, being eight recognized causes of HCPS in Brazil: ANDV (*Necromys lasiurus*), ARQV (*Necromys lasiurus*), JUQV (*Oligoryzomys nigripes*), ARAV (*Necromys lasiurus*), LANV (*Calomys microtis*, *C. callidus*), CASV (*Oligoryzomys utiaritensis*), ANJV (*Oligoryzomys mattogrossae*) and RIOMV (*Oligoryzomys microtis*)^{27,45}.

PATHOGENIC HANTAVIROSES AND ITS RESERVOIRS

Despite several reports involving hantavirus throughout the world, the history of this virus is very long and more than two decades ago, the etiological agent, the HTNV virus, was isolated from the mouse *Apodemus agrarius* (striped field mouse), detected in part by binding of antibodies from patient serum samples to the lung tissues of wild rats captured in the wild and to *Rattus norvegicus* (Brown rat), the host species of the SEOV virus, discovered in 1980, which are predominant reservoirs in nature and in residential areas⁴⁷ also found in other rodent genera such as: *Akodon*, *Necromys*, *Oligoryzomys* and *Calomys*.

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In 2009, in a study conducted in Buenos Aires, Argentine researchers identified Black rats (*Rattus rattus*) in residential and industrial areas, while House mice (*Mus musculus*) and Brown rats (*Rattus norvegicus*) were captured in green areas and slums in that region. , the presence of rodents was favored by the availability and ease of shelter and food⁴⁸, showing the danger of these animals in close proximity to humans.

The disease was associated with infection by the recently discovered Sin Nombre virus (SNV), and its reservoir host the rodent *Peromyscus maniculatus*⁴⁹. The identified virus represented the type species of the family Bunyaviridae, although the first hantavirus to be isolated was the Thottapalayam virus (TPMV) transmitted by shrews *Suncus murinus* (Asian house shrew), in India in 1964, according to Schmaljohn⁵⁰.

Hantavirus studies and analyzes continue at full pace, with the identification of SNV in 1993, around 43 genotypes were reported in related studies in the Americas, associated with clinical cases of HCPS⁵¹. The HV genotype is very abundant, more than 50 confirmed types of HV are currently known, of which at least 28 types can cause human disease, each of them is strictly associated with a unique rodent host, which belongs to one of the three rodent subfamilies^{22,52}.

Mammals such as rodents, bats, shrews and moles are known as reservoir hosts. Although persistent infection may establish and high titers of neutralizing antibodies may accumulate, these reservoirs remain asymptomatic after infection^{31,53}.

The families of rodents from the order Rodentia, from the families Muridae and Cricetidae, which encompass the subfamilies Murinae, Arvicolinae, Neotominae and Sigmodontinae, are the main reservoirs of this viral agent^{51,54,55} (Figure 2). On the American continent, the main reservoirs are wild rodents of the order Rodentia, family Muridae and subfamilies Sigmodontinae and Neotominae. On the Asian and European continents, the main rodents involved belong to the Muridae family and the subfamilies Murinae and Arvicolinae⁵⁵ (Table 1). More currently, they are known to be home to multiple species of shrews and moles (order Eulipotyphla, families Soricidae and Talpidae) throughout Europe, Asia and North America⁵⁶ and also the order Chiroptera⁵⁵ (Table 1).

In evolutionary history, hantaviruses are often considered to have codiverged with their rodent hosts over timescales of millions of years⁵⁷. Other insectivorous mammals from the Soricidae (shrews) and Talpidae (moles) families have shown that the genetic diversity of hantaviruses in associating with a range of hosts across the three continents is great⁵¹.

Rodents of the genus *Apodemus* carry the Hantaan (HTNV), Amur (AMRV), Soochong (SOOV) and Dobrava-Belgrade (DOBV) viruses. The species *Rattus norvegicus*, *R. rattus*, *R. flavipectus* (Buff-breasted rats), *R. losea* (Lesser ricefield rat) and *R. nitidus* (Himalayan field rat), are important reservoirs of the Seoul virus (SEOV). The *Bandicota indica* species carries the Thailand virus (THAIV) and the *Myodes glareolus* (Bank rat) species is a reservoir for the Puumala virus (PUUV). The Tula virus (TULV) has been found in rat species of the genus *Microtus* and in rats of the species *Arvicola amphibius* (European water vole) and *Lagurus lagurus* (Steppe lemming). Rats of the species *Peromyscus maniculatus* carry the Sin Nombre virus (SNV), while the Black Creek Canal (BCCV) and Muleshoe (MULV) viruses have been found in the species *Sigmodon hispidus* (Table 1). The Andes virus (ANDV) and its variants have been isolated in rodents of the genera *Akodon* and *Necromys* and *Oligoryzomys* in South America³⁹. The specimens mentioned belong to the families Muridae, Cricetidae and subfamilies Murinae, Arvicolinae, Neotominae (Figure 2).

The Laguna Negra virus (LANV) was detected in rats of the species *Calomys laucha* (Small vesper mouse) and *Calomys callidus* (Crafty vesper mouse), while the Rio Mamoré virus (RIOMV) infects rodents of the genus *Oligoryzomys*. The Bayou virus (BAYV) infects the species *Oryzomys palustris*, the Cano Delgadito virus (CADV) occurs in the species *Sigmodon alstoni* (Alston's cotton rat), the Choclo virus (CHOV) has been detected in the species *Oligoryzomys fulvescens*, the Sangassou virus (SANGV) was found in African wood mice, species *Hylomyscus simus* (African wood mice)³⁹. All rodents represent the family Cricetidae and subfamily Sigmodontinae, except *Hylomyscus simus* belonging to the family Muridae and subfamily Murinae (Table 1).

Among the viruses and hosts that circulate in Brazil are the Araraquara virus (ARAV), host *Necromys lasiurus*, Castelo dos Sonhos virus (CASV), host *Oligoryzomys utiaritensis* (Utiariti pygmy rice), Juquitiba virus (JUQV), host *Oligoryzomys nigripes*, virus Anajatuba (ANAJV), host *Oligoryzomys fornesis*, Rio Mearim virus (RIMEV), host *Holochilus sciurus*, Laguna Negra virus (LANV), host *Calomys* aff. *Callosus* (Large vesper mouse), Jaborá virus (JABV), host *Akodon montensis* (Montane grass mouse), Rio Mamoré virus (RIOMV), host *Oligoryzomys microtis*³⁷. In this sequence, rodents belong to the Cricetidae family and Sigmodontinae subfamily (Figure 1).

Hantavirus Cardiopulmonary Syndrome (HCPS) is a disease with high human fatality rates, a study on the abundance of rodents in the Atlantic Forest, linked forest restoration and zoonotic diseases, where these researchers observed that forest restoration can reduce abundance of species carrying the virus such as *Oligoryzomys nigripes* (JUQV) in up to 89.29% in 43.43% of the Atlantic Forest territory. For *Necromys lasiurus* (ARAV), abundance decreased by up to 46% in 44% of the Atlantic Forest⁴¹.

The various hantaviruses known to date follow the geographic distribution of their respective reservoirs. The series of cases and the geographic distribution of positive rodents outline a route of occurrence of SCPH (The Center for Food Security & Public Health) cases for Brazil, probably caused by different hantaviruses and associated with different reservoir rodent species (Figure 1).

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NEW POSSIBLE HOSTS FOR HANTAVIRUS

Bats are hosts to many viruses with zoonotic potential and are receiving increasing attention as reservoirs of human transmission in wildlife. However, the role of co-infection in the dynamics of virus transmission in bats is unknown.

Several records have reported that bats can also be infected with hantaviruses, but the participation of these mammals in the epidemiological cycle of the disease has not yet been well established, as some hantaviruses have not yet had their pathogenicity determined in animals and may be apathogenic²⁸. Therefore, many hantaviruses may go unnoticed, as infections will probably go unreported in many areas, particularly in Africa, the Middle East, Central America, the Indian subcontinent and Mongolia, emphasizes Jiang³¹.

Despite being mistakenly considered winged rats, bats have a much greater geographic dispersal capacity than rodents, consequently leading to human outbreaks of viruses carried through their feces, urine and saline; Currently, some considerations regarding these facts are also limited to bat species.

Bats are present throughout the world, with the exception of some very cold regions, playing an important ecological role, mainly in regulating the insect population and pollination of flowers. These mammals are reservoirs of most viruses with zoonotic potential, being more than 200 different viruses found in these animals, such as the agents of rabies, Ebola, SARS-CoV and NiV⁵⁸.

Brazilian researchers⁵⁹ in Northeast Brazil isolated the rabies virus (RABV) in bats Phyllostomidae, Molossidae and non-human primates of the family Callitrichidae (*Callithrix jachus*), emphasizing the urgent need to implement an epidemiological surveillance platform at the phylogenetic scale to track multiple RABV variants that may pose a threat to both humans and animals.

In 2012, only two human-pathogenic hantaviruses were reported in bats from the families Vespertilionidae and Rhinolophidae. First report discovering viral antigens and isolating HTNV from two widely distributed insectivorous species: *Eptesicus serotinus* and *Rhinolophus ferrumequinum*⁶⁰. Sabino-Santos and collaborators⁶⁰ and Araújo⁶¹ presented evidence of a lethal genotype of Andes orthohantavirus (ANDV), Araraquara orthohantavirus (ARQV). Researchers from São Paulo⁶² confirmed serological evidence by isolating ARQV in bats of the species *Molossus molossus*, *Glossophaga soricina* and *Eumops glaucinus* in the urban area of the city of São Paulo/Brazil. (Table 1).

However, in 2013, Chinese researchers⁵⁵ described four new hantaviruses Huangpi virus isolated from *Pipistrellus abramos*; Longquan virus isolated from *Rhinolophus affinis*, *Rhinolophus sinicus* and *Rhinolophus monoceros*; Lianghe virus isolated from *Anourosorex squamipes* and Yakeshi virus isolated from *Sorex isodon* sampled from mammalian species in China and which are distinct from other known hantaviruses. Studies⁵² suggest that bats are likely important hosts for hantaviruses, demonstrating that the order Chiroptera are sources of a wide variety of emerging pathogens, including coronaviruses, filoviruses, henipaviruses, lyssaviruses and arenaviruses.

These expectations were demonstrated by Anthony⁶³ where the identification of coexisting microorganisms is important for the description of the virodiversity that can occur in bats, the support capacity within the bat host and potentially these viral forms can spread to a new host from a single exposure event. Vaheri and collaborators⁵³ emphasize that hantaviruses apparently coevolve with their hosts.

In Brazil, in 2012, in a region of the Atlantic Forest, researchers from São Paulo⁶¹ detected Araraquara hantavirus (ARAV) genomes by RTq-PCR technique in two species of Phyllostomidae bats *Diphylla ecaudata* and *Anoura caudifer* and in three species of marsupials *Micoureus paraguayanus*, *Monodelphis ihering* and *Didelphis aurita*, all from the Didelphidae family. Sumibcay⁶⁴ also reported the detection of Hantavirus in liver tissue from two *Neoromicia nanus* bats, captured in sub-Saharan Africa, where sporadic outbreaks of Ebola Virus Disease (EVD) and Marburg Virus Disease (MVD) normally occur and are limited to sub-Saharan African countries.

Not long ago²⁷, studies showed the isolation of a serotype in neotropical bats in Brazil, the frugivore *Carollia perspicillata* and the common vampire *Desmodus rotundus*. DNA sequencing showed high similarity with the genome of the Araraquara orthohantavirus (ARQV), which belongs to one of the most lethal hantavirus clades, and the Andes virus (ARQV) detected in the blood, urine and organs of *Desmodus rotundus* (Table 1).

In 2010, in the city of Taiwan, researchers carried out a clinical and serological examination of a primate from the Hominidae family, *Pongo pygmaeus*, and detected antibodies with natural hantavirus infection while it was in captivity in the south of that city⁶⁵ (Table 1).

The epidemiological significance of many unconventional hosts may be an alarming factor, and deserves close attention, as this issue does not yet have a defined trajectory, as the threat of hantavirus strains has become worrying, as that studies reported by McElhinney and colleagues⁶⁶ showed that in the United Kingdom and Sweden, epizootic strains of Hantavirus SEOV were detected in pet rats. In 2023, Heuser and collaborators⁶⁷ also investigated the presence of Hantavirus in serology in farmed and wild rats in Germany, detecting the SEOV strain in the analyzed samples, mitigating transmission to the human population.

Although we know that rodents are the main reservoir of this infectious agent; Antibodies against hantavirus have also been found in domestic and wild animals, such as dogs, cats, cattle, pigs, armadillos, bats, marsupials and deer species.

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Domestic animals and rodents live in close proximity to habitats, therefore, transmission from rodents to domestic animals seems possible, where hantavirus endemic regions have been found, as the capture of rodents by these animals promotes contact of infected organs and tissues, making Domestic animals are targets for contamination, as they have sufficient and adequate viral receptors for the entry and replication of these infectious viral agents. The same happens with birds of prey, owls, hawks and eagles that feed on contaminated rodents, which can become infected through contact and food.

An epidemiological cycle was observed with deer mice (*Peromyscus* spp.), consumed in raptor bird nests. Contamination in humans can occur when bird banders come into contact with these birds, running the risk of contracting disease when handling wild vertebrates or climbing into nests for abduction^{68,69} as contact with feces, urine and saliva released by rodents are sources of environmental contamination, in situations where humans come into contact with rodents, such as in professional activities (biologists, geologists, veterinarians) and construction workers. areas of deforestation and reforestation regions⁷⁰.

Ecological and environmental changes, pressures existing in nature are factors that contribute to the influence of the pathogenicity and virulence of the virus. Environmental pressures and factors contribute in a pernicious way, forcing microorganisms to adapt, adopting dangerous forms of contamination for other host species, making these microscopic beings adapted in comparison to the original hosts.

CLINICAL AND PATHOGENIC CHARACTERISTICS OF HANTAVIROSI

The emergence of hantavirus in humans is assessed by several factors that contribute to the persistence of the infection, such as: external environmental factors (temperature, precipitation, relative humidity), soil removal, urbanization quality index, temperature and dryness of the surrounding vegetation, which play significant roles in the density of reservoir hosts and the level of exposure to infectious viruses⁷¹. Another study reported that risk factors for HCPS in South America include being male, engaging in outdoor activities, involvement in agriculture, and living in rural areas²².

Brazilian researchers⁷² investigated rural settlements in Goiás/Brazil and found a 2.57% positive rate for Orthohantavirus, equally distributed between women and men. On the other hand, Santos *et al.*⁷³ similar studies, in the Central-West region of Brazil, demonstrated a higher frequency in men due to their risk behaviors, SCPH affects men in the productive age group and, therefore, is considered a disease occupational. Of the cases reported between 2012 and 2023, in Brazil, males represent 75.7%, with the most affected age groups being, in the case of men, 20-34 years (39.6%), 35-49 years. (33.4%) and 50-64 years old, in that order.

For HFRS infections, as well as Epidemic Nephropathy (EN), a febrile period with incubation ranging from 10 days to 6 weeks presenting: myalgia, headache, abdominal pain and malaise, in addition to neurological, ocular, cardiovascular and gastrointestinal symptoms, are verified⁷⁴.

Hemorrhage can occur as an injection into the conjunctiva and mucosa, presenting vascular leakage, which is often associated with thrombocytopenia, shock and, in a proportion of cases, mental confusion. After the subsequent diuretic phase, which can last months, the convalescence phase begins. The severity and fatality rates of HFRS depend on the causative strain, with Hanntan (HTNV) and Dobrava-Belbrado (DOBV) reaching approximately 10% and 5%, respectively^{53,75}. HFRS due to the Seoul strain (SEOV) can reach a case fatality rate of 2%, while NE induced by the Puumala strain (PUUV) leads to death in 0.08% to 0.4% of patients⁵³.

Hantavirus infection leads directly or indirectly to the activation of signaling pathways and the dysregulation of immune cells, such as CD4+ T cells and CD8+ T cells. The inflammatory response leads to the activation of the complement system, the formation of circulating immune complexes and the secretion of multiple pro-inflammatory cytokines. These cytokines promote endothelial cell dysfunction and capillary leakage. The hemorrhage and coagulopathy appears to be a thrombosis-fibrinolysis imbalance combined with platelet deposition and dysfunction. Severe thrombocytopenia is associated with a more severe disease course in HFRS^{76,77}.

There are at least eight hantavirus genotypes associated with HCPS in Brazil: ANDV, JUQV, ANJV, LANV, ARAV, ARQV, RIOMV and CASV. However, other hantaviruses in the North and Northeast regions of the country may remain unknown. The JUQV and ARAUV serotypes are viruses, carried by *Oligoryzomys nigripes*⁷⁸. This rodent lives in the forests of the Atlantic Forest and the Araucaria forests of southern Brazil, using these environments as a breeding ground for agricultural exploitation and the timber trade. *O. nigripes* is believed to approach and become infected by human hantaviruses when living in natural habitats bordering logging regions⁷⁹.

In the central region of Brazil, in Mato Grosso, an increasing number of HCPS cases in indigenous communities have been registered in different regions. These areas are surrounded by agricultural cities and are responsible for 75% of cases of the disease in the state⁸⁰. The disease scenario has to do with agribusiness in regions of high production, agricultural activities and urban expansion towards the savannah areas that have been favoring the spread of hantavirus. The association of grains produced, agricultural production residues, generating abundant food and the presence of wild rodents in the region are factors that interconnect this epidemiological chain.

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Related studies in the southeastern region of Brazil corroborate this information, and report that changes in the Cerrado ecosystem due to agricultural activities allow for the maintenance of rodent populations and reservoirs of the HCPS virus⁸¹, also associated with existence of environmental degradation due to deforestation of forests and flooding to build dams, forcing wildlife to occupy small extensions of land, concentrating potential reservoirs and contributing to the spread to other animals and humans⁶¹.

Unlike other members of the Bunyaviridae, hantaviruses are not vector-borne, but are transmitted between their vertebrate hosts through aggressive interactions or the inhalation of excreta. These rodents are the main hosts responsible for the transmission of hantavirus in the tropical forests, savannas and humid areas of South America, which have wide radiation in the Neotropical regions and a large number of species with diverse morphological and ecological variations, covering the Amazon, Cerrado and Atlantic Forest. These rodents can transmit different hantaviruses, such as the lethal and emerging SCPVH-causing Orthohantavirus Araraquara (ARAV), and host populations can promote factors that drive variations that influence the dynamics of hantavirus transmission within and between populations⁴⁵.

CONCLUSION

In recent decades, despite intensive research and the extraordinary efforts of modern medicine to eradicate infectious diseases, a number of previously unknown or underestimated pathogens have become a fundamental threat to human health. In the wake of the COVID-19 pandemic, there is a lot of attention and need to understand emerging zoonotic diseases and how we should be prepared for the next pandemic.

Epidemiological surveillance of communicable diseases is one of the most traditional activities related to health. The distribution of pathogens and pathogens is expanding and the differences between “Old World” and “New World” viruses are gradually becoming less obvious. During the last decades, several outbreaks of emerging and re-emerging viral pathogens on the planet have affected human population conditions worldwide. Examples include records of infections such as the hepatitis C virus, Ebola virus, influenza A, H1N1 influenza and, more recently, the difficulties caused by Severe Respiratory Syndrome (SARSCov-2), which have challenged prevention and control measures in healthcare systems. public, leading the scientific community and the medical community to clarify their uncertainties and accelerate knowledge on these groups of infectious microorganisms. Wild species play a key role in the emergence of diseases, providing a “zoonotic reservoir” from which previously unknown pathogens can emerge.

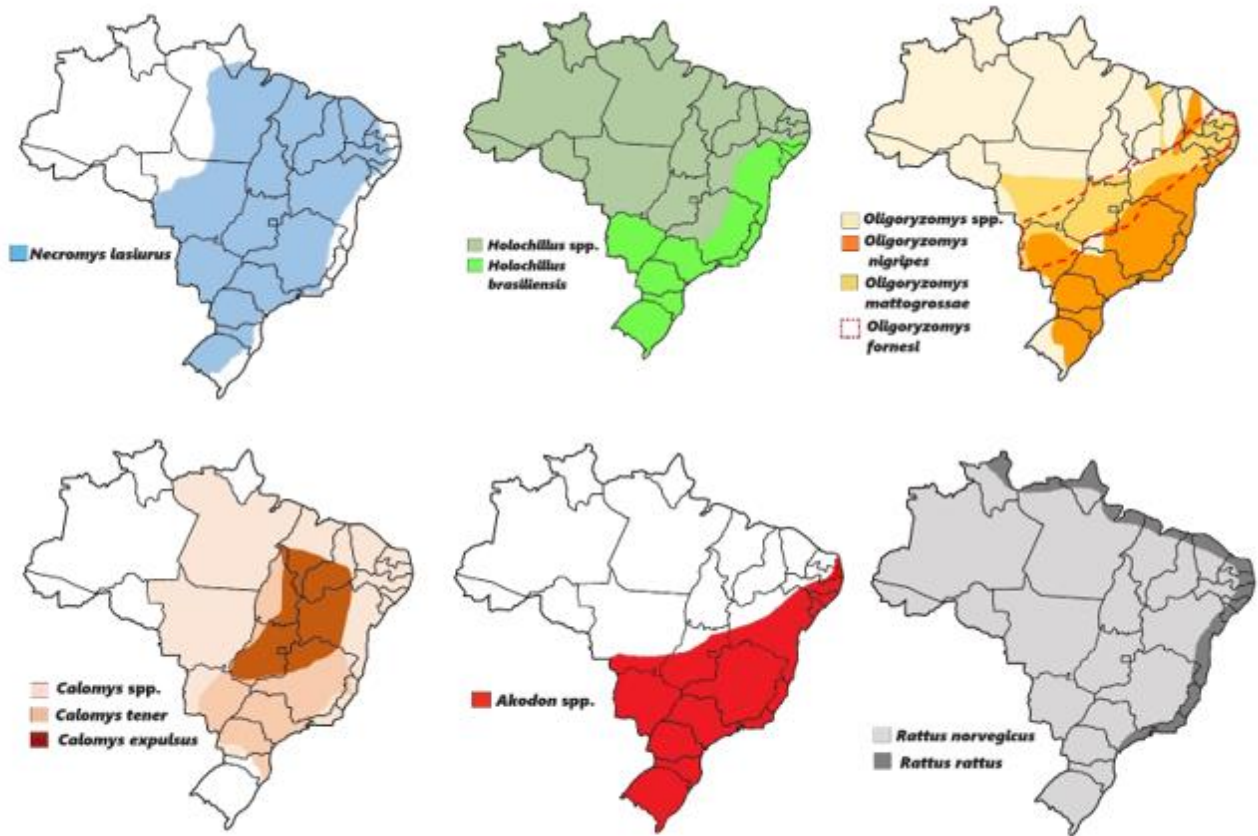
Epidemiological surveillance of infectious diseases is one of the most traditional activities related to health. The distribution of pathogens and pathogens is expanding, and the distinction between “old world” and “new world” viruses is becoming increasingly blurred. Over the past decade, several outbreaks of viral pathogens that have emerged and resurfaced on Earth have affected the condition of humanity and the entire world. Clear examples of these manifestations include the challenges posed by documented infections such as hepatitis C virus, Ebola virus, influenza A, H1N1 influenza and, more recently, severe respiratory syndrome (SARSCoV-2), which defy safety measures. prevention and control of health systems, forcing society, science and the medical community to clarify uncertainties and accelerate knowledge about this group of infectious microorganisms. Wild species play an important role in disease outbreaks by providing “zoonotic reservoirs” from which previously unknown pathogens can emerge.

However, in the last century, outbreaks of several virus-related diseases have emerged or resurfaced, such as the geographic distribution of the West Nile virus, the strengthening of hantaviruses and arenaviruses and the permanence and prolongation of Dengue and other arboviruses such as Zika and Chincungunya. Among zoonotic diseases, small mammals, rodents and bats are the main targets and preferred hosts of several pathogenic viruses, especially infections caused by Hantaviridae, Arenaviridae and Bunyaviridae.

Phylogenetic analyzes suggest that these pathogens may have first appeared in bats, before spreading to rodents, although rodents are currently the best-documented hosts of this viral group. However, although many processes that occur during the pathogenesis of New World hantaviruses may be similar, specific information about the pathogenesis of these viruses is beyond the scope of this review.

With purpose, health surveillance is configured as a set of actions that provide knowledge and detection of any change in the determining and conditioning factors of the environment that interfere with human health, with the purpose of recommending and adopting prevention and control of risk factors and related diseases or injuries. In possession of the aforementioned concepts of health surveillance and social determinants, it is opportune to complement these with the One Health approach. Recently, it has gained prominence and coverage in the face of growing concern about emerging and re-emerging zoonoses and to the detriment of raising awareness about human diseases of animal origin and the multiple diseases that remain zoonotic.

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Source: Based on information from Milholland et al., 2018; Mendes-Oliveira & Miranda, 2015; Bonvicino et al., 2008; Brazil, 2002.

Figure 1. Geographic distribution maps of the main genera and species of rodents in Brazil.

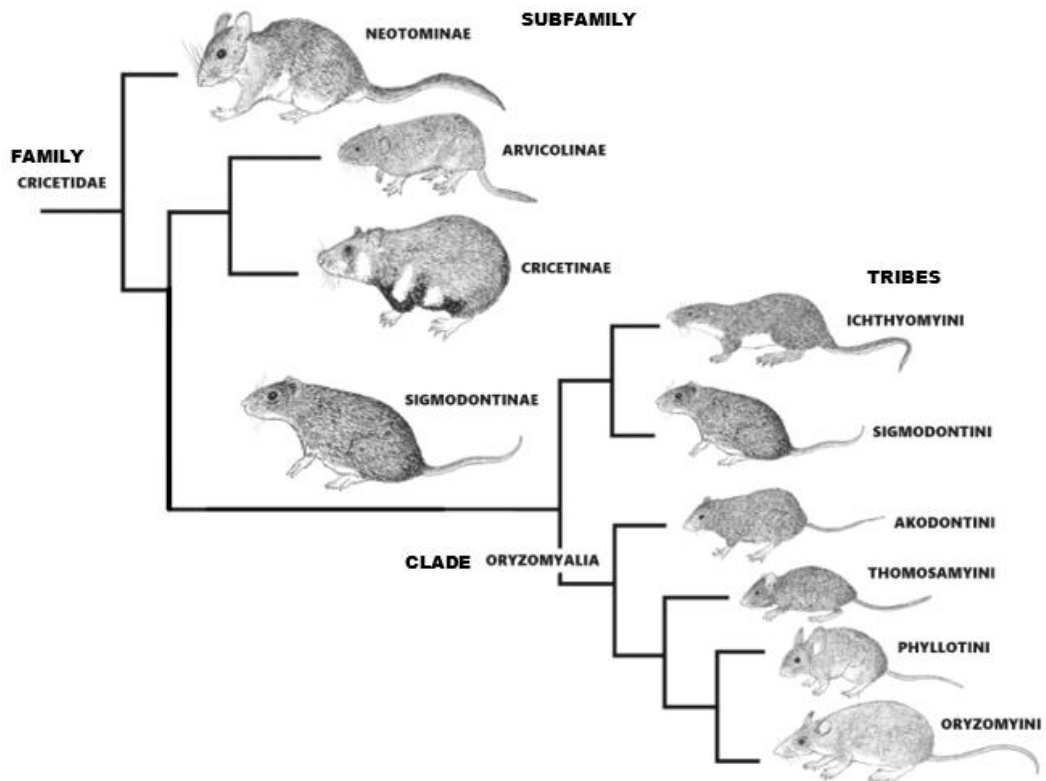


Figure 2. Simplified cladogram of the Cricetidae family, showing the main sigmodontinae lineages portrayed in this study.
 Source: Scientific American. Autor: Darren Naish. <https://blogs.scientificamerican.com/tetrapod-zoology/the-sigmodontines/>

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Table 1. Geographic distribution associated with Hantavirus diseases and their main transmitting species belonging to the Orders Rodentia, Eulipotyphla (Soricomorpha), Chiroptera, Didelphimorphia and Primate and their respective subfamilies.

OLD WORLD - Order: Rodentia (mice and rats)					
Orthohantavirus Sorotype	Acronym	Family/Subfamily	Geographic Distribution	Rodent Host Scientific name	Associated Disease
Amur vírus	AMRV	Muridae/ Murinae	Russia	<i>Apodemus peninsulae</i>	HFRS
Anjzorobe virus	ANZV	Muridae/ Murinae	Madagascar, Cambodia, Chile, China	<i>Rattus rattus</i>	Unknown
Anjzorobe virus	ANZV	Nesomyidae/ Neosomyinae	Madagascar	<i>Eliurus majori</i>	Unknown
Da Bie Shan virus	DBSV	Muridae/ Murinae	China	<i>Niviventer confucianus</i>	Unknown
Dobrava-Belgrade vírus	DOBV	Muridae/ Murinae	Balkans, Turkiye, Russia, Czech	<i>Apodemus flavicollis, A. ponticus, A. sylvaticus</i>	HFRS
Gou virus	GOUV	Muridae/ Murinae	China	<i>Rattus rattus, R. novergicus, R. tanezumi</i>	HFRS
Hantaan vírus	HTNV	Muridae/ Murinae	Russia, China, Korea	<i>Apodemus agrarius, Rattus tanezumi</i>	HFRS
Kurkino virus	KURV	Muridae/ Murinae	Germany	<i>Apodemus agrarius</i>	HFRS
Saaremaa vírus	SAAV	Muridae/ Murinae	Europe	<i>Apodemus agrarius</i>	HFRS/NE
Sangassou virus	SANGV	Muridae/ Murinae	Guinea	<i>Hylomiscus simus, H. alleni</i>	HFRS
Searang virus	SERV	Muridae/ Murinae	Indonesia	<i>Rattus tanezumi</i>	Unknown
Seoul vírus	SEOV	Muridae/ Murinae	Cosmopolita	<i>Rattus norvegicus, R. rattus</i>	HFRS
Sochi virus	SOCV	Muridae/ Murinae	Russia	<i>Apodemus ponticus</i>	HFRS
Soochong vírus	SOO	Muridae/ Murinae	South Korea	<i>Apodemus peninsulae</i>	HFRS
Thailand vírus	THAIV	Muridae/ Murinae	Thailand	<i>Bandicota indica</i>	HFRS
Tigray virus	TIGV	Muridae/ Murinae	Ethiopia	<i>Stenocephalemys albipes</i>	Unknown
OLD WORLD - Order: Rodentia (mice and rats)					
Adler virus	ADLV	Cricetidae/ Arvicolinae	Europe	<i>Microtus majori</i>	HFRS
Baviera virus	BAV	Cricetidae/ Arvicolinae	Germany	<i>Myodes glareolus</i>	HFRS
Bloodland Lake	BLLV	Cricetidae/ Arvicolinae	North America	<i>Microtus ochragaster</i>	Unknown
Fugong vírus	FUGV	Cricetidae/ Arvicolinae	China, Asia	<i>Microtus fortis, M. rufucanus</i>	Unknown
Hokkaido virus	HOKV	Cricetidae/ Arvicolinae	Japan, Sibéria, Asia	<i>Myodes rufocanus, M. rutilus</i>	HFRS/NE
Isla Vista vírus	ISLAV	Cricetidae/ Arvicolinae	North America, Mexico	<i>Microtus californicus</i>	HFRS
Khabarovsk vírus	KHAV	Cricetidae/ Arvicolinae	Russia	<i>Microtus fortis, M. maximowiczii</i>	Unknown
Luxi vírus	LUXV	Cricetidae/ Arvicolinae	China, Asia	<i>Eothenomys eleusis, E. miletus</i>	HFRS
Muju vírus	MUJV	Cricetidae/ Arvicolinae	Asia, Korea	<i>Myodes regulus</i>	HFRS
Pergamino vírus	PRGV	Cricetidae/ Arvicolinae	Central America	<i>Akodon azarae</i>	Unknown

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Prospect Hill vírus	PHV	Cricetidae/ Arvicolinae	Maryland, EUA	<i>Lemmus sibiricus, Microtus pennsylvanicus</i>	Unknown
Puumala vírus	PUUV	Cricetidae/ Arvicolinae	Americas, Escandinavia, Europe, Asia	<i>Clethrionomys glareolus,</i>	HFRS/NE
Tobetsu vírus	TOBV	Cricetidae/ Arvicolinae	Japan	<i>Clethrionomys glareolus</i>	Unknown
Topografov vírus	TOPV	Cricetidae/ Arvicolinae	Siberia	<i>Lemmus sibiricus</i>	Unknown
Tula vírus	TULV	Cricetidae/ Arvicolinae	Russia/Europe	<i>Microtus arvalis, M. rossiaemeridionalis, Lagurus lagurus</i>	HFRS
Vladivostok virus	VLAV	Cricetidae/ Arvicolinae	Russia, Asia	<i>Microtus fortis</i>	Unknown
Yuanjiang vírus	YUVJ	Cricetidae/ Arvicolinae	China	<i>Microtus fortis</i>	Unknown
NEW WORLD - Order: Rodentia (mice and rats)					
Alto Paraguay vírus	ALPV	Cricetidae/ Sigmodontinae	Paraguayan Chaco	<i>Holochilus chacoensis, H. chararius</i>	Unknown
Anajuba vírus	ANAJV	Cricetidae/ Sigmodontinae	Brazil	<i>Oligoryzomys fornesi. O. mato Grossoe</i>	HCPS
Andes vírus	ANDV	Cricetidae/ Sigmodontinae	Argentina, Chile, Uruguay, Brazil	<i>Olig. longicaudatus, Juliomys spp., Loxodontomys microtus</i>	HCPS
Ape Aime vírus	AAIV	Cricetidae/ Sigmodontinae	Eastern Paraguay	<i>Akodon montensis</i>	Unknown
Araraquara vírus	ARAV	Cricetidae/ Sigmodontinae	Brazil, Bolivia	<i>Oligoryzomys microtis, N. lasiurus</i>	HCPS
Araucaria vírus	ARAVU	Cricetidae/ Sigmodontinae	Brazil	<i>Oligoryzomys nigripes</i>	HCPS
Bayou vírus	BAYV	Cricetidae/ Sigmodontinae	North America	<i>Oryzomys palustris</i>	HCPS
Bermejo vírus	BMJV	Cricetidae/ Sigmodontinae	Argentina, Bolivia	<i>Oligoryzomys chocoensis</i>	HCPS
Black Creek Canal vírus	BCCV	Cricetidae/ Sigmodontinae	EUA, Venezuela, Peru	<i>Sigmodon hispidus</i>	HCPS
Calabazo vírus	SLCV	Cricetidae/ Sigmodontinae	Panama	<i>Zygodontomys brevicauda</i>	HCPS
Caño Delgadito vírus	CADV	Cricetidae/ Sigmodontinae	Venezuela	<i>Sigmodon alstoni</i>	HCPS
Castelo dos Sonhos vírus	CASV	Cricetidae/ Sigmodontinae	Brazil	<i>Oligoryzomys longicaudatus, O. utiaritensis, O. eliurus</i>	HCPS
Catacamas vírus	CATV	Cricetidae/ Sigmodontinae	Honduras	<i>Oryzomys couesi</i>	HCPS
Central Plata virus	CPLV	Cricetidae/ Sigmodontinae	Uruguay	<i>Oligoryzomys flavescens</i>	HCPS
Choclo vírus	CHOV	Cricetidae/ Sigmodontinae	Panama	<i>Oligoryzomys fulvescens</i>	HCPS
Hu39694 vírus	Hu39694	Cricetidae/ Sigmodontinae	Argentina	<i>Oligoryzomys flavescens</i>	HCPS
IP37/38	IP37/38	Cricetidae/ Sigmodontinae	Paraguay	<i>Oligoryzomys nigripes</i>	Unknown
Itapua vírus	ITAV	Cricetidae/ Sigmodontinae	Eastern Paraguay	<i>Oligoryzomys nigripes</i>	Unknown
Jaborá vírus	JABV	Cricetidae/ Sigmodontinae	Brazil, Paraguay	<i>Akodon montensis, A. paranaensis</i>	Unknown
Juquitiba vírus	JUQV	Cricetidae/ Sigmodontinae	Brazil, Argentina	<i>Oligoryzomys nigripes, Akodon cursor, Necromys lasiurus</i>	HCPS

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Laguna Negra virus	LANV	Cricetidae/ Sigmodontinae	Brazil, Paraguay, Bolivia, Argentina	<i>Calomys laucha</i> , <i>C. callosus</i>	HCPS
Lechiguanas virus	LECV	Cricetidae/ Sigmodontinae	Uruguay, Argentina	<i>Oligoryzomys flavescens</i>	HCPS
Maciel virus	MCLV	Cricetidae/ Sigmodontinae	Argentina	<i>Necromys obscurus</i> , <i>N. benefactus</i>	HCPS
Maporal virus	MAPRLV	Cricetidae/ Sigmodontinae	Venezuela	<i>Oligoryzomys fulvescens</i> , <i>O. delicatus</i>	Unknown
Maripa virus	MARV	Cricetidae/ Sigmodontinae	French Guiana	<i>Oligoryzomys delicatus</i>	HCPS
Muleshoe virus	MULEV	Cricetidae/ Sigmodontinae	Texas, Nebraska, EUA	<i>Sigmodon hispidus</i>	Unknown
Necocli virus	NECV	Cricetidae/ Sigmodontinae	Colombia	<i>Zygodontomys brevicauda</i>	Unknown
Oran virus	ORNV	Cricetidae/ Sigmodontinae	Argentina	<i>Oligoryzomys longicaudatus</i> , <i>O. chacoensis</i>	HCPS
Pergamino virus	PRGV	Cricetidae/ Sigmodontinae	Argentina	<i>Akodon azarae</i>	Unknown
Playa de Oro virus	OROV	Cricetidae/ Sigmodontinae	Mexico	<i>Oryzomys couesi</i>	Unknown
Rio Mamoré virus	RIOMV	Cricetidae/ Sigmodontinae	Brazil, Bolivia, Peru	<i>Oligoryzomys microtis</i>	HCPS
Rio Mearim virus	RIMEV	Cricetidae/ Sigmodontinae	Brazil	<i>Holochilus sciurus</i>	Unknown
Tunari virus	TUNV	Cricetidae/ Sigmodontinae	Bolivia, EUA, South America	<i>Oligoryzomys</i> spp.	HCPS
NEW WORLD - Order: Rodentia (mice and rats)					
Blue River virus	BRV	Cricetidae/ Neotominae	USA	<i>Peromyscus leucopus</i>	HCPS
Carrizal virus	CARV	Cricetidae/ Neotominae	Mexico	<i>Peromyscus megalopus</i> , <i>Reithrodontomys sumichrasti</i>	HCPS
Convict Creek virus	COCV	Cricetidae/ Neotominae	USA	<i>Peromyscus maniculatus</i> , <i>Microtus californicus</i>	HCPS
El Moro Canyon virus	ELMCV	Cricetidae/ Neotominae	EUA, Mexico	<i>Reithrodontomys megalotis</i>	Unknown
Huitzilac virus	HUIV	Cricetidae/ Neotominae	Mexico	<i>Reithrodontomys megalotis</i>	Unknown
Limestone Canyon virus	LSCV	Cricetidae/ Neotominae	North America	<i>Peromyscus boylii</i> , <i>P. ochraverter</i> , <i>P. spicilegus</i>	Unknown
Monongahela virus	MGLV	Cricetidae/ Neotominae	North America, Canada	<i>Peromyscus leucopus</i> , <i>P. maniculatus</i>	HCPS
Montano virus	MTNV	Cricetidae/ Neotominae	Mexico	<i>Peromyscus beatae</i> , <i>Reithrodontomys sumichrasti</i>	Unknown
New York virus	NYV	Cricetidae/ Neotominae	North America	<i>Peromyscus leucopus</i>	HCPS
Rio Segundo virus	RIOSV	Cricetidae/ Neotominae	Costa Rica, Panama	<i>Reithrodontomys mexicanus</i> , <i>R. creper</i>	Unknown
Sin Nombre virus	SNV	Cricetidae/ Neotominae	EUA, Canada	<i>Peromyscus maniculatus</i>	HCPS
Seoul virus	SEOV	Cricetidae/ Cricetinae	China	<i>Cricetulus barabensis</i>	HFRS
Order: Eulipotyphla (Soricomorpha) (Shrews, moles and hedgehogs)					
Orthohantavirus Serotype	Sigla*	Family/Subfamily	Geographic Distribution	Rodent Host Scientific name	Associated Disease

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Altai virus	ALTV	Soricidae/ Soricinae	Hungary, Russia	<i>Sorex araneus, S. roboratus, S. caecutiens, S. minutissimus</i>	Unknown
Amga virus	MGAV	Soricidae/ Soricinae	Russia	<i>Sorex cecutiens</i>	Unknown
Asama virus	ASAV	Talpidae/ Talpinae	Japan	<i>Urotrichus talpoides</i>	Unknown
Ash River virus	ARRV	Soricidae/ Soricinae	Minnesota, USA	<i>Sorex cinereus</i>	Unknown
Asikkala virus	ASIV	Soricidae/ Soricinae	Europa, Czeçj Republic	<i>Sorex minutus</i>	Unknown
Azagny virus	AZGV	Soricidae/ Crocidurinae	Costa do Marfım	<i>Crocidura obscura</i>	Unknown
Boginia virus	BOGV	Soricidae/ Soricinae	Polônia	<i>Neomys fodiens</i>	Unknown
Bowé virus	BOWV	Talpidae/ Talpinae	Serra Leoa	<i>Crocidura douceti</i>	Unknown
Bruges virus	BRGV	Soricidae/ Soricinae	Europa	<i>Talpa europaea</i>	Unknown
Camp Ripley virus	RPLV	Soricidae/ Soricinae	North America	<i>Blarina brevicauda</i>	Unknown
Cao Bang virus	CBNV	Talpidae/ Talpinae	Vietnan	<i>Anourosorex squamipes</i>	Unknown
Dahonggou Creek virus	DHCV	Talpidae/ Talpinae	China	<i>Scaptonyx fuscicaudus</i>	Unknown
Fox Creek virus	FXCV	Soricidae/ Soricinae	Canada	<i>Sorex palustris</i>	Unknown
Iamonia virus	IAMV	Soricidae/ Soricinae	EUA	<i>Blarina carolinensis</i>	Unknown
Imjin virus	MJNV	Soricidae/ Crocidurinae	Korea	<i>Crocidura lasiura</i>	Unknown
Jeju virus	JJUV	Soricidae/ Crocidurinae	Korea	<i>Crocidura shantungensis</i>	Unknown
Jemez Springs virus	JMSV	Soricidae/ Soricinae	New Mexico, USA	<i>Sorex monticolus</i>	Unknown
Kathmandu virus	TPMV	Soricidae/ Crocidurinae	Nepal	<i>Suncus murinus</i>	Unknown
Kenkeme virus	KKMV	Soricidae/ Soricinae	Russia	<i>Sorex roboratus</i>	Unknown
Kilimanjaro virus	KMJV	Soricidae/ Myosoricinae	Tanzania	<i>Myosorex zinki</i>	Unknown
Lena River virus	LNAV	Soricidae/ Soricinae	Russia	<i>Sorex caecutiens</i>	Unknown
Lianghe virus	CBNV	Soricidae/ Soricinae	China	<i>Anourosorex squamipes</i>	Unknown
Longwan virus	TPMV	Soricidae/ Crocidurinae	China	<i>Suncus murinus</i>	Unknown
Nova virus	NVAV	Talpidae/ Talpinae	Hungary	<i>Talpa europaea</i>	Unknown
Oxbow virus	OCBV	Talpidae/ Talpinae	North America	<i>Neurotrichus gibbsii</i>	Unknown
Powell Butle virus	PWBV	Soricidae/ Soricinae	EUA	<i>Sorex vagrans</i>	Unknown
Qiandao Lake virus	QDLV	Soricidae/ Soricinae	EUA	<i>Sorex cylindricauda</i>	Unknown
Rockport virus	RKPV	Talpidae/ Talpinae	USA	<i>Scalopus aquaticus</i>	Unknown
Sarufutsu virus	SRFV	Soricidae/ Soricinae	Japan	<i>Sorex unguiculatus</i>	Unknown
Seewis virus	SWSV	Soricidae/ Soricinae	Europa, Sibéria	<i>Sorex araneus, S. daphaenodon, S. tundrensis</i>	Unknown
Tanganya virus	TGNV	Soricidae/ Crocidurinae	Guinea	<i>Crocidura theresae</i>	Unknown
Thottapalayam virus	TTPV	Soricidae/ Crocidurinae	India, China, Nepal, Vietnam	<i>Suncus murinus</i>	Unknown
Tualatin River virus	TLNV	Soricidae/ Soricinae	EUA	<i>Sorex trowbridgi</i>	Unknown
Uluguru virus	ULUV	Soricidae/ Myosoricinae	Tanzania	<i>Myosorex geata</i>	Unknown

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Xinyi virus	XYIV	Soricidae/ Soricinae	Taiwan	<i>Anourosorex yamashinai</i>	Unknown
Yakeshi virus	YKSV	Soricidae/ Soricinae	Asia	<i>Sorex isodon</i>	Unknown
Order: Chiroptera (Bats)					
Orthohantavirus Sorotype	Sigla*	Family/Subfamily	Geographic Distribution	Host Scientific name	Associated Disease
Andes virus	ANDV	Rhinolophidae/ Rhinolophinae	Brazil	<i>Rhinolophus ferrumequinum</i>	Unknown
Andes virus	ANDV	Vespertilionidae/ Vespertilioninae	Brazil	<i>Eptesicus serotinus</i>	Unknown
Araraquara virus	ARQV	Phyllostomidae/ Phyllostominae	Brazil	<i>Phyllostomus hastatus</i>	Unknown
Araraquara virus	ARQV	Phyllostomidae/ Carollinae	Brazil	<i>Carollia perspicillata</i>	Unknown
Araraquara virus	ARQV	Phyllostomidae/ Desmodontinae	Brazil	<i>Desmodus rotundus</i>	Unknown
Araraquara virus	ARQV	Phyllostomidae/Glossophaginae	Brazil	<i>Glossophaga soricina</i>	Unknown
Araraquara virus	ARQV	Vespertilionidae/Vespertilioninae	Brazil	<i>Molossus molossus</i>	Unknown
Araraquara virus	ARQV	Molossidae/ Molossinae	Brazil	<i>Eumops glaucinus</i>	Unknown
Araraquara virus	ARQV	Phyllostomidae/ Desmodontinae	Brazil	<i>Diphylla ecaudata</i>	Unknown
Araraquara virus	ARQV	Phyllostomidae/ Glossophaginae	Brazil	<i>Anoura caudifer</i>	Unknown
Araraquara virus	ARQV	Phyllostomidae/ Stenodermatinae	Brazil	<i>Dermanura gnoma</i>	Unknown
Huangpi virus	HUPV	Vespertilionidae/ Vespertilioninae	China	<i>Pipistrellus abramos</i>	Unknown
Laibin virus	LBNV	Emballonuridae/ Taphozoinae	China	<i>Taphozous melanopogon</i>	Unknown
Longquan virus	LQUV	Rhinolophidae/ Rhinolophinae	China	<i>Rhinolophus sinicus, R. affinis, R. monoceros, R. pusillus</i>	Unknown
Magboi virus	MGBV	Nycteridae	Sierra Leone	<i>Nycteris hispida</i>	Unknown
Mouyassue virus	MOYV	Vespertilionidae/ Vespertilioninae	Costa do Marfim	<i>Neoromicia nanus</i>	Unknown
Xuan Son virus	XSV	Hipposideridae/ Hiposiderinae	Vietnam	<i>Hipposideros pomona</i>	Unknown
Order: Didelphimorphia (opossums)					
Orthohantavirus Sorotype	Sigla*	Family/Subfamily	Geographic Distribution	Host Scientific name	Associated Disease

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Araraquara vírus	ARQV	Didelphidae/ Didelphinae	Brazil	<i>Micoureus paraguayanus</i>	Unknown
Araraquara vírus	ARQV	Didelphidae/ Didelphinae	Brazil	<i>Monodelphis ihering</i>	Unknown
Araraquara virus	ARQV	Didelphidae/ Didelphinae	Brazil	<i>Didelphis aurita</i>	Unknown
Order: Rodentia (squirrels and marmots)					
Orthohantavirus Sorotype	Sigla*	Family/Subfamily	Geographic Distribution	Rodent Host Scientific name	Associated Disease
Prospect Hill	PHV	Sciuridae/Xerinae	EUA	<i>Tamias dorsalis</i>	Unknown
Sin Nombre	SNV	Sciuridae/Xerinae	EUA	<i>Tamias dorsalis</i>	Unknown
Prospect Hill	PHV	Sciuridae/Xerinae	EUA	<i>Tamias quadrivittatus</i>	Unknown
Order: Primates (No-human)					
Orthohantavirus Sorotype	Sigla*	Family/Subfamily	Geographic Distribution	Host Scientific name	Associated Disease
Araraquara virus	ARQV	Atelidae/ Alouattinae	Brazil	<i>Alouatta caraya</i>	Unknown
Araraquara virus	ARQV	Cebidae/ Cebinae	Brazil	<i>Sapajus libidinosus</i>	Unknown
Araraquara vírus	ARQV	Callitrichidae/ Callitrichinae	Brazil	<i>Callithrix penicillata</i>	Unknown
Puumala vírus/Tuula virus	PUUV/TULV	Cercopithecidae/ Cercopithecinae	Germany	<i>Macaca mulatta</i> , <i>M. fascicularis</i> e <i>Papio anubis</i>	Unknown
Seoul virus	SEOV	Hominidae/Ponginae	China	<i>Pongo pygmaeus</i>	Unknown
Order: Diptera – Arthropods (mosquito)					
Orthohantavirus Sorotype	Sigla*	Family/Subfamily	Geographic Distribution	Host Scientific name	Associated Disease
Jianxia Mosquito Virus 2	JMV-2	Culicidae/ Culicinae	China	<i>Culex tritaeniorhynchus</i>	Unknown

*Nomenclature of viruses following information from the International Committee on Taxonomy of Viruses (ICTV).

HPS = Hantavirus Pulmonary Syndrome. HFRS = Respiratory Syndrome with Hemorrhagic Fever. NE = Epidemic nephropathy. Unknown = not defined associated with disease.

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