Hantavirus Disease

Hantavirus Fever, Hemorrhagic Fever with Renal Syndrome (HFRS), Nephropathia Epidemica (NE), Hantavirus Pulmonary Syndrome (HPS), Hantavirus Cardiopulmonary Syndrome, Hemorrhagic Nephrosonephritis, Epidemic Hemorrhagic Fever, Korean Hemorrhagic Fever

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Importance

Hantaviruses are a large group of viruses that circulate asymptomatically in rodents, insectivores and bats, but sometimes cause illnesses in humans. Some of these agents can occur in laboratory rodents or pet rats. Clinical cases in humans vary in severity: some hantaviruses tend to cause mild disease, typically with complete recovery; others frequently cause serious illnesses with case fatality rates of 30% or higher. Hantavirus infections in people are fairly common in parts of Asia, Europe and South America, but they seem to be less frequent in North America. Hantaviruses may occasionally infect animals other than their usual hosts; however, there is currently no evidence that they cause any illnesses in these animals, with the possible exception of nonhuman primates.

Etiology

Hantaviruses are members of the genus *Orthohantavirus* in the family Hantaviridae and order Bunyavirales. As of 2017, 41 species of hantaviruses had officially accepted names, but there is ongoing debate about which viruses should be considered discrete species, and additional viruses have been discovered but not yet classified. Different viruses tend to be associated with the two major clinical syndromes in humans, hemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary (or cardiopulmonary) syndrome (HPS). However, this distinction is not absolute: viruses that are usually associated with HFRS have been infrequently linked to HPS and vice versa. A mild form of HFRS in Europe is commonly called nephropathia epidemica.

Some of the viruses that predominantly cause HFRS include Hantaan,* Puumala,* Dobrava-Belgrade,* Seoul,* Amur-Soochong and Gou viruses. (Asterisks indicate names that are officially accepted by the International Committee on Taxonomy of Viruses.) Nephropathia epidemica is mainly caused by Puumala virus or the Saaremaa variant of Dobrava-Belgrade virus. Tula,* Thailand,* Thottapalayam,* Bowe* and Sangassou* viruses have also been implicated in a few clinical cases of HFRS or other febrile syndromes. The viruses that tend to cause HPS include Sin Nombre,* Andes,* Laguna Negra,* Rio Mamore, Muleshoe, Black Creek Canal,* Bayou,* Cano Delgadito,* Choclo,* and other named or unnamed hantaviruses. Andes virus has many variants, including some that were previously considered to be separate viruses, such as Araraquara, Bermejo, Juquitiba, Lechiguanas, Maciel, Oran and Castelo des Sonhos viruses. Monongahela and New York viruses are now considered to be variants of Sin Nombre virus; and Anajatuba and Maripa viruses are variants of Rio Mamore virus.

Some hantaviruses are not known to be pathogenic for any species.

Species Affected

Rodents, insectivores and bats

Known reservoir hosts for hantaviruses include rodents, insectivores (e.g., shrews and moles) and bats. Each virus is thought to be adapted to one or a few species, but spillover rodent, insectivore and bat hosts may not be unusual.

Members of the mouse genus *Apodemus* carry Hantaan, Amur-Soochong and Dobrava-Belgrade viruses. Norway rats (*Rattus norvegicus*) are important reservoir hosts for Seoul virus; however, this virus has also been found in other species of rats including *R. rattus* (black rats), *R. flavipectus*, *R. losea* and *R. nitidus*. Bandicoot rats (*Bandicota indica*) carry Thailand virus, and bank voles (*Myodes glareolus)* are the reservoir hosts for Puumala virus. Tula virus has been found in several species of voles in the genus *Microtus*, in the water vole *Arvicola amphibius* and in the steppe lemming (*Lagurus lagurus*). Deer mice (*Peromyscus maniculatus*) carry Sin Nombre virus, while Black Creek Canal and Muleshoe viruses have been found in cotton rats (*Sigmodon hispidus*). Andes virus and its variants occur in rodents belonging to the South American mouse genera *Akodon and Necromys* and the rice rat genus *Oligoryzomys*. Laguna Negra virus has been detected in the vesper mice *Calomys laucha* and *Calomys callidus*, while Rio Mamore infects members of *Oligoryzomys*.

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Bayou virus infects *Oryzomys palustris*, Cano Delgadito virus occurs in *Sigmodon alstoni,* Choclo virus has been detected in *Oligoryzomys fulvescens*, and Sangassou virus was found in the African wood mouse (*Hylomyscus simus*). Some hantaviruses have also been found in laboratory rats and mice, and Seoul virus has been detected in pet rats. Experimental infections have been established in various laboratory rodents including rats, mice and hamsters.

Shrews and moles carry a number of hantaviruses. The viruses currently known or suspected to cause disease include Thottapalayam virus, which infects an Asian musk shrew, *Suncus murinus*; Bowe virus, which was found in an African musk shrew, *Crocidura douceti*; and Uluguru virus, which was detected in the Geata mouse shrew (*Myosorex geata*).

Bats carry their own hantaviruses, but Hantaan virus and Andes virus (Araraquara variant) have also been reported in these animals. No bat-associated hantaviruses have been found in clinical cases in animals or humans, as of 2018.

Other animal hosts

Animals other than rodents, insectivores and bats can be incidental hosts for hantaviruses. Antibodies to hantaviruses have been found in healthy nonhuman primates housed outdoors, one suspected clinical case was reported in a pet orangutan (*Pongo pygmaeus*), and experimental infections with Puumala, Andes and Prospect Hill viruses have been established in nonhuman primates. Pigs were reported to be infected with hantaviruses in China. They were also susceptible to experimental infection. The identity of the virus used in these experiments is not clear, but it was probably Hantaan virus. Nucleic acids that may belong to Andes virus were detected by PCR in opossums of the species *Micoureus paraguayanus*, *Monodelphis ihering* and *Didelphis aurita* in South America. Virological evidence for hantaviruses has not been reported in other species; however, antibodies to these viruses have been found in cats, dogs, horses, cattle, deer, rabbits/ hares, chipmunks and moose. A Russian study found hantavirus antigens in the lungs of passerine birds, pheasants, doves, herons and owls, and at least one virus was isolated from a passerine bird.

Zoonotic potential

Hantaan, Seoul, Puumala, Dobrava-Belgrade, Sin Nombre, Andes, Laguna Negra, Rio Mamore, Muleshoe, Black Creek Canal, Bayou, Cano Delgadito, Choclo, Amur-Soochong, and Gou viruses are known to be zoonotic. Tula virus, Sangassou virus, Thailand virus, and the shrew-borne Thottapalayam and Bowe viruses have been implicated in a few clinical cases. Antibodies to Uluguru virus were detected in humans, but no clinical cases have been identified to date. Human infections with Bowe and Uluguru viruses were diagnosed by serology, and might have been caused by related viruses. Many hantaviruses have not been linked to any illnesses, but it is unclear whether this is because they are not pathogenic for humans or for other reasons. For instance, people might not be exposed to some reservoir hosts, and the species of virus is not necessarily identified in clinical cases.

Geographic Distribution

Hantaviruses occur worldwide, but the distribution of each virus is limited by the geographic range of its reservoir host(s). Species known to be hantavirus carriers may or may not be infected in a given region.

With the exception of Seoul virus, the viruses circulating in the Western Hemisphere usually cause HPS. Most clinical cases seem to be caused by Sin Nombre virus in North America and Andes virus in South America; however, other viruses can be more prevalent in some regions. Muleshoe, Bayou and Black Creek Canal viruses occur in North America, and Laguna Negra, Rio Mamore, Cano Delgadito and Choclo viruses circulate in Central and South America. In Canada and the U.S., most clinical cases tend to be reported from the western states and provinces, but hantaviruses can be found throughout North America in their reservoir hosts Seoul virus is carried by wild rats throughout the world. It has been found in pet rats in the U.S., Canada and Europe, and probably occurs in these animals in other regions.

The hantaviruses in the Eastern Hemisphere are usually associated with HFRS. Seoul virus and Tula virus can be found in both Europe and Asia, while Dobrava-Belgrade and Puumala viruses circulate in Europe, and Hantaan, Amur-Shoochong, Gou, Thailand and Thottapalayam viruses occur in Asia. There are reports of Puumala or Puumala-like viruses in rodents in Asia. Sangassou, Bowe and Uluguru viruses occur in Africa. There is currently no evidence for hantavirus-associated disease in Australia, although seropositive rodents have been reported.

Transmission

In their rodent hosts, hantaviruses are thought to be transmitted by aerosols and through intense close contact such as biting, grooming and sharing of food. Rodents can shed hantaviruses in saliva, feces and urine. Transplacental transmission does not seem to occur. Infected animals can carry hantaviruses for weeks to years, and they may remain infected for their entire life. In the laboratory, recently infected rodents tend to shed larger amounts of virus, and shedding often decreases significantly after the first 2 months. However, studies on wild populations suggest that animals may transmit some hantaviruses throughout their lifetime. Young rodents can be protected by maternal antibodies. Transmission routes in insectivores and bats may be similar to those in rodents, although few studies have been done. There is little information about hantavirus infections in other animals, but antigens were found in the urine and feces of infected pigs, and pregnant pigs seemed to pass the virus to their offspring across the placenta.

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Whether arthropods have any role in hantavirus transmission is unclear, but mites have been proposed as potential vectors for some agents. A hantavirus (thought to be Hantaan virus) was found in trombiculid mites (chiggers) and gasamid mites in China, and transovarial transmission was demonstrated in both types of mite. Gasamid mites live in rodent nests and all stages feed on these animals. Trombiculid mites occur in the environment, and their larvae feed on various vertebrates. Mites were able to transmit Hantaan virus and Seoul virus to mice in the laboratory. Suggestive evidence also comes from investigations on the prevalence of hantavirus infections and mite infestations of rodents in Asia and the effects of insecticides. There is no convincing evidence that other arthropods are involved in transmitting hantaviruses, although one study from Texas, which found RNA from Bayou virus in mites, also detected this organism in an ixodid tick.

Humans are thought to acquire hantaviruses through contact with infected rodents or their excretions. Many infections seem to occur after inhaling aerosolized dust from rodent urine, droppings or nests disturbed in an enclosed area. Some people have been infected after only a few minutes of exposure to aerosolized virus. Hantaviruses can also enter the body through broken skin, the conjunctiva and other mucous membranes, in rodent bites and possibly by ingestion. Vertical transmission is generally thought to be negligible or nonexistent in humans; however, the possibility of transmission in breast milk was suggested in South America. Some viruses can be isolated from the blood and urine of HFRS patients, and nucleic acids of Andes virus have been detected in blood, respiratory secretions, saliva and urine. However, Andes virus is the only hantavirus reported to be transmitted between people. Transmission is mainly thought to occur during the prodromal stage of the illness or shortly afterward, and it primarily affects family members or others in close contact. Nosocomial transmission of Andes virus has been reported but seems to be uncommon.

In the environment, hantaviruses can survive for a few days to several weeks at room temperature, depending on the humidity, presence of organic matter and exposure to sunlight. Dried viruses seem to lose viability within 24 hours at room temperature.

Disinfection

Hantaviruses are susceptible to many disinfectants including 1% sodium hypochlorite, 70% ethanol, 1-5% peracetic acid and Virkon®. A 10% sodium hypochlorite solution has been recommended for heavily soiled areas. Viruses in solution can be inactivated by heating to 56°C (133°F) for at least 15 minutes. Dried viruses were reported to be inactivated by 2 hours at 56°C.

Infections in Animals

Rodents, Insectivores and Bats

Most studies on hantavirus reservoirs have examined rodents and, to a lesser extent, insectivores; there is little information on these viruses in bats. The infection rate varies between sites and over time, but in some cases, up to 50% of a wild rodent population can be seropositive. Seoul virus has been found in some pet rats in Europe and North America, with seroprevalence rates up to 100% in some colonies, and direct evidence of the virus (by RT-PCR) in up to 80% of these animals. A study from South Korea reported finding antibodies to hantaviruses in 12% of rats and 23% of mice in conventional laboratory facilities and 3% of mice in barrier facilities between 1999 and 2003.

Hantaviruses are not associated with overt disease in their reservoir hosts. However, studies have reported decreased survival and lower weight gains in some wild mice and voles. Domesticated rodents may have clinical signs or lesions when they are experimentally infected with some viruses. Infant rats and mice developed severe illnesses with fatal meningoencephalitis in some of these experiments. Rats and mice over 2-3 weeks of age were unaffected in most studies, but various clinical signs, with pulmonary or renal involvement, have been seen in other species, such as Syrian hamsters. Studies in laboratory rodents administer relatively high doses of virus by injection, and may not reflect exposure to hantaviruses in nature. No clinical signs or lesions have been reported in pet rats naturally infected with Seoul virus.

Serology, immunological techniques to detect antigens, and reverse transcriptase-polymerase chain reaction assays (RT-PCR) can identify hantavirus-infected rodents. The kidneys and lungs seem to be the most reliable organs for detecting hantaviruses at necropsy. Seoul virus nucleic acids have been found in the kidneys, lungs and spleen, among other organs, in captive rats. Virus neutralization tests and ELISAs were used to detect antibodies to this virus in pet rats during some recent outbreaks in people.

To prevent infections in laboratory colonies, wild rodents being added to the colony should be quarantined and tested for hantaviruses. After pet rats caused several human illnesses in North America, rattery owners were advised to quarantine new acquisitions for a month, with serological testing before release. Methods used to control Seoul virus in infected pet rats have included euthanasia of the entire colony or testing and culling of infected animals. During a zoonotic outbreak associated with pet rats, the U.S. instituted mandatory control measures, with lifetime quarantines on rats from exposed colonies that did not test negative or eliminate the virus from the colony. Some other countries have voluntary control programs for these animals.

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Hantaviruses in Other Animals

Antibodies to Puumala and Tula virus were found in some rhesus macaques (*Macaca mulatta*), cynomolgus macaques (*Macaca fascicularis*) and olive baboons (*Papio anubis*) in a captive primate colony housed outdoors in an endemic area. All of these animals were apparently healthy and there was no history of disease that could be attributed to hantaviruses. A suspected clinical case was reported in a pet orangutan in Taipei (Taiwan), China. The illness was characterized by fever, depression/ weakness, anorexia, oliguria, dehydration, vomiting and hypothermia, with elevated liver enzymes, evidence of renal failure and anemia. Antibodies to Seoul virus or a related virus were found in samples collected 2 weeks after the onset of clinical signs, and antibody titers decreased after symptomatic treatment; however, the diagnosis could not be confirmed by detection of the virus. Intratracheal inoculation of Puumala virus into cynomolgus macaques sometimes resulted in lethargy, anorexia, and evidence of kidney disease, with mild proteinuria and/or microhematuria. Intravenous inoculation of cynomolgus macaques and a chimpanzee (*Pan troglodytes*) with Prospect Hill virus caused kidney damage with mild, transient proteinuria and azotemia. Prospect Hill virus is a North American hantavirus, found in *Microtus pennsylvanicus*, that has not been linked to clinical cases in humans. Andes virus did not cause clinical signs in experimentally infected cynomolgus macaques, although they did have transient decreases in lymphocyte numbers.

Neither experimentally infected nor naturally exposed pigs developed lesions or clinical signs. Hantavirus antigens were found in the heart, liver, lung, spleen, kidney, blood and urine of these animals, and in wastes from pigpens. Serological evidence of exposure has been reported in other animals, notably cats and dogs, which are probably exposed to hantaviruses in prey. The seroprevalence was generally 3-10% in cats and 5% in dogs, although one study found a higher rate (23%) in cats with chronic diseases. One study from the U.S. did not detect any seropositive horses, cattle or coyotes in an area where Sin Nombre virus occurs in rodents.

Infections in Humans

Incubation Period

The incubation period for HFRS can range from approximtely one to 6 weeks, while incubation periods of 1-7 weeks have been reported in HPS. Many cases of HFRS and HPS seem to become apparent in about 2-3 weeks.

Clinical Signs

Hantaviruses usually cause one of two syndromes, HFRS or HPS; however, clinical cases that have attributes of both HFRS and HPS are occasionally reported, and some people experience only a nonspecific febrile illness. Asymptomatic infections also occur.

Hemorrhagic fever with renal syndrome

HFRS primarily presents with mild to severe signs related to kidney damage. Classically, the course of the disease has been divided into febrile, hypotensive/ proteinuric, oliguric, diuretic and convalescent stages. These stages are usually more evident in severe disease, and may not be seen in mild cases.

The onset of HFRS is usually abrupt. The initial clinical signs may include fever, chills, prostration, headache and backache. Gastrointestinal signs including nausea, vomiting and abdominal pain may also be seen; in some cases, the pain can be severe enough to mimic appendicitis. There may also be other nonspecific clinical signs, such as injected mucous membranes, photophobia, a flushed face and conjunctivae, or a petechial rash, which usually occurs on the palate or trunk. Temporary visual impairment (e.g., decreased visual acuity) also occurs in some cases. The prodromal stage typically lasts for a few days to a week, and is followed by the onset of renal signs. The first stage is the proteinuric stage. Hypotension may develop during this period and can last for hours to days. Nausea and vomiting are common, and death may result from acute shock. In severe cases of HFRS, the proteinuric stage is typically followed by an oliguric phase, then a diuretic/polyuric phase as kidney function improves. Death can occur at any point, but it is particularly common during the hypotensive or oliguric stages. Kidney failure may occur in severe cases.

Some patients with HFRS also have lung involvement, typically to a lesser extent than in HPS. In many cases, it is limited to mild pulmonary signs or abnormalities on X-ray (especially pleural effusion); however, serious signs including pulmonary edema and impaired pulmonary function are possible. Occasionally, there may be neurological signs, including meningoencephalitis, or clinical signs related to various other organs (e.g., evidence of liver involvement). Thrombocytopenia is common, and hemorrhagic signs including petechiae, hematuria or melena may be seen, especially in more severe cases. Disseminated intravascular coagulation is possible. Full recovery may take weeks or months, but patients usually recover normal kidney function. Some researchers have proposed that chronic renal failure and hypertension might be sequelae in some individuals. Permanent neurological damage has been reported in a few cases.

Hantavirus pulmonary syndrome

Pulmonary signs predominate in HPS. This syndrome is also characterized initially by a nonspecific illness, which usually lasts for 3 to 5 days and is similar to the prodromal stage of HFRS. Respiratory distress and hypotension usually appear abruptly, with cough and tachypnea followed by pulmonary edema and evidence of hypoxia. Cardiac abnormalities such as bradycardia, ventricular tachycardia or fibrillation may also be seen. After the onset of the cardiopulmonary phase, patients can deteriorate rapidly; some may require mechanical ventilation within 24

hours. Thrombocytopenia is common and can occur as early as the prodromal stage. Hemorrhagic signs seem to be rare in patients with HPS in North America, but they are reported more frequently in South America. Kidney damage can be seen, but it tends to be mild. It appears to be more common with Andes, Bayou and Black Creek viruses. Neurological signs have been reported rarely. Although recovery is rapid and patients usually recover full lung function, convalescence may take weeks to months.

Other syndromes

Mild illnesses caused by hantaviruses can have a variety of signs and symptoms that do not necessarily resemble HPS or HFRS. A febrile, nonspecific illness similar to the prodromal stage of HPS has been reported in a region where Choclo virus is common. Some of these patients have pulmonary abnormalities on x-ray, without evidence of respiratory insufficiency; others have no radiological abnormalities, although they may have a cough. Hantaviruses have also been implicated in some cases of fever of unknown origin. One suspected Tula virus infection in a child was characterized by recurrent febrile episodes, a slightly enlarged spleen and a macular, nonpruritic rash on the torso and proximal limbs. An atypical clinical case in one person infected with Seoul virus primarily affected the liver.

Diagnostic Tests

HFRS and HPS are often diagnosed by serology. Antibody titers can usually be detected by the time the clinical signs develop, or soon afterward. Specific IgM or a rise in the IgG titer is diagnostic. ELISAs, immunochromatographic tests and immunofluorescent antibody tests (IFA) are the most commonly used serological tests, but other assays, including immunoblotting and virus neutralization, may also be available. Virus neutralization can distinguish serological reactions to different rodent-borne viruses, but the requirement for live virus limits its use. Antibodies to the hantaviruses carried in insectivores and bats may not be detected with the currently used serological tests.

Clinical cases can also be diagnosed by detecting antigens in tissues with immunohistochemistry, or viral RNA in blood, saliva and tissues with RT-PCR. Some PCR tests use species-specific primers, but tests that can detect multiple hantaviruses have also been published. Nucleic acids may not be found in some patients by the time the symptoms develop. Conversely, one study detected Andes virus nucleic acids in some household contacts before they developed symptoms or became seropositive. Virus isolation can also be used for a definitive diagnosis; however, this is uncommon, due to the risks associated with culturing these viruses. In addition, some hantaviruses have never been successfully isolated in cell culture. Isolated hantaviruses can be identified by virus neutralization.

Treatment

Supportive care is the mainstay of treatment. Intensive care may be required. Ribavirin was reported to be helpful in some cases of HFRS; however, one study of patients with nephropathia epidemica, a mild form of HFRS in Europe, found that this drug was not beneficial. Ribavirin had mixed efficacy in animal models of HPS, and trials in human patients with HPS were disappointing. Some animal models suggest that it may only be effective very early in this syndrome. The administration of antiserum to hantaviruses appeared to be promising in a recent clinical trial in South America.

Prevention

Prevention is based on avoiding exposure to hantavirus carriers and their feces, urine, bodily secretions and tissues. Many clinical cases occur after living or working in an enclosed, rodent-infested space. Cases have also been associated with agricultural activities such as harvesting crops or working with hay. Homes, sheds and other buildings should be rodent-proofed, and food should be stored securely to avoid attracting these pests. Traps or rodenticides can also be helpful. Some websites produced by government agencies, including the Centers for Disease Control and Prevention (CDC) in the U.S., have information on the safe cleaning of rodent-infested areas and droppings. Precautions include airing out the room before starting clean-up, wetting the contaminated area with commercial disinfectant or bleach, and wearing protective clothing and gloves. Wet paper towels or wet mopping are generally recommended as cleaning methods; procedures that might aerosolize the virus, such as sweeping, should be avoided. Special precautions must be taken when cleaning heavily infested areas. In the U.S., detailed advice for this situation may be obtained from health departments.

People who are occupationally exposed to rodents should take precautions to avoid exposure. Depending on the circumstances, this may include gloves, goggles, rubber boots or disposable shoe covers, coveralls or gown, and/or a respirator. Recommendations for various situations are available from CDC and other sources. Pet rat owners should be aware that they might acquire Seoul virus from these animals. Routine precautions should include hand washing after caring for rodents and before eating, drinking or preparing food, together with the avoidance of bites and scratches. Existing breaks in the skin should be covered when handling animals or their bedding and other fomites. Regular cleaning and disinfection of the animals' environment is also recommended. Additional advice and precautions are available from some government agencies and other sources (see Internet Resources). Commercial inactivated vaccines for HFRS caused by Hantaan virus and/or Seoul virus are available in South Korea and China.

Anyone who develops a febrile illness consistent with the early signs of HPS or HFRS should seek medical attention promptly, and inform the attending physician of the occupational risk. Both universal precautions and droplet precautions are now recommended when treating patients infected with Andes virus. Respirators should be used during procedures where aerosolization of virus-containing secretions and tissues is possible. People who have been in contact with someone infected with Andes virus should be monitored for prodromal symptoms.

Morbidity and Mortality

Hantavirus outbreaks are often associated with increased rodent populations or environmental factors that promote human exposure to rodents. Clinical cases are reported to be seasonal in a number of areas. For instance, HPS is more common in late spring and early summer in the U.S., while HFRS occurs more frequently in winter and spring in China.

Worldwide, approximately 150,000 to 200,000 people are estimated to be hospitalized with HFRS each year. Most of these cases occur in Asia, although several thousand illnesses are reported each year in Europe and Russia. Many of the clinical cases in Europe are caused by Puumala virus and are mild. HPS is also relatively common in some parts of South America; however, it seems to be infrequent in North America, with approximately 11-50 cases/ year reported in the U.S., and 0-13 cases/ year in Canada. Clinical cases have been identified very rarely in Africa, but are likely to be underdiagnosed. Some occupations reported to have an elevated risk of exposure to hantaviruses include rodent control workers, field biologists, farmers, forestry workers and military personnel. Activities such as camping or staying in rodent-infested cabins can also increase the risk. Clinical cases caused by Seoul virus have occasionally been associated with pet rats. Smokers appear to be at an increased risk of hantavirus- associated illnesses.

The severity of HFRS and HPS varies with the causative virus and the availability and quality of healthcare. Improved diagnosis and supportive treatments have decreased the case fatality rates for some illnesses, compared to historical reports. The case fatality rate for HFRS ranges from < 0.5% or < 1% in nephropathia epidemica caused by Puumala virus or the Saaremaa strain of Dobrava-Belgrade virus, respectively, to 12% in some other Dobrava-Belgrade virus infections. Amur virus infections are also reported to be severe. Currently, the case fatality rate is reported to be approximately 1-2% for HFRS caused by Seoul virus and 5% for cases caused by Hantaan virus. Rates as high as 10-15% were reported for Hantaan virus in the past. HPS is frequently life-threatening, with case fatality rates estimated to range from 25% to 40% for most viruses. Approximately half of all cases are reported to be fatal in parts of Brazil where Araquara and Paranoá viruses are found, which suggests that these variants might be particularly virulent. Conversely, Laguna Negra virus and Choclo virus seem to cause less severe illnesses, with reported case fatality rates of 15% and 10%, respectively.

Asymptomatic infections and mild clinical cases are suggested by the presence of antibodies in people who have no history of HFRS or HPS. Surveys have found antibodies in approximately 1-12% of the population in many parts of the world. However, seroprevalence rates can be as high as 45% in parts of South America, particularly in one region where Choclo virus circulates and many people are occupationally exposed to rodents. Asymptomatic or mild infections with Sin Nombre virus appear to be uncommon. Hantavirus exposure also seems to be low in the U.S., with studies reporting seroprevalence rates less than 1%. How many people have been exposed to Seoul virus carried by pet rats is unclear. Approximately a third of pet fancy rat owners with no apparent history of hantavirus disease were seropositive in one study in the U.K.

Internet Resources

Centers for Disease Control and Prevention (CDC). Hantaviruses
https://www.cdc.gov/hantavirus/

CDC. Rodent Control.
http://www.cdc.gov/rodents/

European Centre for Disease Prevention and Control. Hantavirus Infection
https://ecdc.europa.eu/en/hantavirus-infection

Government of Canada. Hantaviruses
https://www.canada.ca/en/public-health/services/diseases/hantaviruses.html

Public Health Agency of Canada. Pathogen Safety Data Sheets
https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment.html

Public Health England. Pet Rats, Mice, Hamsters: Reducing the Risk of Infection
https://www.gov.uk/government/publications/pet-rats-mice-hamsters-reducing-the-risk-of-infection

The Merck Manual
http://www.merckmanuals.com/professional

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*Link is defunct.

Table 1: Selected hantaviruses and associated rodent hosts

Hantaviruses Mainly Associated with HPS	
Virus	**Rodent Host(s)**
Andes virus	Oligoryzomys longicaudatus (long-tailed pygmy rice rat),
Andes Central Plata virus (Andes virus variant)	Oligoryzomys nigripes, O. nasutus, O. flavescens
Araraquara virus (Andes virus variant)	Necromys lasiurus
Bermejo virus (Andes virus variant)	*Oligoryzomys chacoensis*
Castelo des Sonhos virus (Andes virus variant)	*Oligoryzomys moojeni, O. utiaritensis*
Juquitiba virus (Andes virus variant)	*Oligoryzomys nigripes*
Lechiguanas virus (Andes virus variant)	*Oligoryzomys flavescens*
Maciel virus (Andes virus variant)	*Necromys benefactus*
Oran virus (Andes virus variant)	*Oligoryzomys longicaudatus, O. chacoensis*
Paranoa virus (Andes virus variant)	unknown
Tunari virus (Andes virus variant)	unknown
Bayou virus	*Oryzomys palustris* (rice rat)
Black Creek Canal virus	*Sigmodon hispidus* (cotton rat)
Cano Delgadito virus	*Sigmodon alstoni*
Choclo virus	Oligoryzomys fulvescens (fulvous pygmy rice rat)
Laguna Negra virus	*Calomys laucha, Calomys callidus*
Muleshoe virus	*Sigmodon hispidus* (cotton rat)
Rio Mamore virus	*Oligoryzomys microtis* (small-eared pygmy rice rat)
Anajatuba virus (Rio Mamore virus variant)	*Oligoryzomys fornesi*
Maripa virus (Rio Mamore virus variant)	unknown
Sin Nombre virus	*Peromyscus maniculatus* (deer mouse)
Monongahela virus (Sin Nombre virus variant)	*Peromyscus maniculatus*
New York virus (Sin Nombre virus variant)	Peromyscus maniculatus (deer mouse); P. leucopus (white-footed mouse)

Hantaviruses Known or Suspected to Cause HFRS or Nonspecific Febrile Illnesses	
Virus	**Rodent Host(s)**
Amur Soochong virus (related to Hantaan virus)	*Apodemus peninsulae*
Bowe virus	*Crocidura douceti* (Doucet's musk shrew)
Dobrava-Belgrade virus	*Apodemus flavicollis* (yellow-necked field mouse), *A. ponticus*
Saaremaa virus . Synonym Dobrava-Aa virus (variant of Dobrava-Belgrade virus)	*Apodemus agrarius* (striped field mouse)
Gou virus (related to Seoul virus)	*Rattus rattus* (black rat), *R. flavipectus, R. norvegicus, Apodemus sp.*
Hantaan virus	*Apodemus agrarius* (striped field mouse)
Puumala virus	*Myodes glareolus* (bank vole)
Sangassou virus	*Hylomyscus simus* (African wood mouse)
Seoul virus	Rattus norvegicus (Norway rat), R. rattus (black rat), R. flavipectus, R. losea, R. nitidus
Thailand virus	*Bandicota indica* (bandicoot rat)
Thottapalayam virus	*Suncus murinus* (musk shrew)
Tula virus	Microtus arvalis (European common vole), M. agrestis (field vole), M. subterraneus, M. levis/ M. rossiaemeridionalis (southern vole), M. gregalis, Arvicola amphibius (water vole), Lagurus lagurus (steppe lemming)
Uluguru virus	*Myosorex geata* (Geata mouse shrew)

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