THE ECOLOGY OF NEW WORLD RODENT BORNE HEMORRHAGIC FEVERS

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Abstract: Few, if any, human settlements are free of peridomestic rodent populations. The threat of rodent borne zoonotic diseases has been widely recognized since the bubonic plague outbreaks of the Middle Ages. In the last decades, outbreaks of human disease caused by the rodent borne hemorrhagic fever viruses, the arenaviruses (family Arenaviridae), and the hantaviruses (family Bunyaviridae, genus *Hantavirus*) have again generated interest in the general public and scientific community regarding the biology of these types of diseases. Recent studies have identified more than 30 new members of these two groups of viruses. Most are associated with rodents in the family Muridae and many are known to be pathogenic. Ongoing studies are investigating aspects of the ecology and systematics of these viruses and their reservoirs. Ecological studies are currently examining modes of transmission between members of the host species, and environmental factors associated with increased frequency of infection. Systematic research is identifying patterns of co-evolution between the viruses and their hosts. The overall goal of these research efforts is develop predictive models that will identify times and places of increased risk and therefore provide an opportunity for risk reduction in these areas. The information resulting from these efforts will benefit individuals who live or work in close proximity to known wild rodent reservoirs and are at risk of contracting rodent borne diseases.

Key words: Arenaviridae, arenavirus, Bunyaviridae, coevolution, hantavirus, hemorrhagic fever, hosts, Muridae, Sigmodontinae, virus, zoonoses

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INTRODUCTION

The discovery of hantavirus pulmonary syndrome (HPS) in 1993 in the southwestern United States, first generated interest in viral hemorrhagic fevers (VHF) in the Americas (Nichol et al. 1993). As a result, there has been a great increase in studies of the ecology and diversity of VHF agents in the viral families Bunyaviridae and Arenaviridae in North, Central, and South America. Of the five genera in the Bunyaviridae, only the members of the genus *Hantavirus* are associated with rodent hosts (Peters 1998). Approximately half of the known *Hantavirus* species have been associated with severe human disease. Arenaviridae is a monotypic family made up of several species in the genus *Arenavirus*. All but one are clearly associated with rodents in the family Muridae, but relatively few of these viruses have been associated

with human disease (Bausch and Ksiazek 2002). In both of these viral genera, the associated rodent species serve as the reservoir host in which chronic infection occurs often with no deleterious effect

Table 1. Rodent borne viral hemorrhagic fevers in the families Bunyaviridae and Arenaviridae. Members of the Family Arenaviridae are noted with an asterisk.

Virus	Host	Distribution of Host Species	Disease
Order Rodentia, family Muridae, subfamily Murinae			
Hantaan (HTNV)	*Apodemus agrarius (mantchuricus)*	C Europe, S to Thrace, Caucasus, & Tien Mtns; Amur River through Korea, to E Xizang & E Yunnan, W Sichuan, Fujiau, Taiwan	Severe HFRS (Lee et al. 1978)
Seoul (SEOV)	*Rattus norvegicus*	Nearly Worldwide	Mild/Moderate HFRS (Lee et al. 1982)
Dobrava (DOBV)	*Apodemus flavicollis*	England, Wales; NW Spain, France, Denmark, S Scandinavia through European Russia, Italy, Balkans, Syria, Lebanon, Israel; Netherlands	Severe HFRS (Avsic-Zupanc et al. 1992)
Saarema (SAAV)	*Apodemus agrarius (agrarius)*	C Europe, S to Thrace, Caucasus, & Tien Mtns; Amur River through Korea, to E Xizang & E Yunnan, W Sichuan, Fujiau, Taiwan.	Mild HFRS (Plyusnin and Morzunov. 2001)
Amur (AMRV)	*Apodemus peninsulae*	SE Siberia from NE China, S throughout NE China and Korea, E Mongolia to SW China, and N Japanese islands	HFRS (Yashina et al. 2001)
Lymphocytic choriomeningitis LCM*	*Mus musculus*	Worldwide	Lymphocytic choriomeningitis (Armstrong and Lillie 1934)
Lassa*	*Mastomys spp.*	Africa south of the Sahara	Lassa fever (Frame et al. 1970)
Order Rodentia, family Muridae, subfamily Arvicolinae			
Puumala (PUUV)	*Clethrionomys glareolus*	France and Scandinavia to Lake Baikal, S to N Spain, N Italy, Balkans, W Turkey, N Kazakhstan; England, SW Ireland	Mild HFRS (Nephropathia epidemica) (Brummer-Korvenkontio et al. 1980)
Order Rodentia, family Muridae, subfamily Sigmodontinae			
Sin Nombre (SNV)	*Peromyscus maniculatus*	Alaska across N Canada, S through USA to S Baja California and NC Oaxaca, Mexico	HPS (Childs et al. 1994)
New York (NYV)	*Peromyscus leucopus*	C and E USA into S and SE Canada, S to Yucatan Peninsula, Mexico	HPS (Hjelle et al. 1995)
Black Creek Canal (BCCV)	*Sigmodon hispidus*	SE USA, interior Mexico to C Panama, N Colombia and N Venezuela	HPS (Rollin et al. 1995)
Bayou (BAYV)	*Oryzomys palustris*	SE USA	HPS (Morzunov et al. 1995)
Muleshoe (MULEV)	*Sigmodon hispidus (texianus)*	SE USA, interior Mexico to C Panama, N Colombia and N Venezuela	HPS (Rawlings et al. 1996)
Monongahela (MONV)	*Peromyscus maniculatus (nubiterrae)*	Alaska across N Canada, S through USA to S Baja California and NC Oaxaca, Mexico	HPS (Song et al. 1996)

Juquitiba (JUQV)	*Unknown*		HPS (Johnson et al. 1999)
Ararquara (ARAV)	*Unknown*		HPS (Johnson et al. 1999)
Castelos dos Sonhos (CASV)	*Unknown*		HPS (Johnson et al. 1999)
Laguna Negra (LNV)	*Calomys laucha*	N Argentina and Uruguay, SE Bolivia, W Paraguay, WC Brazil	HPS (Williams et al. 1997)
Andes (ANDV)	*Oligoryzomys longicaudatus*	Andes of Chile and Argentina	HPS (Levis et al. 1998)
Lechiguanas (LECV)	*Oligoryzomys flavescens*	SE Brazil, Uruguay, Argentina	HPS (Levis et al. 1998)
Bermejo (BMJV)	*Oligoryzomys chacoensis*	W Paraguay, SE Bolivia, WC Brazil, N Argentina	HPS (Levis et al. 1998)
Orán (ORNV)	*Oligoryzomys longicaudatus*	Andes of Chile and Argentina	HPS (Levis et al. 1998)
Hu39694	Unknown		HPS (Levis et al. 1998)
Choclo	*Oligoryzomys fulvescens (costaricensis)*	W and E versants of S Mexico, throughout Mesoamerica, to Ecuador, N Brazil, and Guianas in South America	HPS (Vincent et al. 2000)
Junín*	*Calomys musculinus*	N and C Argentina E Paraguay	Argentine hemorrhagic fever (AHF) (Parodi et al. 1958)
Machupo*	*Calomys callosus*	N Argentina, E Bolivia, W Paraguay, WC to EC Brazil	Bolivian hemorrhagic fever (BHF) (Johnson et al. 1965)
Guanarito*	*Zygodontomys brevicauda*	Savannas from SE Costa Rica through Panama, Columbia, Venezuela, Guianas, to Brazil north of the Amazon River; including Trinidad and Tobago and smaller continental shelf islands.	Venezuelan hemorrhagic fever (VHF) (Salas et al. 1991)
Sabiá*	Unknown	Unknown	Not named (Coimbra et al. 1994)

*Arenaviruses

on the rodent (Mills and Childs 1998, Peters 1998, Salazar-Bravo et al. 2002). Information regarding the reservoir species and distribution of these diseases is presented in Table 1. The purpose of this report is to: 1) give an overview of the rodent-borne diseases in these two viral families, 2) discuss the ecological settings and the current known host/virus pairings in the Americas, and 3) review the precautions which can reduce exposure risk for individuals that are likely to encounter the hosts and the viruses they carry.

BUNYAVIRIDAE

Of the five genera contained in this family (*Bunyavirus*, *Hantavirus*, *Nairovirus Phelebovirus*, and *Tospovirus*) the genus *Hantavirus* is the only genus that is not known to be associated with an arthropod vector (Peters 1998). Most members of this genus are associated with reservoirs that belong to the rodent family Muridae (Peters 1998, Plyusnin and Morzunov 2001, Plyusnin 2002). One species in this group is associated with a shrew in the family Soricidae (Tang et al. 1985). Transmission of disease to humans occurs through contact

with excreta or secreta from infected rodents or inhalation of aerosolized virus from these substances (Nichol et al. 1993, Peters 1998).

Hantaviruses are associated with hemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS). The hosts of HFRS associated viruses belong to two subfamilies (Arvicolinae, Murinae) within the family Muridae. These host species are native to the Old World, although three of them (*Mus musculus*, *Rattus norvegicus* and *Rattus rattus*) now occur worldwide (Lee et al. 1978, 1982; Childs et al. 1994). Host species for HPS-associated viruses belong to the Murid subfamily Sigmodontinae and occur throughout the New World (Schmaljohn and Hjelle 1997, Hall 1981).

HFRS

HFRS, as Korean hemorragic fever, was recognized in the 1950's in Asia, with the isolation of the causative agent coming almost 30 years later. (Earle 1954, Lee et al. 1978). HFRS is mostly confined to the Old World, in the historical range of the various host species (Glass et al. 1994). There are six recognized etiologic agents of HFRS: Hantaan and Dobrava viruses cause severe HFRS, while Seoul, Sereema, Puumala, and Amur viruses are associated with mild to moderate cases. Although HFRS is by far more prevalent than HPS, it is in general, less severe in terms of mortality (Peters et al. 1999). HFRS is a suite of diseases whose duration and severity of symptoms varies with the causative virus, but the following describes the generic clinical course. This disease begins with the onset of high fever that typically occurs 2-3 weeks (range 4-42 days) after exposure. Other symptoms include chills, severe headaches weakness, general muscle aches, anorexia, nausea, and difficulty with urination. The signs of recovery typically begin 9-14 days past the onset of symptoms, with full recovery taking 3-6 weeks. The case fatality rate for HFRS ranges from 0.1% in mild cases caused by Puumala virus, to 15.0% in severe cases caused by either Hantaan, or Dobrava viruses (Bausch and Ksiazek 2002, Peters et al. 1999).

The only HFRS-associated virus known to occur in the Americas is Seoul virus. The native distribution of the host *Rattus norvegicus* (Norway r at) is Eurasia, but they have been introduced nearly worldwide. Although very little data are available regarding Seoul virus infection in the New World, there is evidence that it may be responsible for some acute disease, and a larger number of subclinical or undiagnosed cases (Glass et al. 1994).

HPS

HPS was described in 1993 following an outbreak in the four corners region of the Southwestern United States (Nichol et al. 1993). The identification and isolation of the causative agent was rapid compared to the near thirty-year lag between the recognition of HFRS and the characterization of Hantaan virus. Since the initial description and identification of Sin Nombre virus as the etiologic agent of the Four Corners' cases and *Peromyscus maniculatus* (deer mouse) as the primary reservoir host of this virus, almost thirty more viruses (usually each with a different primary reservoir) have been identified throughout the Americas (Mills and Childs 1998, Plyusnin and Morzunov 2001). Approximately half of the described American *Hantavirus* species are known to cause HPS (Table1). Current data indicate that most HPS cases occur in South America, concordant with the fact that a majority of pathogenic viruses have been described from that region (Peters 1998). Sixteen pathogenic hantaviruses have been identified in North, Central and South America. This list will no doubt increase in

the future as studies continue (CDC, unpublished data).

As with HFRS, HPS symptoms vary depending on the virus, but the generic symptoms are as follows. In most instances an incubation period of up to 21 days is followed by a non-distinct febrile prodrome lasting one to twelve days. The symptoms of this stage include fever, chills, dizziness, weakness, headache, anorexia, muscle aches, variable degrees of nausea, abdominal pain, and diarrhea. This may be followed by a rapid progression over a period of 4-24 hours of decreased blood pressure, difficulty with urination, shock, and pulmonary edema. Pulmonary edema due to vascular leakage distinguishes HPS from HFRS. Mechanical ventilation is usually required for 5-7 days. Recovery begins with the end of the fever and the passing of fluids through urination. Complete recovery requires two weeks to two months. In the United States, the case fatality for HPS is approximately 40% (Duchin et al. 1994, Peters 1998). One outbreak involving human-human transmission has been confirmed with Andes virus in Argentina (Wells et al. 1997, Padula et al. 1998) and cannot be ruled out in a second outbreak involving Andes virus in Chile (Chaparro et al. 1998).

ARENAVIRIDAE

American members of this family were first associated with human disease in the 1950's (Parodi et al. 1958). Currently 19 species in the genus *Arenavirus* are recognized, and 6 of those have been associated with disease in humans (Table 1). This family is divided geographically and phylogenetically, into Old World forms occurring in Eurasia (Ippy, Lassa, Lymphocytic Choriomeningitis, Mobala, and Mopeia viruses) and New World forms occurrring in the Americas (Amapari, Bear Canyon, Flexal, Guanarito, Junín, Latino, Machupo, Parana, Pichinde, Pirital, Oliveros, Sabiá, Tacaribe, Tamiami, and White Water Arroyo viruses) (Clegg 2002).

Only two of the Old World forms, Lassa and Lymphocytic Choriomeningitis (LCM) viruses are known pathogens. In South America; Guanarito, Junín, and Machupo, and Sabiá viruses have been associated with; Venezuelan (VHF), Argentine (AHF), and Bolivian (BHF) hemorrhagic fevers, respectively (Peters 2002). Sabiá, has been associated with a yet unnamed disease similar to AHF. In North America, only White Water Arroyo virus has been potentially associated with disease in humans (CDC 2002).

OLD WORLD ARENAVIRIDAE

Of the Old World pathogenic arenaviruses, Lassa virus causes the greatest human morbidity. Lassa fever is responsible for as many as 300,000 cases with thousands of fatalities each year in West Africa (Bausch et al. 2001). The reservoir was described as *Mastomys natalensis* (Monath et al.1974), but it is now believed that multiple *Mastomys spp.* may be involved (Britton-Davidian et al. 1995). In addition to acquiring this disease from the reservoir host, human-human transmission through direct contact with blood, tissues, or excretions of infected persons has been reported (McCormick and Fisher-Hoch 2002).

Although it can be asymptomatic or manifest by mild symptoms, LCM is of concern due to its worldwide occurrence. The natural host of LCMV is *Mus musculus* (House mouse), which is found in essentially every human settlement (Salazar-Bravo et al. 2002). The preferred habitat of this species is the peridomestic setting, which brings this rodent into frequent contact with humans. Laboratory colonies and pet stocks of Syrian hamsters have also been implicated in the spread of this virus

(Biggar et al. 1975). Some of the documented cases occurred in individuals that had been in the same room as the infected hamsters but had not been in direct contact with the animals, suggesting airborne transmission (Biggar et al. 1975). Early symptoms usually include headache, fever and nausea, with cough and chest pains in some cases. In a small minority of cases (<10%), meningitis appears within 10 days of the initial symptoms. In most cases a full recovery is expected, and the overall case fatality rate is believed to be less than 1% (Childs and Wilson 1994, Peters et al. 1996). The non-distinct symptoms and relatively low case fatality likely contribute to a gross underestimation of the annual number of cases of this disease (Jahrling and Peters 1992).

NEW WORLD ARENAVIRIDAE

Currently, the majority of the pathogens in this group are found in South America. The only potential link to human disease involving a North American *Arenavirus* occurred in the Western United States, where White Water Arroyo virus was identified in an assay based on post mortem samples (CDC 2002). Tamiami virus also has been documented in a serosurvey in the southeastern United States, but no disease has been associated with this virus (Peters 2002). Hemorrhagic fever resulting from arenavirus infection is much more frequent in South America. Before the advent of an efficacious vaccine (Peters et al. 1996), Junín virus infection caused several hundred to a thousand cases of AHF each year on the pampa of central Argentina. AHF cases now number from 10-100 per year. Inhalation of aerosolized excreta from the infected rodent reservoir is the primary mode of transmission to humans (Peters 2002). The pathogenic forms of New World arenaviruses cause hemorrhagic fever with similar symptoms. The most thorough descriptions have resulted from AHF cases. After a 1-2 week incubation period, early symptoms include fever and general muscle aches. These become more intense after 3-4 days and progress to headache, nausea, vomiting, constipation or diarrhea, abdominal pains, dizziness and disorientation. The face and chest are often flushed and severe bloodshot eyes are commonly seen. Muscle tremors involving the tongue and arms, or general convulsions may develop, and some patients become comatose. In extreme cases severe hemorrhaging occurs that often leads to fatal shock. In non-fatal cases recovery begins after approximately two weeks of initial symptoms. Without treatment the case fatality is 25-35%. For AHF, administration of immune serum from recovered patients decreases the case fatality to < 1%. The AHF vaccine has shown signs of effectiveness against some other arenaviruses (Peters et al. 1996, Peters 2002).

ECOLOGICAL SETTINGS OF RODENT BORNE HEMORRHAGIC FEVERS

In the New World, these diseases are primarily associated with rural settings, which encompass the preferred habitat of the sigmodontine hosts. The exceptions are diseases caused by LCMV and Seoul virus (Childs et al. 1992, Childs and Wilson 1994), which are associated with the introduced murid rodents (*Mus musculus* and *Rattus norvegicus*, respectively) that are widely distributed in the peridomestic setting. Data are limited regarding the incidence of these diseases in the Americas, however it is likely that these agents are responsible for a large number of "undiagnosed" illnesses (Childs et al. 1992). These introduced species often cause displacement (or local extinction) of natural resident species. Although in this case,

complete eradication would be desirable from both a public health and ecological perspective, it is unlikely that such an effort is feasible. A more practical alternative would be the implementation of a long-term integrated pest management plan for urban areas. This plan should involve rodent proofing and the elimination of suitable habitat near human residences, in conjunction with the trapping or use of rodenticides on existing rodent populations (Glass et al. 1997, Hopkins et al. 2002). This would have the added benefit of creating a cleaner living environment for the residents of the targeted areas.

In North America, HPS cases have been associated with six *Hantavirus* species maintained in four reservoir hosts; Bayou virus in the marsh rice-rat (*Oryzomys palustris*), Black Creek Canal virus in the hispid cotton-rat (*Sigmodon hispidus*), Monongahela virus in the deer mouse (*Peromyscus maniculatus*), Muleshoe virus also in the cotton-rat, New York virus in the white-footed mouse (*Peromyscus leucopus*), and Sin Nombre virus also in the deer mouse (Childs et al. 1994, Hjelle et al. 1995, Ksiazek et al. 1995, Ksiazek et al. 1997; Rawlings et al. 1996; Rollin et al. 1995) Of these species, the deer mouse has the most general habitat requirements, the broadest geographical distribution and is the most likely to enter the peridomestic environment. The remaining reservoir species are all abundant within their more restricted ranges. The white-footed mouse occurs in the eastern two thirds of the United States and the eastern third of Mexico. In this area they prefer wooded habitats but also utilize brushland in the more arid portions of the range. The hispid cotton rat prefers grassland habitats and occurs in the southeastern one-third of the United States. The marsh rice rat is the most geographically restricted of these species and occurs in wet grasslands in the southeastern United States. Although their range is smaller in area, marsh rice rats often out-number all other rodent species in these areas (Hall 1981, Wilson and Ruff 1999).

South America has a greater diversity of *Hantavirus* species that are known to be pathogenic (Enria et al. 2001). There are ten hantaviruses that have been clearly associated with human disease (Table 1). The reservoir hosts of four of these (Araquara, Castelos dos Sonhos, Juquitiba, and Hu39694) are unknown. The six remaining host-virus pairs are Laguna Negra virus in the small vesper mouse (*Calomys laucha*), Andes virus in the long-tailed pygmy rice rat (*Oligoryzomys longicaudatus*), Lechiguanas virus in the yellow pygmy rice rat (*Oligoryzomys flavescens*), Bermejo virus in the chacoan pygmy rice rat (*Oligoryzomys chacoensis*), Orán virus also in the long-tailed pygmy rice rat, and Choclo virus in the fulvous pygmy rice rat (*Oligoryzomys fulvescens*). A common thread in the biology of the recognized HPS reservoir species is their tolerance or even affinity for disturbed habitats. This characteristic facilitates the passing of pathogens from these rodents into human populations.

The control of these native New World reservoirs of hemorrhagic fevers is considerably more complicated both ethically and biologically than is controlling the urban populations of rats and mice (Mills 1999). All of the HPS reservoir species maintain native populations that are independent of human settlements. The complete eradication of these native species is neither desirable nor practical. Studies have found antibodies to *Hantavirus* and *Arenavirus* species in many host populations that have been extensively surveyed. However, antibody assays are usually non-specific and the presence of antibody does not necessarily indicate the presence of a

pathogenic strain of either of these two viral genera.

For both of hantaviruses and arenaviruses, studies show a close link in the evolution of the viruses and their hosts (Plyusnin and Morzunov 2001, Salazar-Bravo et al. 2002). This is most apparent when the host-virus phylogenies are placed side by side. It is fairly clear that an early ancestral form of *Hantavirus* was present before the division of the rodent family Muridae into the subfamilies Arvicolinae, Murinae, and Sigmodontinae approximately 30 million years ago (Plyusnin and Morzunov 2001). This history is similar in the Arenaviradae where viral clades are also divided between the Murinae and Sigmodontinae (Salazar-Bravo et al. 2002).

Ecological and laboratory investigations of the rodent hosts of hantaviruses and arenaviruses have revealed much regarding the natural history of infection in the hosts (Botten et al. 2002, Douglass et al. 2001, Glass et al. 1998, Hutchinson et al. 1998, Mills et al. 1992, Mills and Childs 1998, Sabitini et al. 1977). Males are more frequently infected than females. Older individuals are more likely to be infected than younger individuals. In all age classes, those with visible scars are more likely to be infected than are those without scarring. Once an individual rodent is infected and develops antibodies to the virus, those antibodies may persist for life. Pups borne to infected dams have maternal antibody, which is generally protective for the first few months of their life. In *Hantavirus* infections virus shedding is most intense in the first few weeks post infection, but may persist in reduced (or even sporadic) levels throughout the life of the rodent (Botten et al. 2002). When taken together, these data are quite informative regarding the nature of the host-virus relationship. The age bias and the presence of maternal antibody in juveniles indicates horizontal (transmission by contact) rather than vertical (mother to offspring) transmission patterns among post juvenile rodents. The increased frequency of antibody in males suggests that transmission is likely due to antagonistic encounters, which are more frequent between males than females. This is further supported by the correlation between scarring and antibody prevalence. Finally, field studies have revealed relationships between environmental conditions (e.g., rainfall and winter temperatures), rodent population densities, rates of inter-host transmission, and the risk of human disease (Mills et al. 1997, Yates et al. 2002). The continuation of these types of studies will contribute to the development of accurate predictive models for these and perhaps other rodent-borne diseases (Mills and Childs 1998).

EXPOSURE RISKS AND RECOMMENDED PRECAUTIONS

Recommendations for risk reduction for HPS can be found in the July 26, 2002 Morbidity and Mortality Weekly Report (Mills et al. 2002). This document can be obtained from the Centers for Disease Control and Prevention in Atlanta or on the internet: http://www.cdc.gov/mmwr/PDF/rr/rr5109.pdf. Because of the similar physical properties of the viruses and the overlapping host taxa, these recommendations can be equally applied to arenaviral diseases. The lipid envelop characteristics of hantaviruses and arenaviruses causes them to be labile in the environment outside of the cells of a living host. Additionally, it makes them easy to inactivate using household disinfectants such as Lysol or a 10% bleach solution. The following activities have been associated with elevated risks of exposure to one of these viruses: living in rodent infested structures, cleaning rodent infested structures, visiting areas with high numbers

of infected rodents, maintaining live wild-caught rodents in captivity, using contaminated (with rodent excreta) machinery and equipment, agricultural activities, and hiking or camping in areas with infected rodents. Individuals who live or work in structures with signs of rodent infestations should rodent-proof the structures, clean up rodent excreta, then use kill traps or rodenticide to remove the animals present. Rodent-proofing is conducted by sealing any holes that rodents could use to gain entry into a structure, using steel wool or wire screening. Cleaning should involve wetting the area with a disinfectant solution, using rubber gloves; then wiping or mopping (never sweeping) the area. Again wearing rubber gloves, trapped rodents should be sprayed with disinfectant, double bagged, and disposed of with the household trash. Clean up of particularly heavy rodent infestations, or buildings associated with a confirmed case of HPS should best be left to public health or pest-control professionals. In addition to the precautions outlined above, these professionals should wear coveralls, rubber boots, a fitted HEPA respirator with N-100 or P-100 filters, and eye protection.

Some occupations are associated with increased risk of infection. These occupations include, but are not limited to, mammalogists (Childs et al. 1995), pest control specialists, and building inspectors. Specific recommendations have been published for personnel who trap or handle wild rodents as part of their vocation (Mills et al. 1995, or http://www.cdc.gov/ncidod/dvrd/spb/mnpages/rodentmanual.htm). Individuals in these occupations should be familiar with the early symptoms of HPS. If symptoms appear, a physician should be contacted and informed of the potential exposure to hantavirus. If the physician suspects HPS, a blood sample should be submitted for testing through the appropriate local or state public health agency.

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