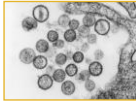


S l i d e 1	<p>Hantavirus</p> <p><i>Hemorrhagic Fever with Renal Syndrome (HFRS), Hantavirus Pulmonary Syndrome (HPS), Hemorrhagic Nephrosonephritis, Epidemic Hemorrhagic Fever, Korean Hemorrhagic Fever, Nephropathia Epidemica (NE)</i></p>	
S l i d e 2	<p>Overview</p> <ul style="list-style-type: none"> • Organism • History • Epidemiology • Transmission • Disease in Humans • Disease in Animals • Prevention and Control 	<p>In today’s presentation we will cover information regarding hantavirus and its epidemiology. We will also talk about the history of the disease, how it is transmitted, species that it affects (including humans), and clinical and necropsy signs observed. Finally, we will address prevention and control measures, as well as actions to take if hantavirus is suspected.</p>
S l i d e 3	<p>THE ORGANISM</p>	
S l i d e 4	<p>The Organism</p> <ul style="list-style-type: none"> • Hantaviruses <ul style="list-style-type: none"> - Genus <i>Hantavirus</i> - Family Bunyaviridae • Group of antigenically distinct viruses carried in rodents and insectivores • More than 20 hantavirus species • Only genus not arthropod-borne 	<p>Hantaviruses (genus <i>Hantavirus</i>, family Bunyaviridae) are a group of antigenically distinct RNA viruses carried in rodents and insectivores (shrews and moles). Each hantavirus is endemic in one, or at most, a few specific rodent or insectivore hosts, to which it is well adapted. At least 20 hantaviruses have been identified, but estimates of the exact number of viruses vary. Newly identified hantaviruses are often named for the location where the virus is found; however, some of these viruses are later reclassified. [Photo: Electron micrograph of Sin Nombre (“without a name”) hantavirus, the most common serotype seen in the U.S. Source: CDC Public Health Image Library]</p>
S l i d e 5	<p>The Organism</p> <ul style="list-style-type: none"> • Different viruses cause different disease syndromes in humans <ul style="list-style-type: none"> - HFRS: Hemorrhagic fever with renal syndrome - HPS: Hantavirus pulmonary syndrome 	<p>In humans, the consequences of infection depend with the virus. Different hantaviruses cause hemorrhagic fever with renal syndrome (HFRS) and hantavirus pulmonary syndrome (HPS), the two syndromes seen in humans.</p>

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HFRS-Associated Viruses		
Serotype	Host	Location
Hantaan	<i>Apodemus agrarius</i> (Striped field mouse)	Asia, Far East Russia
Dobrava	<i>A. agrarius</i> <i>A. flavicollis</i> (Yellow neck mouse)	Europe Balkans
Seoul	<i>Rattus norvegicus</i> (Norway brown rat) <i>R. rattus</i> (Roof rat)	Worldwide
Puumala	<i>Clethrionomys glareolus</i> (Red bank vole)	Europe

The most important hantaviruses causing HFRS are Hantaan virus, Puumala virus, Dobrava virus and Seoul virus. Other hantaviruses such as Amur virus are also associated with this disease. HFRS includes several diseases that formerly had other names, including Korean hemorrhagic fever and epidemic hemorrhagic fever. "Nephropathia epidemica" is sometimes used for a mild form of HFRS, which is often caused by Puumala virus or Saaremaa virus.

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HPS-Associated Viruses		
Serotype	Host	Location
Sin Nombre	<i>Peromyscus maniculatus</i> (Deer mouse)	Central and Western U.S Canada
Monongahela	<i>P. maniculatus</i>	Eastern U.S. Canada
New York	<i>P. leucopus</i> (White-footed mouse)	Eastern U.S. Canada
Bayou	<i>Oryzomys palustris</i> (Rice rat)	Southeast U.S.
Black Creek Canal	<i>Sigmodon hispidus</i> (Cotton rat)	Southeast U.S.

Hantavirus pulmonary syndrome is caused by a number of hantaviruses in North and South America. In the United States and Canada, the Sin Nombre virus (with its Monongahela and New York variants) is responsible for most cases. HPS can also result from infection by the Muleshoe, Bayou, and Black Creek Canal viruses, as well as other named or unnamed hantaviruses.

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HPS-Associated Viruses		
Serotype	Host	Location
Andes	<i>Oligoryzomys longicaudatus</i> (Long-tailed pygmy rice rat)	Argentina Chile
Oran (Andes variant)	<i>O. longicaudatus</i>	Northwest Argentina
Lechiguanas (Andes variant)	<i>O. flavescens</i>	Central Argentina
Hu39694 (Andes variant)	Unknown	Central Argentina
Juquitiba	Unknown	Brazil

In South and Central America, Andes virus and its variants are important causes of HPS; Choclo, Castelo Dos Sonhos, Juquitiba, Bermejo, Maciel and other hantaviruses can also cause this syndrome. Some hantaviruses have yet been not been linked to human disease, either because they are not pathogenic for humans or because their rodent hosts are unlikely to pass the virus to humans.

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This map depicts the geographic distribution of the various hantaviruses in the Western Hemisphere. The host vector is listed with the virus name.

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HISTORY

Hantaviruses are not new diseases, but rather, newly emerging diseases.

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History: Europe and Asia

- American Civil War
- World Wars I and II
 - 1913: Russia
 - 1932: Russia
 - 1932: Manchuria
 - 1934: Sweden
 - Nephropathia epidemica

Center for Food Security and Public Health, Iowa State University, 2013

Hantavirus disease outbreaks have occurred as far back as American Civil War times. In Europe, there are records of hemorrhagic fever syndrome (HFRS) during World War I and II. What are thought to be the first outbreaks of hantavirus causing HFRS were reported in Russia in 1913 and 1932. Japanese troops in Manchuria reportedly had cases in 1932 and cases referred to as Nephropathia Epidemica (NE) in Sweden appeared in 1934.

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History: Europe and Asia

- 1951-1954: Korea
 - 3,200 U.N. troops affected
 - Hantaan River separated N. & S. Korea
- 1977
 - "Hantaan" virus isolated, characterized
- 1979
 - Similar virus found in laboratory workers in Japan and Europe
 - "Seoul" virus

Center for Food Security and Public Health, Iowa State University, 2013

HFRS was first recognized by western physicians from 1951 to 1954 when 3,200 cases of a debilitating, acute, febrile illness were reported among United Nations forces in Korea. The soldiers were living in foxholes while stabilizing the contested border between North and South Korea and had close contact with rodents. Isolation of the organism, named "Hantaan" virus, occurred in 1977. In 1979, a virus similar to Hantaan caused hemorrhagic fever in laboratory workers that had contact with rats in Japan and Europe. This virus was carried by *Rattus norvegicus*, *R. rattus* and named Seoul virus after the site of the initial studies. The ongoing shipping of these laboratory rats worldwide lead to the dissemination of the Seoul virus.

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History: U.S.

- 1993: Four Corners region
 - Sudden onset respiratory failure identified in healthy young people
 - 12 fatalities
 - Antibodies to hantavirus detected
- Additional surveillance and testing
 - 1700 small mammals
 - 30% had antibodies to hantavirus
- Sin Nombre virus identified

Center for Food Security and Public Health, Iowa State University, 2013

Hantavirus-associated disease was first reported in the United States in the 1990s during an outbreak in the Four Corners region. Several young and healthy members of the Navajo Nation in New Mexico presented to the Indian Health Service physicians with a sudden onset of respiratory failure in May 1993, and by June, twelve people had died. Initial results of acute and convalescent sera against Hantaan, Seoul, and Puumala virus antigens showed cross-reactive antibodies. However, the pulmonary form observed in this outbreak was unlike any other clinical presentation of hantavirus. The Department of Public Health for New Mexico, along with the Centers for Disease Control and Prevention, became involved and set up surveillance and testing. Nearly 1700 small mammals representing 31 species were subsequently captured and tested. Almost half of the mammals captured were deer mice (*Peromyscus maniculatus*) and 30% had antibodies to virus, named Sin Nombre Virus.

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The Four Corners Outbreak

- May 1993
 - First clinical case
 - Abrupt fever, myalgia, pulmonary edema
- June 1993
 - 12 fatalities
 - Unexplained Adult Respiratory Distress Syndrome (ARDS)
 - Sera cross-reacted with Hantaan, Seoul, Puumala virus
 - Rodents trapped - deer mouse main reservoir

Center for Food Security and Public Health, Iowa State University, 2013

Several young and healthy members of the Navajo Nation in New Mexico presented to the Indian Health Service physicians with a sudden onset of respiratory failure in May 1993, and by June, twelve people had died. It was originally diagnosed as unexplained Adult Respiratory Distress Syndrome (ARDS). Clinical signs included an abrupt fever, myalgia, headache, and cough, followed by acute progressive pulmonary edema, leading to respiratory failure and hypotension and death 2-10 days after onset. The Department of Public Health for New Mexico along with the Centers for Disease Control and Prevention became involved and set up surveillance and testing. Initial results of acute and convalescent sera against Hantaan, Seoul, and Puumala virus antigens showed cross-reactive antibodies. It had taken a pulmonary form which was unlike any other clinical presentation of hantavirus. Nearly 1700 small mammals representing 31 species were subsequently captured and tested. Almost half of the mammals captured were deer mice (*Peromyscus maniculatus*) and 30% had antibody the now named Sin Nombre Virus.

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The Four Corners Outbreak

- Winter and spring 1993
 - Drought for several years followed by snow and rain
 - Vegetation blossomed and rodent population grew tenfold
- Virus isolated and named
 - Sin Nombre Virus (SNV)
- Newly emerging virus has been present since 1959
 - 38 year old Utah man

Center for Food Security and Public Health, Iowa State University, 2013


The sudden outburst of cases is attributed to the weather patterns that occurred in the Four Corners area. Prior to 1993 there had been a drought for several years. By spring of that year, heavy snows and rainfall helped drought-stricken plants and animals to revive and grow in larger-than-usual numbers. With plenty of vegetation for food and protection, the deer mice reproduced so rapidly that there were ten times more mice in May 1993 than there had been in May of 1992. An increase in mice numbers, coupled with their high infection rate, increased the risk to humans who shared habitats with mice in rural areas. The virus was isolated 1 month after the first report of cases and named Muerto Canyon virus, then Four Corners virus, and finally Sin Nombre Virus (SNV – “virus without a name”). Cases did occur prior to 1993, but a sharp rise in 1993 led to recognition of the disease. One of the prior cases was a 38 year old Utah man that had died from an illness compatible with hanta in 1959. Researches located his lung tissue and utilizing current technology, were able to isolate SNV in 1994. Earliest case diagnosed by immunohistochemistry in postmortem tissues was a patient who died in 1978.

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Four Corners Outbreak

- Contributing factors
 - Drought followed by heavy snow and rain
 - Large increase in plant and animal numbers, especially deer mice
 - High infection rate



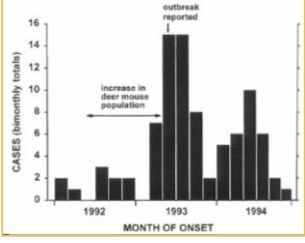
WorldAtlas.com

The sudden outburst of cases is attributed to the weather patterns that occurred in the Four Corners area. Prior to 1993 there had been a drought for several years. By spring of that year, heavy snows and rainfall helped drought-stricken plants and animals to revive and grow in larger-than-usual numbers. An increase in mouse numbers, coupled with a high infection rate, increased the risk to humans who shared habitats with mice in rural areas. [Photo: Map showing the Four Corners region of the United States. Source: worldatlas.com]

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Epidemic Curve of Four Corners Outbreak



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An epidemic curve of the first 100 cases of HPS in the Four Corners outbreak through December of 1994. It shows that HPS did occur prior to the major outbreak in 1993 but it took the cluster of clinical cases to realize the potential threat to human health.

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EPIDEMIOLOGY

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Geographic Distribution


- Found worldwide
 - Each virus range limited by host range
- HPS-causing viruses
 - North, Central, and South America
 - U.S.: mostly Western states
- HFRS-causing viruses
 - Europe and Asia

Hantaviruses are found worldwide in rodents and insectivores. The distribution of each virus is usually limited by the geographic range of its specific host(s). The viruses that cause hantavirus pulmonary syndrome seem to occur only in North, Central and South America. In the U.S., most cases are seen in the western states, but infections have been reported throughout the country. HFRS is mainly seen in Europe and Asia; however, one agent, the Seoul virus, can be found worldwide in its rat host, and has been associated with a few cases of HFRS in the United States. Although clinical cases have not been reported from Africa or the Middle East, antibodies to hantaviruses have been reported among humans in both regions, and a hantavirus was recently discovered in the African wood mouse (*Hylomyscus simus*). There is currently no evidence for hantavirus-associated disease in Australia, but it is likely that hantaviruses are carried in some Australian rodents or insectivores.

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Common Rodent Reservoirs

- United States, except the Southeast
 - Deer mouse
- Southeast U.S.
 - Cotton rat
 - Rice rat
- Eastern
 - White-footed mouse
- The house mouse is not a carrier!

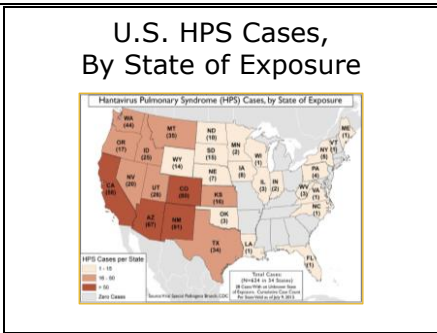


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As noted previously, the natural host of hantavirus is rodents. The deer mouse (*Peromyscus maniculatus*) is the primary carrier in all areas of the United States, except the southeast. There the carriers tend to be the cotton rat (*Sigmodon hispidus*) and the rice rat (*Oryzomys palustris*). The eastern United States also deals with the white-footed mouse (*Peromyscus leucopus*). It is important to remember that the house mouse is not a carrier. It is unknown whether any of the animals other than the natural rodent hosts are epidemiologically important.

[Photo: (Top) Deer mouse, *Peromyscus maniculatus*. Source: Wikimedia Commons; (Middle) Cotton rat, *Sigmodon hispidus*. Source: CDC Public Health Image Library; (Bottom) House mouse, *Mus musculus*. Source: Wikimedia Commons]

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As of July 9, 2013, a total of 624 cumulative cases of hantavirus pulmonary syndrome have been reported in the United States. This map depicts the cases per state (where the individual was exposed). Source: Centers for Disease Control and Prevention at <http://www.cdc.gov/hantavirus/surveillance/state-of-exposure.html>.

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Risk Factors for Infection

- Human exposure to rodents
 - Increased rodent populations
 - Environmental factors
 - Occupational exposures
 - Rodent control workers, field biologists, farmers, forestry workers, military
 - Recreational exposures
 - Camping, rodent-infested cabins
- Cases peak in spring/early summer

Hantavirus outbreaks are often associated with increased rodent populations or environmental factors that lead to increased human exposure to rodents. HPS tends to peak in late spring or early summer. HFRS tends to peak with human agricultural activities in spring and fall. Occupations that may be at higher risk of infection include rodent control workers, field biologists/ mammalogists, farmers, forestry workers and military personnel. Activities such as camping or staying in rodent-infested cabins can also increase the risk.

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Morbidity and Mortality: Humans

- Seroconversion
 - Europe: 1 to 8%
 - Varies by country and virus
 - Russia>Finland>Sweden>Others
 - U.S.: 0.2 to 0.5%
 - South America: 1 to 40%

Approximately 1-8% of the population has antibodies to hantaviruses in Europe; the seropositivity rate varies with the country and specific virus. In Europe, HFRS is most common in Russia (3000 cases), Finland (1000 cases) and Sweden (300 cases), with 100 or fewer cases seen annually in other countries. In the U.S., 0.2-0.5% of the general population is seropositive for hantaviruses. In South America, 1-40% of the population has antibodies to hantaviruses, and HPS is also more common.

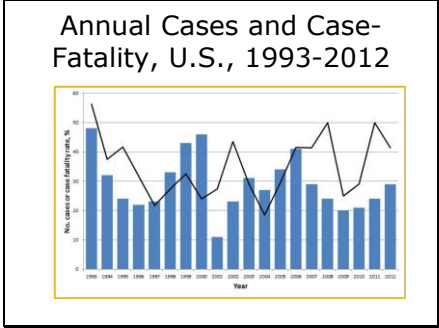
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Morbidity and Mortality: Humans

- Case fatality rate
 - Puumala virus: 0.1 to 0.4%
 - Seoul virus: 1 to 5%
 - Dobrava virus: 7 to 12%
 - Hantaan virus: 10 to 15%
 - Sin Nombre virus (HPS): 40 to 60%
 - Muleshoe, Black Creek Canal, Bayou viruses: >40%
 - Andes virus variants: 43 to 56%

Different hantaviruses tend to cause mild, moderate or severe disease. The mortality rate also varies with the availability of healthcare services. The case fatality rate is approximately 0.1% to 0.4% for Puumala virus (the most commonly reported infection in Europe), 1-5% for Seoul virus, 7-12% for Dobrava virus, and 10-15% for Hantaan virus. The estimated case fatality rate is 40-60% for HPS caused by Sin Nombre virus. The case fatality rate for Muleshoe, Black Creek Canal and Bayou viruses is also greater than 40%. Andes virus infections have a similar case fatality rate (43-56%), but the mortality rates for some variants may be lower: the case fatality rate is 9-29% for Laguna Negra virus and 8-40% for Lechiguanas virus and Oran virus. Choclo virus infections have a case fatality rate of approximately 25%.

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This graph shows the annual number of cases (bars) and case-fatality (line) for hantavirus pulmonary syndrome, in the United States, from 1993 (year first detected in the U.S.) to 2012. Source: Centers for Disease Control and Prevention at <http://www.cdc.gov/hantavirus/surveillance/annual-cases.html>.

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TRANSMISSION

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Transmission


- Animals
 - Virus spread by aerosols or bites
 - Virus shed in saliva, feces, urine
 - Viral shedding highest during early stages of infection
- Humans
 - Incidental hosts
 - Infected by contact with infected rodents or their droppings

Each hantavirus has one or possibly a few specific rodent or insectivore hosts. In these host populations, infections can be spread in aerosols and via bites. Rodents can shed hantaviruses in saliva, feces and urine. Infected animals carry these viruses for weeks to years, and sometimes for life. Transient infections are also possible. Recently infected animals tend to shed larger amounts of virus; generally, virus shedding decreases significantly by approximately 8 weeks after infection. Transmission routes may vary with the specific virus; for example, some hantaviruses are more readily isolated from the urine than others. Humans can become incidental hosts when they contact infected rodents or their excretions.

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Transmission

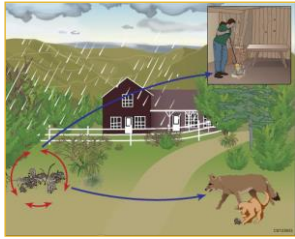
- Humans
 - Aerosolization of rodent urine, droppings, or nests in enclosed areas
 - Entry through broken skin, conjunctiva, other mucous membranes
 - Rodent bites
 - Ingestion
 - Vertical transmission (rare)



Often, rodent urine, droppings or nests are disturbed in enclosed areas; the viruses are then inhaled in aerosolized dust. Infection can sometimes occur after only a few minutes of exposure to aerosolized virus. Hantaviruses can also be transmitted through broken skin, the conjunctiva and other mucous membranes, by rodent bites and possibly by ingestion. Vertical transmission is generally thought to be negligible or nonexistent; however, data suggesting the possibility of hantavirus transmission in breast milk have been reported from South America. Person-to-person spread has not been seen in HPS cases in North America or HFRS in Eurasia, but occurs occasionally with the Andes virus in Argentina. [Photo: Aerosolization of rodent urine can occur when sweeping. Source: CDC Public Health Image Library]

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Transmission



This image, from CDC, illustrates potential hantavirus transmission routes for humans.

Image: CDC.

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Transmission

- Other animals
 - Pigs
 - Shed virus and urine and feces
 - May also transmit virus vertically
 - Other species
 - Antibodies to hantaviruses reported
 - No virus shedding
- Infected animals not linked to human cases

Whether animals other than rodents, shrews and moles can shed hantaviruses is uncertain. Studies from China suggest that hantavirus-infected pigs can excrete antigens in urine and feces, and may also pass the virus to their offspring across the placenta. Antibodies to hantaviruses have been reported in other species, but they have not been reported to shed these viruses. No infected animals have been linked to human cases.

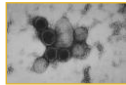
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Risk of Contracting HPS

- Work, play, or live in closed spaces where rodents are actively living
- Hikers and campers
- Construction and utility workers
 - Enter crawl spaces under buildings
 - No serological evidence in 522 samples
- Traveling to and within hantavirus areas is not a risk factor

Center for Food Security and Public Health Iowa State University, 2013


Poor housing conditions, agricultural activities, wilderness camping, and other outdoor activities have help predispose people to the spread of infection if rodents are actively living in those same areas. Hikers and campers can also be exposed when they use infested trail shelters or camp near other rodent habitats. Construction and utility workers can be exposed when they work in crawl spaces under houses or in vacant buildings that may have a rodent population. Out of 522 samples taken from various occupational groups with frequent contact with rodents and their excreta (farm workers, laborers, professionals, home repairers, service industry and park service workers, heating and plumbing contractors, utility workers, and technicians) there was no serological evidence of SNV infection. Travel to and within all areas where hantavirus infection has been reported is not considered a risk factor for infection with HPS. However, recent research results show that many people who have become ill with HPS got the disease after having been in frequent contact with rodents and/or their droppings for some time. In addition, many people who have become ill reported that they had not seen rodents or their droppings at all.

<p>S l i d e 3 2</p>	<p style="text-align: center;">DISEASE IN HUMANS</p>	
<p>S l i d e 3 3</p>	<p style="text-align: center;">Incubation in Humans</p> <ul style="list-style-type: none"> • HFRS <ul style="list-style-type: none"> - 1 to 6 weeks • HPS <ul style="list-style-type: none"> - 7 to 39 days (Andes virus) - 9 to 33 days (Sin Nombre virus) • Infections range from asymptomatic to severe 	<p>Hantaviruses usually cause one of two diseases, HFRS and HPS; however, other syndromes may also be possible. The incubation period for HFRS is 1-6 weeks. Incubation periods of one week to 39 days and nine to 33 days have been reported in patients with HPS from Andes virus and Sin Nombre virus, respectively. Depending on the virus, hantavirus infections vary from asymptomatic to severe. [Photo: Transmission electron micrograph (TEM) showing the appearance of a number of virus particles, or “virions”, of the hantavirus known also, as the Sin Nombre virus (SNV). Source: CDC Public Health Image Library]</p>
<p>S l i d e 3 4</p>	<p style="text-align: center;">Hemorrhagic Fever with Renal Syndrome</p> <ul style="list-style-type: none"> • Severity varies with virus • Disease stages in severe cases <ul style="list-style-type: none"> - Febrile - Hypotensive/proteinuric - Oliguric - Diuretic - Convalescent 	<p>The severity of HFRS varies with the causative agent. Hantaan, Dobrava and Amur virus infections usually cause severe symptoms. Seoul virus generally results in more moderate disease, while Puumala and Saaremaa (Dobrava) virus infections are typically mild. 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.</p>
<p>S l i d e 3 5</p>	<p style="text-align: center;">Hemorrhagic Fever with Renal Syndrome</p> <ul style="list-style-type: none"> • Abrupt onset fever, chills, aches • Onset of renal signs <ul style="list-style-type: none"> - Proteinuria→ oliguria→ polyuria - Hypotension - Nausea and vomiting - Kidney failure - Lung or neurological signs • Patients usually recover 	<p>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. Patients may also develop injected mucous membranes, photophobia, temporary visual impairment, a flushed face and conjunctivae, or a petechial rash, which usually occurs on the palate or trunk. This 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 phase of the disease and can last for hours or days. Nausea and vomiting often occur, and death may result from acute shock. In severe cases, this 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 phases. In severe cases, kidney failure may be seen. Some cases have lung involvement (to a lesser extent than in HPS) or neurological signs. Hemorrhagic signs or tendencies including petechiae, hematuria or melena may also be seen, particularly in more severe cases. Disseminated intravascular coagulation can occur. Full recovery may take weeks or months, but patients usually recover normal kidney function.</p>

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Hantavirus Pulmonary Syndrome

- Initial phase
 - Fever, myalgia, headache
- Cardiopulmonary phase
 - Abrupt respiratory distress
 - Cough
 - Tachypnea
 - Pulmonary edema
 - Cardiac abnormalities



Hantavirus pulmonary syndrome is usually characterized by pulmonary rather than kidney disease. The initial phase usually lasts for 3 to 5 days; the clinical signs during this period are similar to the prodromal stage of HFRS, and may include fever, myalgia, headache, chills, dizziness, malaise, lightheadedness, nausea, vomiting and sometimes diarrhea. Arthralgia, back pain and abdominal pain are occasionally seen. Respiratory distress and hypotension usually appear abruptly, with cough and tachypnea followed by pulmonary edema and evidence of hypoxia. Cardiac abnormalities can occur, and may include bradycardia, ventricular tachycardia or fibrillation.

[Photo: This x-ray reveals mid-stage bilateral pulmonary effusion due to severe HPS (hantavirus pulmonary syndrome) in the chest cavity. Source: D. Loren Ketai, MD, CDC Public Health Image Library]

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HPS: Clinical Presentation

Most Frequent	Frequent	Other
Fever	Headache	Shortness of breath
Chills	Nausea	Dizziness
Myalgias	Vomiting	Arthralgia
	Diarrhea	Back pain
	Abdominal pain	Chest pain
	Cough	Sweats

This table, adapted from CDC, summarizes the symptoms of HPS according to frequency.

Source: <http://www.cdc.gov/hantavirus/technical/hps/clinical-manifestation.html>.

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Hantavirus Pulmonary Syndrome

- Disease progression
 - May be rapid after onset of cardiopulmonary phase
 - May require hospitalization and mechanical ventilation
- Other symptoms
 - Mild kidney disease possible
 - Hemorrhagic disease rare



After the onset of the cardiopulmonary phase, the disease usually progresses rapidly; patients may be hospitalized and require mechanical ventilation within 24 hours. Kidney disease can also be seen, but it tends to be mild; kidney damage occurs more often with the Andes, Bayou and Black Creek viruses. Hemorrhagic signs are rare in patients with HPS in North America, but more common in South America. Although recovery is rapid and patients usually recover full lung function, convalescence may last for weeks or months. Asymptomatic or mild infections appear to be rare with Sin Nombre virus, but may be more common with some South American hantaviruses.



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Hantavirus: Other Infections

- Some mild infections do not resemble HPS or HFRS
- May cause of fever of unknown origin in Asia
- Several atypical cases also diagnosed in Europe

Mild cases can have a variety of signs and symptoms that do not necessarily resemble HPS or HFRS. Hantavirus infections have been suspected in fever of unknown origin in some Asian countries. In Europe, Tula virus infections were found in two patients. One case occurred in a 12-year-old boy in Switzerland who had been bitten by a rodent and developed paronychia, recurrent febrile episodes, a slightly enlarged spleen and a macular, nonpruritic rash on his torso and proximal limbs. The other patient was an adult with fever, renal disease and pneumonia. The Tula virus infection was suspected but not proven to be the cause of the disease in both cases.

<p>S I d e 4 0</p>	<p style="text-align: center;">Diagnosis in Humans</p> <ul style="list-style-type: none"> • Virus isolation <ul style="list-style-type: none"> - May be difficult - Some viruses have never been isolated • Serology <ul style="list-style-type: none"> - Immunofluorescent antibody test (IFA) - ELISA - Immunoblot - Virus neutralization 	<p>A definitive diagnosis can be made if the hantavirus is isolated from the patient; however, recovery is not always successful. In addition, some hantaviruses (including Sin Nombre virus) have never been isolated in cell culture. If viruses are found, they can be identified by virus neutralization. Hantavirus infections are often diagnosed by serology. Either the presence of specific IgM in acute phase sera or a rise in IgG titer is diagnostic. Serological tests include the immunofluorescent antibody test (IFA), enzyme-linked immunosorbent assays (ELISA), immunoblotting and virus neutralization. Commercial ELISA and/or immunoblot assay kits have been developed for Dobrava, Hantaan, Puumala, Seoul, Sin Nombre and some other viruses. Hantaviruses can cross-react in some serologic assays. [Photo: Blood tubes. Source: Danelle Bickett-Wedde/CFSPH]</p>
<p>S I d e 4 1</p>	<p style="text-align: center;">Diagnosis in Humans</p> <ul style="list-style-type: none"> • Immunohistochemistry <ul style="list-style-type: none"> - Tissues • RT-PCR <ul style="list-style-type: none"> - Blood or tissues - Can differentiate some viruses 	<p>Hantavirus infections can also be diagnosed by finding antigens in tissues with immunohistochemistry. Viral RNA can be detected in blood or tissues with reverse transcriptase-polymerase chain reaction assays (RT-PCR). PCR assays that can differentiate some hantaviruses have been described; one published assay identifies Dobrava, Hantaan, Seoul and Puumala viruses. Real-time RT-PCR has been described for some viruses.</p>
<p>S I d e 4 2</p>	<p style="text-align: center;">Treatment in Humans</p> <ul style="list-style-type: none"> • Supportive care • Intensive care may be required • Ribavirin <ul style="list-style-type: none"> - HFRS only 	<p>Supportive care is the mainstay of treatment. Intensive care may be required. Ribavirin may be helpful in cases of HFRS, but has not been effective for HPS to date.</p>
<p>S I d e 4 3</p>	<p style="text-align: center;">DISEASE IN ANIMALS</p>	
<p>S I d e 4 4</p>	<p style="text-align: center;">Species Affected</p> <ul style="list-style-type: none"> • Hantaviruses found naturally in: <ul style="list-style-type: none"> - Rodents <ul style="list-style-type: none"> • Up to 50% seropositive • About 10% of deer mice seropositive for Sin Nombre virus - Insectivores (shrews and moles) • Most species carry only one virus 	<p>Hantaviruses are found naturally in various species of rodents and insectivores (shrews and moles). Each virus is thought to be carried mainly by one species of animal; however, sometimes a species can carry more than one hantavirus, and some hantaviruses may infect more than one host. The infection rate varies between sites and over time, but in some cases, up to 50% of a rodent population can be seropositive. On average, approximately 10% of deer mice are seropositive for Sin Nombre virus. [Photo: “Deer mouse”, <i>Peromyscus maniculatus</i>, which has been determined to be one of the reservoirs and transmitters of Hantavirus. Source: CDC Public Health Image Library]</p>

<p>S I d e 4 5</p>	<p style="text-align: center;">Disease in Animals</p> <ul style="list-style-type: none"> • Rodents <ul style="list-style-type: none"> - Can carry viruses but not usually do not become ill - Sporadic reports of clinical illness <ul style="list-style-type: none"> • Decreased survival • Decreased weight gain • Fatal pulmonary disease • Death (neonates) • Meningoencephalitis 	<p>Hantaviruses can be carried lifelong, and are not usually associated with overt disease in their reservoir hosts. However, studies have reported decreased survival in bank voles (<i>Myodes glareolus</i>) infected with Puumala virus and deer mice infected with Sin Nombre virus, as well as lower weight gains in infected male deer mice. Hamsters infected with Andes virus may develop fatal pulmonary disease similar to HPS. Hantavirus infections can also kill neonatal rodents. Fatal meningoencephalitis occurs in infant laboratory mice (<i>Mus musculus</i>) experimentally infected with Hantaan virus, as well as rats infected with Seoul virus. Maternal antibodies seem to be protective during the period of susceptibility. Rats and mice over the age of 2-3-weeks do not usually develop clinical signs. Infant mice do not seem to be susceptible to disease caused by Puumala or Sin Nombre viruses.</p>
<p>S I d e 4 6</p>	<p style="text-align: center;">Disease in Animals</p> <ul style="list-style-type: none"> • Other species <ul style="list-style-type: none"> - Can also be infected but little evidence of clinical illness - Antibodies found in: <ul style="list-style-type: none"> • Cats and dogs • Swine • Horses and cattle • Deer • Rabbits/hares and chipmunks • Moose 	<p>Species other than rodents and insectivores can be infected by hantaviruses, but there is little or no evidence that these animals become ill. Antibodies to some hantaviruses have been found in cats, dogs, swine, horses, cattle, deer, rabbits/ hares, chipmunks and moose. In one study, 10% of healthy cats in the United Kingdom and 23% of cats with chronic diseases were seropositive. Other studies have reported lower rates. Horses, cattle and coyotes were seronegative in one U.S. survey.</p>
<p>S I d e 4 7</p>	<p style="text-align: center;">PREVENTION AND CONTROL</p>	
<p>S I d e 4 8</p>	<p style="text-align: center;">Prevention and Control</p> <ul style="list-style-type: none"> • Prevent exposure to rodents and their excretions <ul style="list-style-type: none"> - Occupational exposures - Exposures in the home - Agricultural exposures 	<p>Hantavirus infections can be prevented by avoiding exposure to rodents and their excretions. Many cases of HPS and HFRS occur after living or working in an enclosed, rodent-infested space; however, some patients have reported no known contact with rodents or their feces. HFRS has also been associated with agricultural activities, such as harvesting crops or working with hay. [Photo: Cotton rat, <i>Sigmodon hispidus</i>, whose habitat includes the southeastern United States, and way down into Central and South America. Source: CDC Public Health Image Library]</p>
<p>S I d e 4 9</p>	<p style="text-align: center;">Prevention and Control</p> <ul style="list-style-type: none"> • Rodent control in and around the home • CDC recommendations <ul style="list-style-type: none"> - Seal up - Trap up - Clean up 	<p>The primary strategy for preventing human exposure to rodent diseases is effective rodent control in and around the home. This is achieved by eliminating any food sources, sealing even the smallest entries into homes, and successfully trapping rodents in and around the home. The CDC summarizes this by recommending: seal up, trap up, and clean up. [Photos: Prevention measures to keep rodents out of the home. Source: Centers for Disease Control and Prevention]</p>

<p>S I d e 5 0</p>	<p style="text-align: center;">Cleaning and Disinfection</p> <ul style="list-style-type: none"> • Safe cleaning practices for rodent-infested areas and droppings <ul style="list-style-type: none"> – Wet area with disinfectant – Clean with paper towels, then mop or sponge – Avoid procedures that aerosolize virus (e.g., sweeping) – Wear rubber gloves and mask – Contact health department for guidance 	<p>The CDC website has information on the safe cleaning of rodent-infested areas and droppings. Precautions include airing out the room before starting clean-up, and wetting the area with commercial disinfectant or bleach. Infested areas should be cleaned with paper towels, followed by mopping or sponging. Procedures that might aerosolize the virus, such as sweeping, should be avoided, and protective clothing and gloves should be worn while cleaning. Special precautions must be taken when cleaning heavily infested areas; a local, state or federal health department should be contacted for detailed guidelines. [Photo: Spraying rodent feces with bleach solution. Source: Centers for Disease Control and Prevention]</p>
<p>S I d e 5 1</p>	<p style="text-align: center;">Disinfection</p> <ul style="list-style-type: none"> • 1% sodium hypochlorite <ul style="list-style-type: none"> – 10% sodium hypochlorite solution recommended for heavily soiled areas • 2% glutaraldehyde • 70% ethanol • Detergents • Acid (pH 5) • Heat (60° C for at least 30 minutes) 	<p>Hantaviruses are susceptible to many disinfectants including 1% sodium hypochlorite, 2% glutaraldehyde, 70% ethanol and detergents. A 10% sodium hypochlorite solution has been recommended for heavily soiled areas. Hantaviruses are also susceptible to acid (pH 5) conditions. In addition, they can be inactivated by heating to 60° C for at least 30 minutes.</p>
<p>S I d e 5 2</p>	<p style="text-align: center;">Prevention and Control</p> <ul style="list-style-type: none"> • Occupational exposures <ul style="list-style-type: none"> – Wear recommended PPE <ul style="list-style-type: none"> • Detailed guidance available from CDC – Seek medical attention promptly if a febrile illness develops – Follow universal precautions in human healthcare settings – Quarantine and test laboratory rodents • No vaccine available 	<p>People who are occupationally exposed to rodents should take additional precautions to prevent infection. Depending on the circumstances and type of exposure, this may include gloves, goggles, rubber boots or disposable shoe covers, coveralls or gown, and/or a respirator (as of 2008, the CDC recommends a N-100 filter type respirator). In the U.S., detailed precautions for a variety of situations, including exposure to rodent blood and organs, are available from the CDC. 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. Hospitals should follow universal precautions when treating patients with Andes virus infections. Vaccines for hantaviruses are in development, but are not yet available in the U.S. To prevent infections in laboratory colonies, wild rodents should be quarantined and tested for hantaviruses.</p>
<p>S I d e 5 3</p>	<p style="text-align: center;">Additional Resources</p> <ul style="list-style-type: none"> • Center for Food Security and Public Health <ul style="list-style-type: none"> – www.cfsph.iastate.edu • CDC <ul style="list-style-type: none"> – www.cdc.gov/hantavirus/ • World Health Organization <ul style="list-style-type: none"> – www.who.int/ith/diseases/hantavirus/en/ <p style="text-align: center;"><small>Center for Food Security and Public Health, Iowa State University, 2013</small></p>	
<p>S I d e 5 4</p>	<p style="text-align: center;">Acknowledgments</p> <p>Development of this presentation was made possible through grants provided to the Center for Food Security and Public Health at Iowa State University, College of Veterinary Medicine from the Centers for Disease Control and Prevention, the U.S. Department of Agriculture, the Iowa Homeland Security and Emergency Management Division, and the Multi-State Partnership for Security in Agriculture.</p> <p><small>Authors: Kerry Leadem Larson, DVM, MPH, PhD, DACVPM; Anna Rovid Spickler, DVM, PhD; Raiford Davis, DVM, MPH; Danielle Bickett-Weddie, DVM, MPH, PhD, DACVPM Reviewer: Glenda Dvorak, DVM, MPH, DACVPM</small></p>	<p>Last reviewed: August 2013</p>