Hantavirus: Clinical Insights, Emerging Evidence, and What Every Healthcare Worker Should Know

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The North American deer mouse has been determined to be one of the reservoirs and transmitters of the hantavirus. Credit: James Gathany, CDC

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A recent episode of *Transmission Interrupted*, "From Mice to Medicine: Exploring Hantavirus and Protecting Healthcare Teams," brought together Dr. Steven Bradfute (University of New Mexico Health Sciences Center) and Dr. Gaby Frank (Johns Hopkins Special Pathogens Center) to unpack what we know — and still don't know — about Hantaviruses, their ecology, clinical presentation, and implications for healthcare workers and the public.

Epidemiology: Where Hantavirus Lives, and How It Spreads

Hantaviruses are a diverse group of pathogens in the Bunyaviridae family, with more than two dozen species that can infect humans. The type of illness depends heavily on the strain and region.

Two major clinical syndromes

Hantavirus Cardiopulmonary Syndrome (HCPS)

- Found primarily in the Americas
- Caused largely by Sin Nombre virus (U.S.) and Andes virus (Argentina/Chile)
- Begins with flu-like symptoms and can progress abruptly to severe respiratory failure

Hemorrhagic Fever with Renal Syndrome (HFRS)

- Occurs mainly in Europe and Asia
- Associated with viruses such as Puumala, Hantaan, and Dobrava

Among all hantaviruses, Andes virus is the only one known to spread person-to-person.

Rodent reservoirs & transmission routes

Infection occurs through inhalation of aerosolized rodent urine, feces, saliva, or disturbed nesting material**,** especially in enclosed or poorly ventilated spaces.

Common scenarios include:

- Cleaning dusty garages, sheds, attics, barns, or crawl spaces
- Opening or tidying unused cabins or storage buildings
- Working outdoors in rural or wooded areas

- Handling rodent-contaminated food or stored goods

Why human cases remain rare

Despite widespread rodent infection, human disease is uncommon. Possible reasons include:

- Mild or subclinical infections that go undetected
- Misdiagnosis due to nonspecific symptoms
- Environmental influences on viral aerosol survival
- Differences in human behaviors and exposure patterns
- Genetic variability among viruses

European data suggest only about 15% of Hantavirus infections are clinically recognized, hinting at underdiagnosis elsewhere as well.

Prevalence of Hantavirus in New Mexico

Dr. Bradfute and his team investigate how prevalent Sin Nombre virus is across New Mexico — the U.S. state with the highest known HCPS incidence.

Key insights from his research include:

- The virus is far more widespread among small mammals than previously believed
- Detected in multiple rodent species, not just deer mice
- Found in areas with known human cases and areas with *no* documented cases
- Viable virus has been isolated from rodent feces

These findings suggest that human infection risk is influenced by microenvironment, climate, human behavior, and viral stability. However, additional research is needed to better understand transmission dynamics and human risk given the diversity of rodent carriers.

The full episode shares the surprising story behind how this research journey began. Listen now.

Diagnosis: Recognizing a Rapidly Progressing Illness

Early HCPS can mimic flu or other viral syndromes, making diagnosis challenging. The key is recognizing symptom evolution, laboratory clues, and conducting a thorough exposure and travel history.

Clinical Staging of HCPS

HPS follows a predictable clinical progression:

1. Prodromal phase (3–5 days): fever, chills, myalgias, headache, GI symptoms
2. Cardiopulmonary phase: abrupt onset of pulmonary edema, hypoxia, and shock
3. Diuretic phase (in survivors): brisk diuresis as capillary leak resolves
4. Convalescent phase: rapid clinical improvement but fatigue may continue for weeks

This staging is useful for clinicians recognizing early deterioration.

The Importance of Symptom, Exposure, and Travel History

Symptoms to ask about

- Fever, chills
- Severe myalgias
- Gastrointestinal symptoms, sometimes severe
- Shortness of breath developing early in illness
- Rapid decline, sometimes within hours

Timeline: Ask further back than usual

HCPS incubation can be up to six weeks — much longer than typical respiratory viruses. Most clinical screening tools ask about exposures within the last 7-30 days; for Hantavirus, clinicians should ask about the past 6 weeks, especially regarding environmental exposures.

Exposure history

Instead of asking whether someone “saw rodents,” clinicians should focus on dust-disturbing activities where rodent contamination could be aerosolized:

- Cleaning or sweeping dusty indoor spaces
- Opening sealed structures (sheds, cabins, basements)
- Handling items with rodent droppings, nests, or contaminated stored goods
- Outdoor work such as forestry, wildlife management, or agricultural activities

Travel history

Ask about recent trips to:

- The Four Corners states: Arizona, New Mexico, Colorado, and Utah
- Argentina or Chile (risk for Andes virus, which can spread person to person)
- European or Asian regions where HFRS viruses are endemic

Combining symptom progression, specific laboratory findings, and an expanded exposure/travel timeline gives clinicians the best chance of identifying HCPS early.

Laboratory Clues (“The Classic Five”)

Dr. Frank highlights a set of findings that strongly suggest HCPS when clustered together:

1. Thrombocytopenia
2. Hemoconcentration
3. Left shift without toxic granulation
4. More than 10% immunoblasts
5. Rapid onset of respiratory compromise

The presence of four or more of these strongly suggests HCPS.

Testing

Two primary diagnostic approaches were discussed in the podcast:

- PCR: useful because viremia persists through illness
- Serology: IgM typically positive at symptom onset

The podcast also notes the need for faster, point-of-care diagnostics, especially in rural settings where HCPS cases often present.

Reporting and Confirming Hantavirus Cases

A confirmed case requires compatible illness plus:

- Positive IgM
- Rising IgG titers
- Positive immunohistochemistry
- Positive PCR

HCPS is a nationally notifiable condition, meaning providers must report suspected cases promptly.

Clinicians should notify local or state health departments and may contact the CDC Emergency Operations Center (770-488-7100) for consultation, testing support, and confirmatory diagnostics.

Clinical Care: Supportive Management and Early Escalation

There is no specific antiviral treatment for Hantavirus in the United States. Care is supportive and must be proactive, precise, and rapidly escalated when needed. Suspected HCPS is a medical emergency, and patients should be cared for in an ICU-level setting as early as possible, even before diagnosis is confirmed.

Mortality

The U.S. case fatality rate for HCPS is approximately 35–40%, largely due to the rapid cardiopulmonary decline.

Early Recognition and Stabilization

HCPS often begins with nonspecific viral symptoms but can progress to severe respiratory distress within hours.

Patient management should include:

- Close monitoring of cardiac function
- Careful fluid administration: excessive IV fluids worsen non-cardiogenic pulmonary edema
- Supplemental oxygen as needed
- Intubation and mechanical ventilation if respiratory failure develops
- Use of vasopressors rather than fluid boluses for hypotension
- Early transfer to a facility with extracorporeal membrane oxygenation (ECMO) capability

Additional Clinical Considerations for Healthcare Workers

While the podcast focused on core recognition and management principles, several additional clinical considerations are important for frontline providers:

- Empiric broad-spectrum antibiotics are appropriate until bacterial infection is excluded
- Manage fever and pain appropriately
- Most patients develop hypotension within 24 hours
- Pulmonary edema and hypoxia typically worsen rapidly
- Without early supportive care, most deaths occur within 24–48 hours of the onset of cardiopulmonary phase

Poor prognostic indicators include:

- Lactate >4.0 mmol/L
- Cardiac index <2.2 L/min/m^2
- Severe myocardial depression, arrhythmias, or electromechanical dissociation

Survivors often experience a polyuric phase and recover rapidly, though fatigue may persist for weeks.

Infection Prevention and Control (IPC)

Healthcare Worker Guidance

Most Hantaviruses (e.g., Sin Nombre):

- No documented person-to-person transmission
- Standard precautions recommended
- Use respiratory protection for aerosol-generating procedures
- Use eye protection and gloves when handling respiratory secretions

Andes virus:

The only known Hantavirus with confirmed person-to-person transmission.

Dry VHF PPE with respiratory protection is sufficient for Suspect and Confirmed Andes Hanta patients which includes:

- Fluid resistant gown (AAMI Level 3 or 4) or coverall
- Gloves
- Eye and face protection
- Fit-tested N95 or PAPR
- Strict isolation precautions, including AIIR when available

Public Guidance for All Strains

To reduce the risk of exposure:

- Never sweep or vacuum rodent droppings
- Wet contaminated areas with 10% bleach for five minutes before wiping
- Wear gloves and, ideally, an N95 when handling contaminated materials
- Seal off potential entry points where rodents may enter homes and storage areas
- Store food in rodent-proof containers

Final Thoughts

This episode highlights the importance of understanding exposure risks, recognizing early clinical red flags, and acting quickly when HCPS is suspected. It also underscores how much remains unknown — from rodent ecology to human susceptibility and viral behavior.

Resources for Healthcare Workers

CDC: Clinician Brief: Hantavirus Pulmonary Syndrome (HPS)

About the Experts

Dr. Steven B. Bradfute, PhD, is an Assistant Professor in the UNM Center for Global Health and Department of Internal Medicine. Dr. Bradfute received his PhD in Immunology from Baylor College of Medicine (2005) and completed a postdoctoral fellowship at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), where he studied immune responses to hemorrhagic fever viruses, including the filoviruses (ebolaviruses, marburgviruses, and cuevaviruses). While continuing to study filoviruses, Dr. Bradfute has expanded his work to include other emerging and re-emerging viral pathogens, such as hantaviruses, equine encephalitis viruses, Zika virus, and the novel coronavirus SARS-CoV-2. As there are few treatments or vaccines available for many of these viruses, the Bradfute lab studies immunology, therapeutics, diagnostics, and vaccine development for these important pathogens.

Dr. Maria (Gaby) Frank, MD, FACP, SFHM, is a hospitalist, Professor of Medicine PAR, and the Director of Johns Hopkins' Special Pathogens Center at Johns Hopkins Hospital in Baltimore, Maryland, one of the 13 Regional Emerging Special Pathogen Treatment Centers (RESPTCs). The Johns Hopkins Hospital (JHH) is a premier 1000-bed non-profit academic medical center within the larger Johns Hopkins Health System, one of the leading health care systems in the United States. The 5-hospital health system in the Baltimore-Washington area has 2513 beds (354 intensive care unit beds) and serves approximately 7 million people. JHH provides a full range of clinical services, including specialty care for both adults and pediatric patients. The Johns Hopkins Hospital was ranked number one in the nation by U.S. News & World Report for 22 years of the survey's 30-year history. Before joining Johns Hopkins, Dr. Frank was the Medical Director of the biocontainment unit at Denver Health and Hospital Authority. In her role as the medical director of BCU, she served as the site Principal Investigator for the NIH-sponsored ACTT trial and is actively involved in the National Emerging Special Pathogen Training and Education Center (NETEC) and Special Pathogens Research Network (SPRN). Dr. Frank received her medical diploma from the University of Buenos Aires in Buenos Aires, Argentina, and completed a residency in Internal Medicine and another in Emergency Medicine in Argentina. She immigrated to the U.S. in 2004, where she completed another Internal Medicine

Residency at the University of Colorado, joining as faculty after graduation. Her areas of interest include emergent special pathogens, and disaster preparedness and response.

Jill Morgan, RN, is a nurse at Emory University Hospital. She has been on Emory's biocontainment team for over 15 years where she has cared for patients with Ebola virus disease and Lassa fever. Jill is co-lead for the PPE working group for NETEC, the National Emerging Special Pathogens Training and Education Center and has recently been appointed to the National Academies Committee on Personal Protective Equipment and Workplace Safety and Health.