

Hantavirus pulmonary syndrome in the Americas

Hantavirus pulmonary syndrome (HPS) was first identified in 1993 in the southwestern United States of America, when an outbreak produced 39 cases, more than half of whom died (1). Subsequently, outbreaks have been documented in Argentina (1992[identified retrospectively]–1996), Brazil (1993), Paraguay (1996), and Chile (1997). Sporadic cases have occurred in those same countries as well as Bolivia, Paraguay, and Uruguay. The number of known cases now exceeds 432, of which some 75% have been in Argentina and the United States (2 and unpublished data).

Hantavirus disease has long been known in Asia and Europe. However, Old World hantaviruses produce hemorrhagic and nephrotic pathophysiology rather than the pulmonary manifestations seen in the New World (3). In the Americas, each strain of hantavirus associated with HPS has its reservoir in a single species of rodent. All American hantaviruses are maintained by members of the subfamily *Sigmodontinae* (order: *Rodentia*; family: *Muridae*) (4). Andes virus, the strain responsible for an outbreak in southern Argentina, infects the long-tailed pygmy rat (*Oligoryzomys longicaudatus*). This same animal also infests Chile and was probably implicated in the outbreak in that country. Sin Nombre virus, the hantavirus responsible for the outbreak in the United States that led to the recognition of HPS, is found in the deer mouse (*Peromyscus maniculatus*). Other American rodents reported to be infected with hantaviruses include Argentine rice rats (*Oligoryzomys flavescens*), grass field mice (*Akodon azarae*) and dark field mice (*Bolomys obscurus*); Paraguayan vesper mice (*Calomys laucha*); and United States cotton mice (*Sigmodon hispidus*) (2).

EXPOSURE AND TRANSMISSION

Humans contract hantavirus infection by inhaling aerosols of fresh or dried excreta (feces, urine, or saliva) from colonized rodents. People can also be infected by touching the mouth or nose after handling a contaminated object (2). Strong evidence supports a hypothesis that the 1996 HPS outbreak in Argentina was fueled in part by person-to-person transmission. Five physicians and one hospital receptionist developed the disease after being exposed to patients, but only two of these health care

workers recalled seeing rodents during the 6 weeks prior to their illness, and traps in the homes of four of them yielded no rodents (5, 6). In contrast, epidemiologists have concluded that person-to-person transmission of HPS has not occurred in the United States. A survey of 266 New Mexican health workers who were exposed to HPS patients revealed that none had developed the disease. Moreover, some of these workers had not taken precautions to avoid contact with blood or respiratory secretions from their patients, and some had administered unprotected mouth-to-mouth resuscitation or accidentally pierced themselves with needles contaminated with patients' blood (3).

SYMPTOMATOLOGY

Once exposure occurs, HPS incubates for up to 6 weeks until the onset of signs and symptoms. The syndrome consists of a constellation of non-specific flu-like symptoms (fever, headache, myalgia, gastrointestinal symptoms) with marked hypotension and shortness of breath that progresses rapidly to respiratory failure. In Chile only, petechiae have been observed in pediatric cases (6). HPS should be suspected in previously healthy patients who develop such symptomatology, particularly if they have recently been exposed to rodents. A clinical diagnosis can be made in the presence of compatible symptoms and history, a chest X-ray showing pulmonary infiltrates, and four hematologic findings: left-shift neutrophilic leukocytosis, hemoconcentration, thrombocytopenia, and circulating immunoblasts. Confirmation of the diagnosis requires, in addition, laboratory documentation of hantavirus RNA by enzyme-linked immunosorbent assay (ELISA) or Western Blot test, polymerase chain expansion, or immunohistochemistry (7).

TREATMENT AND DISEASE OUTCOME

After the early phase of illness, an overwhelming immune reaction to the presence of hantavirus, rather than any cytopathic activity of the virus, seems to drive the pathology of HPS (5). To date, there is no specific treatment. Patient management is supportive, focused on respiratory and circulatory support with oxygen and fluids in an intensive care setting. Fluids should be administered with extreme caution to avoid exacerbating fluid buildup in the lungs. Because the potential for person-to-person transmission of HPS is unknown,

physicians and nurses who treat patients, and other health care workers who handle specimens, should use barrier protective techniques to avoid exposure to hantavirus (2). There has been one report of a patient recovering from HPS cardiopulmonary failure following administration of nitric oxide ventilation (8). A double-blind, placebo-controlled trial of the antiviral agent ribavirin, begun in the United States, is currently being expanded to include Chilean patients.

The crude mortality rate due to HPS is approximately 40% to 50% (9). The swiftness with which the patient seeks help is a critical life-or-death determinant. Patients who survive the crisis recover quickly and apparently without sequelae.

PREVENTION AND CONTROL

On September 26, 1997, the Directing Council of the Pan American Health Organization, made up of Ministers of Health from all the countries in the Americas, resolved to intensify measures to detect and control HPS. PAHO urges physicians to notify health authorities of any known or suspected case of the disease. Pursuant to the resolution of its Directing Council, the Organization is currently establishing a network for laboratory diagnosis, reagent production, virological and ecological research, and surveillance. It previously funded studies in Argentina aimed at identifying hantavirus reservoirs and evolving control measures, funded Argentine virologists to study hantavirus in the United States, and facilitated a technical agreement between Argentina and Chile for collaboration in training, surveillance, and health education (2).

Public education about HPS should be fashioned to avoid inducing panic, since the disease is rare. Any measure that reduces the potential for human exposure to infected rodents, their habitats or their excreta should be encouraged. The United States Centers for Disease Control and Prevention recommends clearing grass around dwellings and applying rodenticide in infested areas. In cleaning rodent nests or burrows or droppings from dwellings or workplaces, individuals should first douse them with household bleach, alcohol, or other disinfectant. Wearing a face mask during such activities is advised. Abandoned or unused buildings should be opened up and aired thoroughly before they are occupied. Anyone who sleeps outside should inspect the campsite for signs of rodents and go elsewhere if any are present. Food should be stored in rodent-proof containers, and garbage promptly discarded, burned, or buried (2, 4, 10).

INCREASED INCIDENCE AND IDENTIFICATION

According to PAHO Director Dr. George Alleyne, "Hantaviruses form part of a wider issue, that of emerging diseases and the need to intensify epidemiological surveillance" (2). Although HPS has only recently been identified, it appears to have been present in the Americas for a long time. Native Americans in the United States have been aware of rises in deaths of healthy young men associated with high rainfall and burgeoning rodent populations going back at least as far as 1933 (10). A case has been diagnosed in preserved tissues from a patient who died in 1959 (1). In addition, the wide genetic variation of hantavirus strains in the United States suggests that the disease and its hosts have been paired through a considerable stretch of co-evolution (1). However, even if HPS has had a protracted unrecognized existence in the Americas, it is possible that climate change, human population growth, human penetration into new ecological zones, and other factors have resulted in an increase in incidence, and that it is this increase, together with advances in disease awareness, that has led to identification of HPS (2).

SINOPSIS

El síndrome pulmonar por virus Hanta en las Américas

La infección por virus Hanta, cuadro nefrótico y hemorrágico documentado desde la antigüedad en países de Asia y Europa, se presenta en las Américas en la época moderna con una nueva cara. Conocida por síndrome pulmonar por virus Hanta, la infección americana se caracteriza por una serie de síntomas respiratorios similares a los de la influenza, con hipotensión grave y disnea progresiva que lleva a la insuficiencia respiratoria y, en 40 a 50% de los casos, a la defunción.

Varias cepas virales son las responsables del trastorno y cada cepa tiene por reservorio una especie particular de roedores. El contagio se produce por inhalación de partículas de las materias excretadas por roedores infectados o por contacto con objetos contaminados. Hay datos que podrían indicar la posible transmisión del virus entre seres humanos.

Ante la gravedad de este nuevo problema de salud pública, la OPS está intensificando las medidas para la detección y control del síndrome pulmonar por virus Hanta, entre las que figuran el establecimiento de una red de laboratorios encargados de diagnosticar la enfermedad, preparar reactivos para su detección, investigar la ecología del virus causal y mantener una vigilancia de casos activa.

REFERENCES

1. Khan AS, Rima FK, Armstrong LR, Holman RC, Bauer SP, Graber J, et al. Hantavirus pulmonary syndrome: the first 100 US cases. *J Infect Dis* 1996;173:1297-1303.
2. Pan American Health Organization. Health ministers approve intensified fight against hantavirus. News release. 29 September 1997.
3. Wells RM, Young J, Williams RJ, Armstrong LR, Busico K, Khan AS, et al. Hantavirus transmission in the United States. *Emerg Infect Dis* 1997;3:361-365.
4. World Health Organization. Hantavirus pulmonary syndrome in the Americas. *Wkly Epidemiol Rec* 1997;72(41):305-306.
5. Wells RM, Sosa Estani S, Yadon ZE, Enria D, Padula P, Pini N, et al. An unusual hantavirus outbreak in southern Argentina: person-to-person transmission? *Emerg Infect Dis* 1997;3:171-174
6. Centers for Disease Control and Prevention. Hantavirus pulmonary syndrome—Chile, 1997. *MMWR* 1997;46(40):949-950.
7. Centers for Disease Control and Prevention. Case definitions for infectious conditions under public health surveillance. *MMWR* 1997;46(no. RR-10).
8. Texas Tech University. Hantavirus pulmonary syndrome. [Internet site] Available at: <http://www.ttu.edu/newspubs/newsrel/news177.htm>. Accessed 12 December 1997.
9. Benenson AS, ed. *Control of communicable diseases manual*. Sixteenth Edition. Washington, D.C.: American Public Health Association; 1995.
10. Centers for Disease Control and Prevention. Hantavirus pulmonary syndrome. [Internet site] Available at: <http://www.cdc.gov/ncidod/diseases/hanta/html/hv94cont.htm>. Accessed 12 December 1997.