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Hantavirus in Indian Country: The First Decade in Review

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When bubonic plague ravaged London in 1665, on hand to witness the event was author Daniel Defoe. Although he was only five years of age at the time, he built on that experience to craft a journalistic narrative of the epidemic, his *Journal of the Plague Year*. He relates that: "It was about the beginning of September, 1664, that I, among the rest of my neighbours, heard in ordinary discourse that the plague was returned again in Holland . . . whither, they say, it was brought, some said from Italy, others from the Levant, among some goods which were brought home by their Turkey fleet."[1] The plague was not native to Europe. It first emerged there three hundred years earlier, in 1348, and became known as the Black Death. It killed one-third of the population in just five years, about 25 million people.[2] Perhaps 200 million people died by the end of the fourteenth century. The London epidemic witnessed by Defoe probably left one hundred thousand dead, about a fifth of the city's population.

A catastrophe of this magnitude is no longer part of our common experience. Plague, cholera, smallpox, typhus, and similar contagions have been banished to history or the Third World. These natural disasters have no visible cause and spread with alarming speed. When they suddenly appear on our doorstep we are quite rightly shaken. And when the disease is unknown to science, we are thrown back to the world experienced by Defoe's Londoners, albeit with confidence that scientists will soon have an explanation if not an answer.

Hantavirus first emerged in the spring of 1993 on the Navajo Reservation. Although it is by no means an "Indian disease"—there are four times as many cases of hantavirus pulmonary syndrome (HPS) among non-Indians (see table 1)—it has disproportionately affected Native Americans. Hantavirus is carried by the ubiquitous deer mouse. Close contact with mice in a dwelling

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is strongly associated with hantavirus and the resulting illness, HPS. The disease has been fatal in 37 percent of cases. Outbreaks of the illness in the Southwest are associated with bursts in the deer mouse population, which are in turn a response to changing climate patterns. The background level of infection in the West appears to be increasing as well, perhaps a result of more thorough diagnoses. Inadequate rural housing, especially common in western Indian Country, heightens the risk of contracting this disease. Hantavirus and HPS pose an enigma. Although signs of the virus are widespread throughout the West, the incidence of the disease is quite low, especially when compared with such everyday risks as auto accidents. The virus is everywhere, but few people get sick. Why? Answering this question poses a continuing challenge to research as well as to defining public health policy to combat the illness.

The course this illness takes is terrifying, as graphically described in this article. Defoe's observation of the plague years is not out of place: "The contagion despised all medicine; death raged in every corner; and had it gone on as it did then, a few weeks more would have cleared the town of all, and everything that had a soul. Men everywhere began to despair; every heart failed them for fear; people were made desperate through the anguish of their souls, and the terrors of death sat in the very faces and countenances of the people" (par. 800).

HANTAVIRUS EMERGENT: NAVAJOLAND 1993

An outbreak of a severe respiratory illness began in the Four Corners region of Arizona, New Mexico, Colorado, and Utah in May 1993. The first victim to attract notice, on May 14, was "a young Navajo long-distance runner who died of sudden pulmonary edema after attending the funeral of his fiancee."[3] The young man was nineteen; his fiancée was twenty-one.[4]Three days later, a total of five deaths attributed to acute respiratory distress syndrome among previously healthy adults was reported by the Indian Health Service.[5] By June 17, twenty-four cases were being investigated in the region, including twelve deaths. The cause of these deaths was a complete mystery. The initial diagnosis of the first seventeen patients included: pneumonia (seven cases), abdominal pain (three cases), acute respiratory distress syndrome (two cases), cardiopulmonary arrest (two cases), and a variety of other causes (three cases). Among the diagnoses also considered were "pneumonic plague, leptospirosis, inhalational anthrax, rickettsial infections, pulmonary tularemia, atypical bacterial and viral pneumonias, legionellosis, meningococcemia and other sepsis syndromes, and illnesses caused by viruses not commonly seen in the United States (flavivirus, arenavirus, and bunyavirus)."[6] This was a new and frightening disease that hid behind the symptoms of more common afflictions, making it difficult to diagnose.

Through a "fortuitous" set of circumstances, the work of a mammalogist studying a booming deer mouse population in the region in combination with prior work of the Department of Defense in characterizing Hantaan virus—which had affected American troops in the Korean war—led to the rapid identification of the cause of these illnesses and deaths.[7] It is a virus of the family

Table 1
HPS Cases January 1993–July 2004

Characteristic	Total	%
Reported cases	366	100%
Gender		
Male	227	62%
Female	139	38%
Race		
White	284	78%
American Indian	71	19%
Black	6	2%
Asian	3	1%
Ethnicity		
Hispanic	45	13%
Case fatality		
Dead	135	37%
Age (years)	Mean=37	[10-75]

(Source: Centers for Disease Control and Prevention, "Case Information: Hantavirus Pulmonary Syndrome Case Count and Descriptive Statistics," http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/caseinfo.htm.)

Bunyaviridae, genus *Hantavirus*.[8] It is typical to name the species of a virus after its place of discovery. The hantaviruses take their name from the Hantaan River separating North and South Korea. The American variant of the virus—found only in the Americas—was first identified in the Canyon del Muerto (literally, "Canyon of the Dead").[9] This was not encouraging. Another name, "Four Corners virus," was also briefly used and then rejected, possibly because it implied the virus was limited to this area. Finally, the appellation "sin nombre" ("no name" in Spanish) was conferred, and it is now designated the Sin Nombre virus (SNV). The deer mouse is identified as its reservoir and host. It causes hantavirus pulmonary syndrome (HPS) in humans, sometimes more accurately called hantavirus cardiopulmonary syndrome (HCPS).[10]

HPS Risk

As of 6 July 2004, the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, had confirmed 366 cases of the illness in the United States since January 1993.[11] Thirty-seven percent of these died. Seventy-five percent of cases occurred in rural areas. Cases have been identified in thirty-one states, some attributable to other variants of the virus, but 93 percent of cases have come from seventeen western states. Native Americans account 19 percent of the victims of HPS, although they comprise less than 2 percent of

Table 2
Relative Risk of HPS in Selected At-risk Populations: 1993–2004[a]

Region:	United States	Western states	Western Hispanic	Southwest	Native West
Population 2000[b]	281,422.4	91,629.6	22,841.0	49,354.0	1,611.3
At-risk population	78,748.5	18,176.0	2,136.8	5,393.6	854.5
HPS cases	366	341	42	203	66
Incidence rate/ 100K[c]	0.46	1.88	1.97	3.76	7.72
Relative risk					
US population	1.0	4.1	4.3	8.2	16.8
Western states	—	1.0	1.1	2.0	4.1

[a]The at-risk population is 133.3% of the rural population. Seventeen western states account for 93% of HPS cases. These states (cases) are: Arizona (36), California (40), Colorado (30), Idaho (18), Kansas (14), Montana (23), Nebraska (6), Nevada (14), New Mexico (60), North Dakota (7), Oklahoma (2), Oregon (5), South Dakota (7), Texas (25), Utah (23), Washington (27), Wyoming (4). The time frame for reporting cases is January 1, 1993, through July 6, 2004, a period of 138 months. *(Source: Centers for Disease Control and Prevention, "Case Information: Hantavirus Pulmonary Syndrome Case Count and Descriptive Statistics," http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/caseinfo.htm.)*

[b]Population in 1000s. *(Source: US Census Bureau, "Table GCT-P6. Race and Hispanic or Latino: 2000 Data Set: Census 2000 Summary File 1 (SF 1) 100-Percent Data Geographic Area: United States (and various states)–Urban/Rural and Inside/Outside Metropolitan Area," http://factfinder.census.gov/.)* The tables enumerate rural and urban populations by race. *Hispanic* is the Hispanic-Latino at-risk population in the Western states. *Southwest* is California, Nevada, Arizona, Colorado, New Mexico, and Utah. *Native West* refers to rural Native Americans in the seventeen western states, mostly, but not necessarily, resident in tribal areas.

[c]Incidence rates are the number of persons affected per 100,000 in the population, usually calculated on an annual basis. The rates shown on the table are the cumulative cases per 100,000 in the population as it was in 2000. This averages the relative risk from January 1993 to July 2004.

the population in the Great Plains and West.[12] Statistically, cases have occurred among Native Americans ten times more frequently than their numbers in the general population of the West would suggest, a crude statistic that merits refinement.[13]

While the Sin Nombre virus was first discovered in Indian Country, and there was initial fear that it constituted an "Indian disease," in terms of total numbers, most of the victims have been Euro-Americans. Studies in South America have even found indigenous peoples with high rates of exposure to a Sin Nombre–like virus but with no reports of illness.[14] However, no such immunity has been found in North America. Deer mice live everywhere in the rural West, and 75 percent of HPS victims lived in rural areas as well. Most of

the remaining victims, 25 percent of HPS cases, reported recent visits to rural areas. Not everyone in the West is at risk for HPS. The actual at-risk population can be estimated by combining the rural census population with an estimate of visitors in a 75 percent to 25 percent proportion, mathematically 133.3 percent of the rural population. Most HPS cases have occurred in the rural West, in that part of the American landscape that is also home to much of Indian Country.

Rural residents and frequent visitors to rural areas in the western states are four times more likely to contract HPS than other Americans nominally in the at-risk population (see table 2). There is an added risk to living in the Southwest. The hispanic segment of the at-risk population in the West is no more at risk than the general at-risk population, but Native Americans are at four times the risk of other rural Westerners (see table 2). Three factors account for this increased risk: (1) Native Americans comprise a larger share of the at-risk population in the Southwest; (2) the Southwest is prone to epidemic outbreaks of the disease; and (3) Native Americans often live in poorer quality housing more vulnerable to mice during epidemic outbreaks of the disease. The first two of these factors can be demonstrated empirically; the third is open to interpretation. While the number of cases of HPS is quite small, many continue to go undetected.[15] It is prudent to consider the available data as a sample representative of a greater threat. Hantavirus has been around for centuries, perhaps thousands of years. It is up to those of us living in the rural West to learn to adapt to it. The risk of contracting HPS varies with where you live, not who you are.

HPS Cases

The case descriptions of this disease are alarming. This is a highly lethal disease that is very difficult to diagnose. Early symptoms are similar to the flu, pneumonia, or other respiratory illnesses. After exposure to the virus, the incubation period of HPS is two to three weeks, followed by the onset of flu-like symptoms that can persist for three to ten days.[16] This leads into the cardiopulmonary phase, which can end in death in just twenty-four hours. There is no treatment for the disease other than supportive intensive care, although an antiviral drug has been tried (with unremarkable success) and passive immunotherapy using plasma from HPS survivors may offer an effective therapeutic intervention.[17] The following case report is abstracted from the *New England Journal of Medicine:*

> A nineteen-year-old man living in rural New Mexico presented to an emergency department with a one-day history of fever, myalgia [muscle pain], chills, headache, and malaise; he did not have dyspnea or cough. The patient had been in excellent health and was a marathon runner; his fiancee, with whom he had lived, had died two days earlier of a rapidly progressive respiratory illness. His temperature was 39.4°C [102.9°F], his heart rate was 118 beats per minute, his blood pressure was 127/84 mm Hg, and his respiratory rate was 24 breaths per minute.

> The physical examination was normal. The patient was treated with erythromycin [an antibiotic used to treat respiratory infections such as pneumonia, but ineffective against viral diseases like HPS], amantadine [a drug effective against influenza A], and acetaminophen [a common painkiller] and then discharged.
>
> Two days later, the patient presented at a clinic with persistent symptoms plus vomiting and diarrhea. His temperature was 36°C [96.8°F], his heart rate was 80 beats per minute, his blood pressure was 90/70 mm Hg, and his respiratory rate was 22 breaths per minute. The physical examination was normal, with clear lung fields on auscultation; the patient was discharged with no change in the diagnosis or therapy. . . . The day after discharge, the patient had acute respiratory failure and cardiopulmonary arrest and could not be resuscitated.[18]

Another report, about the search for the cause of this illness, noted: "The death that set the search into motion was that of a young man who feverishly began gasping for air as he was heading to his fiancee's funeral. Family and friends in the car had tried to comfort him before they realized that this was more than grief. He was dead by the time they got him to the hospital. An autopsy found the small blood vessels in his lungs had sprung hundreds of leaks, causing his fluid-clogged lungs to swell to twice normal size, drowning him in blood."[19]

This is a virus that strikes young and healthy adults and older children with an often rapidly fatal disease. The case history of a twenty-seven-year-old woman in California notes: "Twenty hours after admission, the patient noted progressive chest tightness that was not alleviated by oxygen. The patient developed acute respiratory distress syndrome and had recurrent cardiopulmonary arrests. She died 40 h after she was hospitalized."[20] A report of HPS cases in Alberta, Canada, observed that: "The median duration of hospitalization was 9 days (range, 6–85 days) for those who survived [14 cases], and for those who died [5 cases], the median interval from presentation to death was 2 days (range, 1–5 days)."[21]

There is no evidence that the Sin Nombre virus can be transmitted from person to person. No caregivers have contracted the illness after coming into contact with patients that have the disease, even after attempting mouth-to-mouth resuscitation.[22] The virus can persist outside its host reservoir for only a few days before exposure to air and sunlight kill it. People are cautioned to avoid entering and cleaning closed buildings without thoroughly airing and disinfecting the interior. Any disturbance of dirt and dust inside the structure by sweeping or vacuuming can atomize the virus, leading to the risk of inhalation and infection. The virus is small, even for viruses, with a diameter of less than five microns. A high-efficiency particulate air (HEPA) filter is required for protection. An early study found that 70 percent of HPS cases were associated with cleaning a building that had signs of rodent infestation. More recently, researchers have suggested that exposure in a confined space, such as a home, may account for up to 80 percent of hantavirus infections.[23]

The CDC reports that the HPS outbreak was predictable. Navajo elders observed a correspondence between the heavy winter-spring rains—and consequent bumper crop of piñon nuts, and the deer mice that feed on them—and the appearance of an "illness enters through the mouth, the nose or the eyes, and . . . usually attacks the strongest and healthiest of the Navajo people."[24] Navajo oral history noted similar outbreaks in 1918 and 1933–34: "Healers say that when mice enter the home, they put people at risk of infection, as people come into contact with mice droppings and urine . . . . Therefore, traditional medicine prescribes avoiding mice, keeping them out of the hogans, and isolating food supplies."[25]

REGIONAL ECOLOGY AND HANTAVIRUS INCIDENCE

The Navajos' observations have been validated by research. The deer mouse, *Peromyscus maniculatus,* is the reservoir and host for this disease. This animal has been described as "the most numerous mammal in North America," a "quintessential generalist."[26] It is found throughout the United States and Canada except along the Atlantic seaboard and in the Southeast. It is a rural and suburban dweller, less common in urban settings, where it faces competition from other rodent species. It enters homes in search of food and nesting sites, often in a seasonal cycle. The hantavirus is shed by the animal through saliva, feces, and urine, whereby the virus can become airborne and inhaled by humans.[27]

Exposure to the virus is influenced by (1) the density of the deer mouse population, (2) the proportion of mice infected, and (3) the rate the virus is shed by the host. "Specifically, large-scale population declines [or increases] seem to affect not only the likelihood of rodent-human encounters, but also the likelihood that a given encounter involves a rodent that is shedding large amounts of virus."[28] As their population increases, mice began competing and fighting with each other for territory. The virus is passed through wounds, infecting a growing share of the population. A ten-fold increase in the mouse population, accompanied by a five-fold increase in the proportion of mice infected, could result in a fifty-fold increase in exposure risk. This helps explain the low rate of the illness in most years, punctuated by dramatic outbreaks in the years or seasons when the mouse population increases.

Deer Mouse Ecology and HPS: Southwest

There are two distinct phases of hantavirus infection in the Southwest. The background or endemic rate of infection is quite low, on the order of four to six cases annually. This low rate of incidence is contrasted with epidemic or outbreak periods such as that experienced in the Four Corners in 1993–94, when fifty-six cases were reported. It is estimated that the deer mouse population had increased by at least ten-fold in 1993 after a wet and warm winter and spring. The Sevilleta National Wildlife Refuge in central New Mexico reported a twenty-fold increase in the deer mouse population in 1993 as the abnormal rainfall in turn increased food supplies for mice.[29] These weather

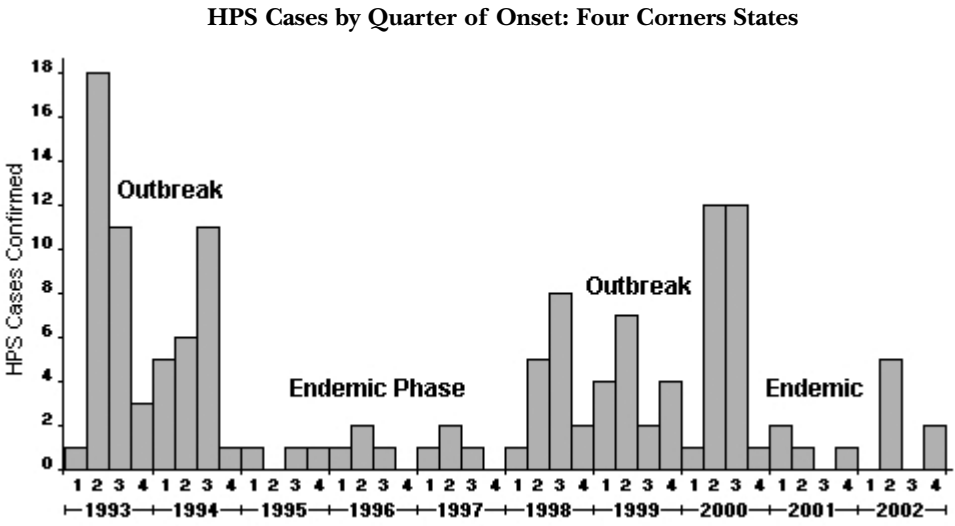

FIGURE 1. *(Source: Centers for Disease Control and Prevention, "Hantavirus Pulmonary Syndrome Cases by Region, United States, as of July 6, 2004," Teaching Materials Epidemiology Slide 3. Available at http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/epislides/episl3.htm.)*

conditions were related to the El Niño southern oscillation, which peaked again in the late 1990s. There were 115 cases during five outbreak years from 1993 through 2002, five times the twenty-two cases that occurred during the other half of the decade. In 1993, at Red Mesa on the Southern Ute Reservation in Colorado, hantavirus was detected in 50 percent of the deer mouse population near the home of a person who died of HPS. But a subsequent forty-one-month surveillance of the deer mouse population in the same area observed a prevalence rate of just 9.6 percent.[30]

A large study in California found a prevalence of SNV antibodies of 11.8 percent in the deer mouse population between 1975 and 1995.[31] This rate varied from 0.7 percent in inland valleys and urban areas, to 11.6 percent along the coast, to 14.5 percent in the foothills and mountains of the Sierra Nevada Range. Where cases of HPS were reported, this increased to an average of 26.8 percent and to a maximum of 50 percent. When it was discovered that 71.4 percent of the deer mice on Santa Cruz Island (one of the California Channel Islands) tested positive for SNV antibodies, a congressman called for the closure of the Channel Islands National Park, although none of the islands in the park had unusually high prevalence rates. Nonetheless, a congressional hearing was held to investigate the risk.[32]

The at-risk population in the Four Corners is 12.9 percent Native American, compared to 3.8 percent in the Northwest, the High Plains, California, and Nevada. Thus, a larger share of the at-risk population is Native American in the region where outbreaks have been frequent; twenty cases of

HPS among Native Americans can be attributed to these factors alone. Another six cases have been identified in other parts of the West. But this leaves about forty cases unexplained, all occurring in the Four Corners.[33] About one-quarter of all HPS cases nationally to date are attributable to outbreaks in the Four Corners.

Deer Mouse Ecology and HPS: Montana (Northwest and High Plains)

Outside the Four Corners region a fairly consistent background or endemic incidence of HPS cases is reported, averaging 4.2 cases per quarter. There is a modest seasonal trend. Through the entire decade, cases reported in the fourth quarter reflect a decline from those reported the preceding third quarter. This can be attributed to declines in the deer mouse population in late fall and the winter months.

Montana has been the focus of studies representing the range of biomes found on the northern high plains and intermountain Northwest.[34] The climate in this region is cooler than that in the Southwest, and the winters are cold. Parts of the region are often covered in snow for long periods. There have been no epidemic outbreaks in this part of the country. The seasonal peaks in the deer mouse population differ from those in the Southwest and are less pronounced. A long-term study of the deer mouse population in six different sites around Montana revealed that the population numbers can peak in either or both the spring and the fall. The seasonal peaks, while still large, are smaller than those in the Four Corners. The five-year study found the average seasonal peaks in populations to be about five times the lows.[35] This is in sharp contrast to the ten-fold, and even twenty-fold, increases observed in the Four Corners prior to the 1993–94 outbreak.

HPS Cases by Quarter of Onset, Outside Four Corners Region

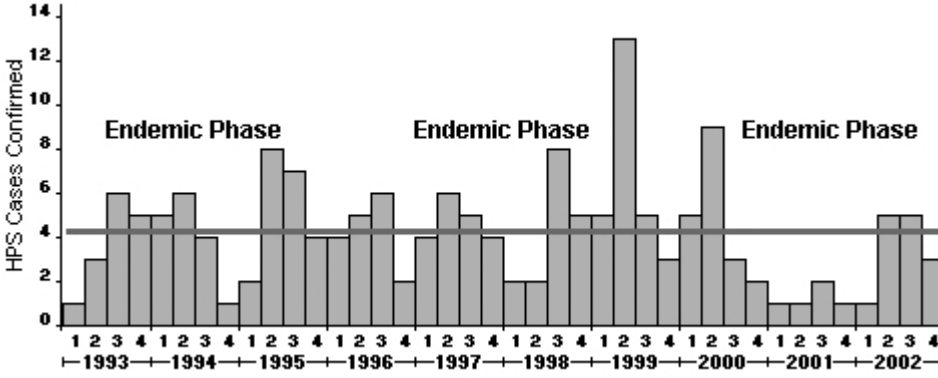

Figure 2. *(Source: Centers for Disease Control and Prevention, "Hantavirus Pulmonary Syndrome Cases by Region, United States, as of July 6, 2004," Teaching Materials Epidemiology Slide 3, http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/epislides/episl3.htm.)*

A report of HPS cases in northern Alberta, Canada, noted that about 80 percent of cases occurred in spring and fall—half in the spring and half in the fall.[36] This pattern is consistent with the peaks and lows in the deer mouse population reported in Montana. In all, nineteen cases were identified in Alberta between 1989 and June 1998, but half (ten) of these occurred over the single year between June 1997 and June 1998, suggesting that a climatic event increased the deer mouse population. This unexplained cluster of cases offers the possibility that the low endemic incidence of the disease in the north-west states could be subject to an epidemic outbreak, although none has yet been observed. No climatic events have been linked to these cases in the research literature.

The endemic incidence of HPS in the Four Corners can readily be estimated. There were 22 cases during the five years when there were no outbreaks, compared to 115 cases during five years of outbreaks over the decade from 1993 through 2002. There have been no new outbreaks since. A straight substitution—22 cases for 115, a difference of 93 cases—provides a reasonable estimate of the endemic incidence in the region. There have been 149 cases of HPS reported in the Four Corners to 6 July 2004—93 cases attributable to outbreaks, 56 cases reflecting the endemic incidence of HPS. Statistically, there is no difference in the endemic incidence rate between the north-west states, Four Corners states, and California-Nevada (x^2=0.23, p < .90, df=2, two-tailed test). The endemic risk is greatest in Montana, Idaho, and Washington, although the difference is not statistically significant (x^2=3.22, p < .20, df=2, two-tailed test).[37] The low relative risk in the southern plains states actually hides the clustering of HPS cases in the western portions

Table 3
Endemic Relative Risk of HPS in Selected At-Risk Populations: 1993–2004[a]

Population:	Western states	Hispanic[b] West	California and Nevada	Four Corners	North-West states	Montana[b] ID and WA	Southern Plains
Population 2000	91,458.6	22,841.0	35,869.9	13,484.1	13,401.5	8,090.3	28,702.1
At-risk (1000s)	18,176.0	2,136.8	2,735.5	2,658.1	4,610.9	2,549.1	8,171.9
Endemic HPS cases	248	42	54	56	91	68	47
Incidence	1.36	1.97	1.97	2.11	1.97	2.67	0.58
Relative risk	1.0	1.4	1.4	1.5	1.4	2.0	0.4

[a]The *Four Corners* states are Arizona, New Mexico, Colorado, and Utah. The *north-west states*—the Pacific Northwest and northern High Plains—are: Washington, Oregon, Idaho, Montana, Wyoming, North Dakota, and South Dakota. The *Southern Plains* states are Nebraska, Kansas, Oklahoma, and Texas.

[b]The *Hispanic West* is a subset of the western states; the Montana, Idaho, and Washington grouping is a subset of the north-west states.

of these states. Parts of these states have an ecology similar to that of Colorado and New Mexico, and parts have one similar to Missouri and Arkansas—where no cases have been reported—and to Louisiana, where just one case has been reported.

Given the cumulative incidence rate in the at-risk population in Montana, Idaho, and Washington, about three cases would be expected in the Native American population to date (the at-risk Native American population was 99,500 in 2000). At least one case in Montana has been confirmed, as well as other possible cases in the Pacific Northwest.[38] A second Montana case, identified as a resident of the Blackfeet Indian Reservation, was reported in May 2004.[39] Native Americans in these states are at least at the same risk as other rural residents. It is reasonable to conclude that the endemic risk is similar for rural Indians and non-Indians alike from the western Great Plains to the Pacific Coast; it is possibly a little higher in the Northwest for both Native and non-Native groups.

Two studies in Montana have focused on the prevalence of antibodies to SNV in mice captured in urban and suburban homes around Butte and in and around rural ranches at three sites in west-central Montana. In the Butte study, individual mice captured in seven of the twenty-five participating homes tested positive for SNV, a home exposure rate of 28 percent over a period of three years (1996–99). In the rural study, mice were captured inside buildings that people entered on a regular basis, in outbuildings entered only occasionally, around the perimeters of buildings, and in the general vicinity of structures.

About one-quarter (24.5 percent) of the captured deer mice were infected with hantavirus. The averages were subject to wide fluctuations, ranging from no mice captured testing positive to SNV in some months to as many as 70 percent testing positive in others. Prevalence of SNV was highest in the first half of the year and declined sharply in the fall; on average it was

Table 4
Deer Mice Captured at Rural Ranch Sites and Numbers Infected with Sin Nombre Virus, Montana 1996–99

Sample % Captured:	Inside Buildings Used		Outside Buildings		Captured and Tested	
	Regularly	Irregularly	Perimeter	Distant	Number	Infected
Anaconda[a]	8%	4%	—	88%	1,132	23.2%
Butte	23%	17%	16%	44%	705	28.8%
Cascade	42%	21%	16%	21%	348	19.6%
Averages	18%	11%	8%	63%	2,185	24.5%

(Source: Amy J Kuenzi et al., "Antibody to Sin Nombre Virus in Rodents Associated with Peridomestic Habitats in West Central Montana," American Journal of Tropical Medicine and Hygiene *64, nos. 3–4 (2001): 137–46.)*

[a]The Anaconda and Butte sites are located in rural areas near those communities. Cascade is a small town southwest of Great Falls, near the ranch capture site.

highest in and around buildings (38.0 percent) and lower at sites in natural settings well away from homes (16.5 percent).[40]

As of 6 July 2004, twenty-three cases had been confirmed in Montana by the CDC since 1993. While many case reports indicate that victims had significant exposure to deer mice, others are somewhat baffling. University of Montana freshman Lauren Howell contracted HPS in the fall of 2000. The following report is abstracted from the university newspaper (*folfing* is disc golf, played with a Frisbee):

> Only nineteen years old, Howell spent two months in a Missoula hospital battling hantavirus, a rare disease that can be fatal. Howell fell into a coma for two weeks, during which her vital signs crashed and she suffered a stroke, paralyzing her left side.
>
> She now walks with a quad-cane while she attempts full recovery.
>
> Howell was one of four Montanans confirmed with the hantavirus in 2000 and one of fifteen to ever contract the disease. Three Montanans have died from the disease, which showed its first case in the state in 1993. She believes she contacted hantavirus, which is commonly spread by rodents, from either folfing in Pattee Canyon or hiking near the Rattlesnake trailhead in late August or early September.
>
> At the end of February, Howell will travel to the University of New Mexico to be a part of a research study on the hantavirus. Howell said the hantavirus could possibly have a lasting effect on her kidneys.[41]

Summary: HPS Epidemiology 1993–2004

Measured against the at-risk population in a region, Native Americans in the Southwest are about three times as likely to get HPS than others at risk in the region, even after adjusting for the greater proportion of Native Americans living in rural areas. No comparable differences are found outside the region. The at-risk population in the Four Corners is 12.9 percent Native American, compared to 3.8 percent in the Northwest, High Plains, California, and Nevada. About twenty cases of HPS can be attributed to this larger at-risk population. This leaves about forty cases among Native Americans in the Southwest unexplained, an incidence rate of 11.70 for Native Americans compared to 3.76 for the region (from table 2). Thus, the incidence rate for Native Americans is 3.11 times higher than that for the region as a whole. No differences are found outside the region. The deer mouse population can fluctuate wildly in the Southwest. During the initial 1993 outbreak in the Four Corners, the deer mouse population expanded twenty-fold after an unusually warm and wet winter and spring. This was related in turn to a major climatic cycle, the El Niño. In contrast, seasonal variations in Montana can lead to a five-fold increase in the deer mouse population but without the dramatic population bursts observed in the Southwest. The dynamic relationship between environmental factors, population numbers, and rates of SNV infections in deer mice are complex and not well understood. What is clear is that

HPS occurs in outbreaks in the Southwest that can be anticipated in the wake of major climatic events. Elsewhere there is a steady background level of infection clustered in the spring and fall.

Since most cases of HPS are related to exposure to the virus in confined spaces, usually a home or cabin, it is reasonable to associate differences in the incidence of HPS cases in the Four Corners with differences in housing quality. But there is no reliable way to measure this. The 2000 census stated that 31.9 percent of Navajo homes lacked plumbing, compared to 0.6 percent for the United States as a whole, a measure of housing quality. A 1990 study noted 40 percent of 176 homes surveyed on the Navajo Reservation had no running water, but only 2.9 percent of these reported any mice in the home.[42] Significant mouse infestations cannot be inferred from conventional measures of housing quality. Another study in a "Native American community in northwestern New Mexico," observed that mice were trapped in five of thirty-five control homes (14.3 percent) in just a three- to four-week period.[43] However, the study cautioned that its "statistical power" was limited since the experiment took place during "a period of low rodent abundance (August–November 2000)." There are no measures of the rates of infestation in non-Indian homes for comparison. While observation suggests that housing quality is the determining factor for increased risk of HPS in the Four Corners, this cannot be empirically demonstrated.

THE ENIGMA OF HANTAVIRUS INFECTION

Why do some people get the disease while others in like situations do not? The evidence presents an enigma. While most people who contract HPS likely do so through exposure in and around a home (70 to 80 percent), in many cases only casual outdoor exposure has been found. The virus is short-lived in open air and sunlight, making such cases even more puzzling. The disease is rare. There are eighteen million people in the at-risk population in the West—tens of thousands of ranches, farms, and homes where people routinely encounter deer mice—but only an average of thirty-three cases have been reported annually, including the outbreaks in the Southwest. Researchers have found significant numbers of infected mice (about 25 percent) in homes and ranches in Montana, but no cases of HPS are reported from those same homes. Yet a coed goes hiking and contracts the disease. It skips younger children and the elderly, the latter a segment of the population that is often vulnerable to infectious diseases due to weakened immune systems. The flu killed sixty-five thousand people in the United States in 2000, 90 percent over the age of sixty-five.[44] About 6 percent of the population in the West is seventy-five or older. Yet no cases of HPS have been reported in this age group, where twenty-two cases would have been expected (x^2=22.69, p<.001, df=1, two-tailed test) based solely on their numbers in the population. The clustering of cases in a single household is also uncommon.[45] Although the initial two victims shared a trailer, more often the disease singles out individuals, ignoring other members of the same household, as well as neighboring households exposed to the same deer mouse population. HPS remains a comparatively rare disease even in areas

where it is fairly common. All this suggests that there is a low threshold to infection but that exposure to the virus is rare, despite the fact that the virus and its host are found everywhere in the rural West.

People who work in close contact with deer mice should be at greater risk for exposure to the virus than the general population. This hypothesis was tested in a sample of farm workers in southern New Mexico and western Texas. But the study concluded, "While these populations [of workers] showed a high level of risk, we did not find a drastic increase in the prevalence of infection."[46] Only about 1 percent of the farm workers had antibodies for the virus in their blood. An earlier study examined a large (n=494) high-risk group of workers in the Four Corners area and found none that tested positive for exposure to the hantavirus, even though the majority reported handling rodents, entering or cleaning closed spaces, and working in areas with mouse droppings.[47] Only two cases of HPS have been diagnosed in southern New Mexico compared to the scores of cases in the Four Corners. Research into the dynamics of hantavirus infection is very much a work in progress, and the following analysis is best viewed as reasoned speculation based on available evidence.

Deer mice are the long-term hosts for the hantavirus but are not immune from its effects. Mice usually survive the initial infection and actively shed the virus during this phase, which may be as brief as a month. The mouse builds its own immunity to SNV, after which the virus remains at a low level. One interpretation of these results suggests that "the rodent immune system is decreasing the amount of virus, thereby decreasing the quantity of infectious virus shed in excreta. This assumption, in turn, suggests that the infection rates of at-risk groups . . . are low, despite the high frequency of infection and broad geographic range of *P. maniculatus* [deer] mice, because deer mice secrete the highest amount of infectious virus during the early or acute stages of disease, when antibodies to SNV are absent."[48] This may help explain why most cases are traced to exposure to deer mice in the home, but not all homes with mice lead to cases of HPS. Once infected, mice develop an immunity to reinfection. It may be a matter of when mice enter a home, at what phase of their infection cycle, that determines the risk of contracting HPS. If the infection threshold is low in people, then cases that follow from incidental outdoor activities are also explained. Exposure to a single mouse actively shedding the virus may be all that is needed to contract the disease, and this exposure is in fact rare.

The enigmatic character of hantavirus infection is reflected in this cautionary statement from the CDC, which urges people to take no chances: "Anything that puts you in contact with rodent droppings, urine or nesting materials can place you at risk for infection."[49] It may be that the frequency with which someone happens to come into contact with mice is a determining factor, not the intensity of that exposure. "*Anything* that puts you in contact" poses a risk. The question may be moot, since mouse infestations increase both the frequency and intensity of possible exposure to the virus. But the CDC consensus is the foundation for public health policy. Should housing be constructed with the intention of rendering it mouse proof to eliminate all possibility of home exposure to hantavirus, or just mouse resistant to reduce

the number of mice entering homes and to reduce the intensity of exposure? The distinction is relevant since the current building code for mobile homes specifies only the latter, and trailers have been identified as a risk factor for HPS on the Navajo Reservation.[50] Given the uncertainties, it is prudent to avoid all exposure to deer mice.

RISK AND PUBLIC POLICY

People have a well-observed indifference to threats that are not howling on their doorstep.[51] Defoe observed "that where the plague was in its full force, there indeed the people were very miserable, and the consternation was inexpressible. But a little before it reached even to that place, or presently after it was gone, they were quite another sort of people; and I cannot but acknowledge that there was too much of that common temper of mankind to be found among us all at that time, namely, to forget the deliverance when the danger is past" (par. 700). Hantavirus presents a very low public health threat, but the disease masks as many other possible afflictions and the course of the illness is appalling in its speed and lethality. This is the kind of threat that produces both casual indifference when the disease is absent and diffuse fear and hysteria when outbreaks occur. Responses to the threat can be summarized under two broad categories: public health and health care, and societal adaptation.

Health Care: Research, Prevention, Diagnosis, and Treatment

The volume of research on the hantavirus over the past decade is stunning. A search on PubMed/Medline produces twenty-five hundred published research reports. This reflects a lot of energy focused on a disease that is a minor public health threat. Perhaps the emergence of this virus, which has been around for centuries, poses an unacceptable affront to medical science and public health. Whatever the motivation, much has been learned and more will be learned. There is a clear need to better understand the dynamics of the transmission of the disease so that more effective preventive measures can be taken. Prevention would also be served by the development of a vaccine, and at least one report exists of a vaccine that has been effective in primates.[52] This could be useful in high-risk areas when outbreaks occur.

Public education flows from research and this review is a part of that process. Most HPS cases are associated with contact with deer mice in confined spaces, usually in and around the home. Strategies to reduce this exposure are the most effective means to reducing the risk of contracting the disease. A short list of sources for additional information, including the National Park Service rodent exclusion manual, follows this text.

Surveillance of rodent populations is a common public health practice. Deer mouse populations are routinely sampled to determine if the rate of hantavirus infection is increasing. Ideally, such increases should trigger a warning to area health-care providers to be alert for possible HPS cases. The importance of this warning is underscored by the tragic case of Hardy Haceesa. A Navajo then twenty-three years old, Haceesa was a resident of rural

Nageezi, New Mexico, about fifty miles southeast of Farmington. In April 1998 he came down with the symptoms of HPS. When he presented at the Indian Health Service hospital in Shiprock, he was diagnosed with bronchitis, treated for that illness, and sent home. When his condition worsened, he was taken to the San Juan Regional Medical Center in Farmington, where he was diagnosed with hepatitis, treated, and again sent home. His condition further worsened and was taken back to Farmington the following day. He was then placed on a ventilator and airlifted to the University of New Mexico Hospital in Albuquerque, where he was diagnosed with HPS and subsequently died. Treatment came too late to give him a fighting chance. Despite living in the region where hantavirus first emerged with devastating impact, and despite the availability of a reliable diagnostic test, two medical centers failed to accurately diagnose his illness.[53] Hantavirus is a rare disease that presents symptoms similar to many more common illnesses. An early warning of an outbreak should increase vigilance among health care providers.

Societal Adaptation

Mouse-proofing homes is the most effective strategy for reducing the risk of HPS. This can be reflected in building codes. Such codes routinely incorporate requirements to protect structures and their occupants from smoke and fire, structural failure, termites, and damage from hurricanes. The motto of the International Code Council, the group that crafts the building code used across the West, is "Setting the Standard for Building Safety." An effective code standard could help designers and contractors build rodent-proofing features into a structure rather than adding them on after the fact. The federal government sets standards for trailers since they can be transported across state lines. The current rodent exclusion standard in the trailer code (24 CFR Part 3280.307) states:

> (c) Where adjoining materials or assemblies of materials are of such nature that separation can occur due to expansion, contraction, wind loads or other loads induced by erection or transportation, sealants shall be of a type that maintains protection against infiltration or penetration by air, moisture or vermin.
>
> (d) Exterior surfaces shall be sealed to resist the entrance of rodents.

This is not much of a standard. The code needs to specify the use of materials and practices in areas of the structure particularly vulnerable to providing openings for mice, such as the entry areas of utilities. This is a reasonable societal adaptation to the threat of hantavirus.

Current housing projects point out the importance of making mouse-proofing an integral aspect of building codes. Two respected universities, Pennsylvania State University and the University of Washington, are engaged in projects to build straw-bale structures on reservations.[54] Other groups have also adopted straw-bale construction as an "answer" to providing affordable

"sustainable" housing in Indian County. These efforts are laudable, but are straw-bale homes safe? Straw-bale structures use bales of straw to form the walls and provide support for the roof. The straw bales are sealed inside and out with only a thin layer of vulnerable plaster or stucco applied directly to the straw. These buildings are literally constructed of nesting material for mice, and even their advocates note they are often infested.[55] The builders need to consider what steps should be taken to assure these structures do not pose an excessive risk of contracting HPS in the rural West, where hantavirus is at large.

HANTAVIRUS AT LARGE

The risk of HPS is slight, but it is persistent and lethal. Because symptoms mask as so many other diseases, many cases may go unreported and undiagnosed. The Southwest is vulnerable to outbreaks due to periodic explosions in the deer mouse populations. These usually occur after a warm and wet winter. As this essay is being written (winter 2005), Southern California is experiencing record rainfalls. Is this indicative of an increasing HPS risk? Much of the West has been in a drought since the late 1990s. As the drought period ends, will the mouse population rebound with an increased incidence of the HPS across the West? These questions underscore the permanence of hantavirus in the rural West. The only choice open to us is to learn to adapt to this risk by minimizing exposure to deer mice. This is of particular importance to Indian Country. The National American Indian Housing Council reports, "In Tribal areas, *40 percent* of homes are overcrowded and have serious physical deficiencies" (emphasis in original) and two hundred thousand units are needed today to provide adequate housing.[56] Perhaps it is best said that hantavirus is not so much an Indian disease as is poor housing; hantavirus merely follows. The following was reported in May 2004:

> A woman from Glacier County is hospitalized in Great Falls with hantavirus, the state health department said Monday. It's the second case of hantavirus reported this spring. A Flathead County man died of the disease in late March. . . . The state agency identified the woman, in her 20s, as a resident of the Blackfeet Indian Reservation."[57]

SOURCES OF ADDITIONAL INFORMATION

Most of the research articles cited in this review are available online; some—*JAMA, New England Journal of Medicine*—require an online subscription. The easiest form of access is through PubMed (see below).

1. Centers for Disease Control and Prevention, "All About Hantaviruses," http://www.cdc.gov/ncidod/diseases/hanta/hps/index.htm (accessed 1 May 2005). This is the most authoritative and current source for information on hantavirus, HPS cases, precautionary measures, and related subjects.

2. James N. Mills et al., "Hantavirus Pulmonary Syndrome—United States: Updated Recommendations for Risk Reduction," *Morbidity and Mortality Weekly Report* 51, no. RR-9 (26 July 2002): 1–12. Available at: Centers for Disease Control and Prevention, http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5109a1.htm (accessed 1 May 2005). This is the current scientific and public health consensus statement on avoiding hantavirus infection.
3. Gerard Hoddenbach, Jerry Johnson, and Carol Disalvo, "Rodent Exclusion Techniques: A Training Guide for National Park Service Employees," rev. ed. (Washington, DC: National Park Service, 2005). Available at: National Park Service, www.nps.gov/public_health/inter/info/general/NPS_RP_Manual_v2.pdf (accessed 1 May 2005). This is the definitive manual for mouse proofing, newly revised with updated links and appendices, including worksheets for evaluating structures, as well as case reports.
4. PubMed: The National Library of Medicine provides free public access to its online medical database, Medline. About four thousand medical journals are routinely indexed. Key search terms are: hantavirus, HPS, HCPS, Sin Nombre virus, SNV, Hantaan virus. Available at: NCBI, "PubMed," http://www.ncbi.nlm.nih.gov/entrez/query.fcgi (accessed 1 May 2005) or use a search engine to find "PubMed."

NOTES

1. Daniel Defoe, *Journal of the Plague Year* (London, 1722; repr. Project Gutenberg, 2001), par. 1. Available at: Project Gutenberg, "Welcome to Project Gutenberg," http://www.gutenberg.net/etext95/jplag.txt (accessed 4 June 2004). Defoe's most famous work is *Robinson Crusoe*. All subsequent quotations from Defoe are from this edition and will be referenced by paragraph in the text.

2. Thirteen/WNET New York, Educational Broadcasting Corporation, "Secrets of the Dead: Mystery of the Black Death," 2002. Available at: PBS, "Secrets of the Dead," http://www.pbs.org/wnet/secrets/case_plague/ (accessed 1 May 2005). BBC News Online, "Black Death and Plague 'Not Linked,'" 12 April 2002. Available at: BBC News, http://news.bbc .co.uk/1/hi/ health/1925513.stm (accessed 1 May 2005).

3. Richard P. Wenzel, "A New Hantavirus Infection in North America," *New England Journal of Medicine* 330 (1994): 1004–5.

4. Jeffrey S. Duchin et al. for the Hantavirus Study Group, "Hantavirus Pulmonary Syndrome: A Clinical Description of 17 Patients with a Newly Recognized Disease," *New England Journal of Medicine* 330 (1994): 949–55.

5. Ibid.

6. Ibid.

7. Wenzel, "A New Hantavirus Infection," 1005.

8. The Eurasian variant of the hantavirus was known before the virus was discovered in the New World. It is responsible for a disease identified as hemorrhagic fever with renal syndrome (HFRS). There are probably five hundred thousand cases of this disease each year, mostly in Asia, with a fatality rate ranging from 0.1 percent to 10 percent depending on the strain of the virus. Only an extremely rare variant is found in the Western Hemisphere. See Connie Schmaljohn and Brian Hjelle, "Hantaviruses: A Global Disease Problem," *Emerging Infectious Diseases* 3, no. 2 (April–June 1997): 95–104.

9. An anonymous reviewer of this article noted that Canyon del Muerto (just north of the Canyon de Chelly) was the scene of a Navajo massacre in the nineteenth century. Genetic analysis has determined that the Sin Nombre virus (SNV) is closely related to variants found throughout the Americas, more distantly to hantaviruses elsewhere. SNV was not brought to the Western Hemisphere by Europeans or by soldiers returning from Asia.

10. It has been suggested that the name of the disease be refined to hantavirus cardiopulmonary syndrome (HCPS) to better reflect its progression.

11. Centers for Disease Control and Prevention, US Department of Health and Human Services, "Case Information: Hantavirus Pulmonary Syndrome Case Count and Descriptive Statistics," 6 July 2004, http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/caseinfo.htm (accessed 1 May 2005). An additional thirty-three cases have been confirmed prior to January 1993.

12. US Census Bureau, "Resident Population by Race and State: 2000," *Statistical Abstract of the United States: 2002,* 222nd ed. (Washington, DC: US Census Bureau, 2003), Table 24.

13. The CDC reports that 19 percent of HPS cases (71) have been Native American, with 93 percent of cases reported in the West; see Centers for Disease Control and Prevention, US Department of Health and Human Services, "Case Information." But Native Americans account for only 1.76 percent of the population in the West (Arizona, California, Colorado, Idaho, Kansas, Montana, Nebraska, Nevada, New Mexico, North Dakota, Oklahoma, Oregon, South Dakota, Texas, Utah, Washington, and Wyoming). Thus, Indians are 11.37 times more likely to be victims of HPS than other western Americans (rounded to "ten times" in the text).

14. Jorge Ferrer et al., "High Prevalence of Hantavirus Infection in Indian Communities of the Paraguayan and Argentinean Gran Chaco," *American Journal of Tropical Medicine and Hygiene* 59, no. 3 (1998): 438–44.

15. CBS News, "Hantavirus Often Misdiagnosed," 30 October 2002. Available at: CBS News, "Hantavirus Often Misdiagnosed, http://www.cbsnews.com/stories/2002/10/30/eveningnews/main527537.shtml (accessed 1 May 2005). This CBS News report cited an unnamed federal health official who stated that HPS may kill more than one hundred people a year. Dr. Brian Hjelle, director of the Emerging Virus Research Center at the University of New Mexico, agreed: "It wouldn't surprise me to find that there were a hundred fatal cases a year that we're missing." At the observed fatality rate of 37 percent, this means that 270 cases go undetected annually, compared to the average thirty-two that have been confirmed.

16. "Review of 11 case-patients with well-defined and isolated exposure to rodents suggests that the incubation period of HPS is 9 to 33 days, with a median of 14–17 days"; quoted in Joni C. Young et al., "The Incubation Period of Hantavirus Pulmonary Syndrome," *American Journal of Tropical Medicine and Hygiene* 62, no. 6 (2000): 714–17.

17. L. E. Chapman et al. for the Ribavirin Study Group, "Intravenous Ribavirin for Hantavirus Pulmonary Syndrome: Safety and Tolerance During 1 Year of Open-Label Experience," *Antiviral Therapy* 4 (1999): 211–19; Chunyan Ye et al., "Neutralizing Antibodies and Sin Nombre Virus RNA after Recovery from Hantavirus Cardiopulmonary Syndrome," *Emerging Infectious Diseases* 10, no. 3 (March 2004): 478–82.

18. Duchin et al., "Hantavirus Pulmonary Syndrome," 954.

19. Sylvia Wrobel, "Serendipity, Science, and a New Hantavirus," *The FASEB Journal* 9 (October 1995); Sylvia Wrobel/Federation of American Societies for Experimental Biology (FASEB), "Serendipity, Science, and a New Hantavirus," http://www.faseb.org/opar/hanta.html (accessed 7 December 2003).

20. Douglas J. Passaro et al., "Predominant Kidney Involvement in a Fatal Case of Hantavirus Pulmonary Syndrome Caused by Sin Nombre Virus," *Clinical Infectious Diseases* 33 (2001): 263–64.

21. Robert Verity et al., "Hantavirus Pulmonary Syndrome in Northern Alberta, Canada: Clinical and Laboratory Findings for 19 Cases," *Clinical Infectious Diseases* 31 (2000): 942–46.

22. Rachel M. Wells et al., "Hantavirus Transmission in the United States," *Emerging Infectious Diseases* 3 (July–September 1997): 361–65.

23. Brian Hjelle and Gregory E. Glass, "Outbreak of Hantavirus Infection in the Four Corners Region of the United States in the Wake of the 1997–1998 El Niño Southern Oscillation," *The Journal of Infectious Diseases* 181 (2000): 1569–73.

24. Centers for Disease Control and Prevention, US Department of Health and Human Services, "Navajo Medical Traditions and HPS," 21 September 2000, http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/navajo.htm (accessed 7 December 2003).

25. Ibid.

26. Charles H. Calisher et al., "Natural History of Sin Nombre Virus in Western Colorado," *Emerging Infectious Diseases* 5 (January–February 1999): 132.

27. James N. Mills, "Statement on Hantavirus Exposure at National Parks. Before the House Committee on Resources, Subcommittee on National Parks and Public Lands, June 29, 1999," http://www.hhs.gov/asl/testify/t990629c.html (accessed 7 December 2003).

28. John D. Boone et al., "Infection Dynamics of Sin Nombre Virus after a Widespread Decline in Host Populations," *American Journal of Tropical Medicine and Hygiene* 67, no. 3 (2002): 314; Dale Netski, Brandolyn H. Thran, and Stephen C. St. Jeor, "Sin Nombre Virus Pathogenesis in *Peromyscus maniculatus," Journal of Virology* 73, no.1 (1999): 585–91.

29. David M. Engelthaler et al., "Climatic and Environmental Patterns Associated with Hantavirus Pulmonary Syndrome, Four Corners Region, United States*," Emerging Infectious Diseases* 5, no. 1 (January–February 1999): 87–94.

30. Calisher et al., "Natural History of Sin Nombre Virus."

31. Michele Jay et al., "Seroepidemiologic Studies of Hantavirus Infection Among Wild Rodents in California," *Emerging Infectious Diseases* 3, no. 2 (April–June 1997): 183–90.

32. Maureen Finnerty, "Statement of Maureen Finnerty, Associate Director, Park Operations and Education, National Park Service. Before the House Subcommittee on National Parks and Public Lands, Committee on Resources, Regarding the Presence of Hantavirus at Channel Islands National Park, June 29, 1999," http://resourcescommittee.house.gov/archives/106cong/parks/99jun29/finnerty.htm (accessed 1 May 2005).

33. Dr. Brian Hjelle of the Emerging Virus Research Center at the University of New Mexico estimates that 80 to 90 percent of Native American cases have occurred

in the Four Corners, an estimate he considers authoritative but not precise due to inadequacies in the HPS case database (personal communication, 30 June 2004).

34. Richard J. Douglass et al., "Longitudinal Studies of Sin Nombre Virus in Deer Mouse–Dominated Ecosystems of Montana," *American Journal of Tropical Medicine and Hygiene* 65, no. 1 (2001): 33–41; Amy J. Kuenzi et al., "Antibody to Sin Nombre Virus in Rodents Associated with Peridomestic Habitats in West Central Montana," *American Journal of Tropical Medicine and Hygiene* 64, nos. 3–4 (2001): 137–46; Amy J. Kuenzi et al., "Sin Nombre Virus in Deer Mice Captured Inside Homes, Southwestern Montana," *Emerging Infectious Diseases* 6, no. 4 (July–August 2000): 386–88.

35. Douglass et al., "Longitudinal Studies," 34.

36. Verity et al., "Hantavirus Pulmonary Syndrome."

37. The endemic relative risk is greatest in Montana-Idaho with a relative risk of 2.7 compared to the Four Corners or California-Nevada (x^2=9.23, $p < .01$, df=2, two-tailed test). There have been twenty-seven cases reported in Washington, but just five in Oregon, a very unlikely statistical difference ($x^2 = 8.29$, $p < .01$, df=1, two-tailed test), suggesting that cases are being missed.

38. Hjelle, personal communication.

39. Indianz.com, "Blackfeet Reservation Woman Reported with Hantavirus," 4 May 2004, http://www.indianz.com/News/2004/001602.asp (accessed 1 May 2005).

40. According to Kuenzi et al., "Antibody to Sin Nombre Virus," 142: "Average prevalences of antibody to SNV over the course of the study were 21.6 % (SD = 11.86, n = 31) at Anaconda, 25.5% (SD = 13.4, n = 31) at Butte, and 20.9% (SD =16.8, n = 31) at Cascade." The *n* is the number of months during which rodents were captured in the study. The statistics are for all rodents captured, not just deer mice.

41. Trisha Miller/Montana Kaimin Online, "UM Student Recovering from Fight with Hantavirus," 1 February 2001, http://www.kaimin.org/Feb2001/2-1-01/news1_2-1-01.html (accessed 7 December 2003).

42. Mark C. Wolff et al., "A Case-Control Study of Risk Factors for *Haemophilus Influenza* Type disease in Navajo Children," *American Journal of Tropical Medicine and Hygiene* 60, no. 2 (1999): 263–66.

43. A. S. Hopkins et al., "Experimental Evaluation of Rodent Exclusion Methods to Reduce Hantavirus Transmission to Residents in a Native American Community in New Mexico," *Vector Borne Zoonotic Diseases* 2, no. 2 (Summer 2002): 61–68.

44. Ali H. Mokdad et al., "Actual Causes of Death in the United States, 2000," *JAMA* 291, no. 10 (10 March 2004): 1238–45.

45. A CBS News report quoted Dr. Brian Hjelle of the University of New Mexico: "Case clusters with hantavirus are very unusual so you can extrapolate from that there are probably quite a lot of individual cases where someone dies and they're not diagnosed," said Hjelle. See CBS News, "Hantavirus."

46. Liza M. Gonzalez et al., "Prevalence of Antibodies to Sin Nombre Virus in Humans Living in Rural Areas of Southern New Mexico and Western Texas," *Virus Research* 74 (2001): 177–79.

47. P. S. Zeitz, "Assessment of Occupational Risk for Hantavirus Infection in Arizona and New Mexico," *Journal of Occupational and Environmental Medicine* 39 (May 1997): 463–67.

48. Netski et al., "Sin Nombre Virus Pathogenesis," 590. This observation is confirmed by Boone et al., "Infection Dynamics of Sin Nombre Virus." Douglass et al.,

"Longitudinal Studies," found that infected juvenile mice are less likely to survive, the first study to document a detrimental effect of the virus on mice.

49. Centers for Disease Control and Prevention, US Department of Health and Human Services, "Who Is at Risk of Getting HPS, and Why?" http://www.cdc.gov/ncidod/diseases/hanta/hps/noframes/at_risk.htm (accessed 1 May 2005). Medical consensus is the *opinion* of experts based on their knowledge of a disease. It is not necessarily a statement of scientific fact. Medicine is charged with taking action despite incomplete knowledge.

50. Hjelle, personal communication.

51. See, for example, Ian Burton, Robert W. Kates, and Gilbert F. White, *The Environment as Hazard* (New York: Oxford University Press, 1978), and Mary Douglas, *Risk Acceptability According to the Social Sciences* (New York: Russell Sage Foundation, 1985).

52. Ye et al., "Neutralizing Antibodies and Sin Nombre," and D. M. Custer et al., "Active and Passive Vaccination against Hantavirus Pulmonary Syndrome with Andes Virus M Genome Segment-Based DNA Vaccine," *Journal of Virology* 77, no. 18 (September 2003): 9894–905.

53. Leslie Linthicum, "$2.1 Million Awarded in Hantavirus Misdiagnosis," *Albuquerque Journal*, 13 June 2001.

54. The American Indian Housing Initiative is supported by several Penn State partners, including the Schreyer Honors College, Alumni Association, Rock Ethics Institute, Hamer Center for Community Design Assistance, Kellogg Leadership for Institutional Change Initiative, and College of Engineering's Leonhard Center for the Enhancement of Engineering Education. The Red Feather Development Group, a national nonprofit housing and community development organization, serves as the liaison between Penn State and the American Indians. Amy Milgrub Marshall, "Students, Faculty Join Forces to Improve Living Conditions for American Indians," *Penn State Outreach Magazine*, 4, no. 3 (2002). Available at: http://www.outreach.psu.edu/News/magazine/Vol_4.3/joinforces.html (accessed 20 April 2005).

55. See for example, Kelly Hart, "Green Home Building: Natural Building Techniques: Strawbale," 1 August 2003, http://www.greenhomebuilding.com/strawbale.htm (accessed 1 May 2005).

56. National American Indian Housing Council, "Indian Housing Data," 22 February 2002, http://naihc.indian.com/housingdata.htm (accessed 10 March 2004).

57. Montana Forum, "Second Hantavirus Case Reported in Glacier Co.," http://www.montanaforum.com/modules.php?op=modload&name=News&file=article&sid=33 (accessed 12 July 2004).