A 45-year-old woman was living with her husband in a 2-year-old home in a semirural area of the northeastern United States. On a Monday in mid-May, she went fishing and stuck herself with a fishhook; on the same day, she developed fever. Clinic physicians prescribed erythromycin because they were concerned about possible infection from the fishhook wound. On Tuesday, the patient developed body aches and chills, and went to a local medical clinic. On Thursday, she had severe coughing, vomiting, and diarrhea; so she went to the emergency room of the local hospital. She had developed breathing difficulty and was found by radiography to have bilateral pneumonia. Her oxygen saturation value was very low, and the physician diagnosed adult respiratory distress syndrome (ARDS). The patient was transferred to a regional hospital.

She was placed in isolation in an intensive care unit. Her oxygen saturation value was now 65%. She also was thrombocytopenic, with platelet count of 65,000 cells/µl, and she was experiencing abdominal pain. Her WBC count was 17,400 cells/µl, with 41% band neutrophils, and her hematocrit was high (50.2%). She also had profound lactic acidosis. Her clinical condition deteriorated rapidly, and she was placed on a ventilator almost immediately after arriving in intensive care. The patient died the following day.

The family had a cat and a dog that spent time inside and outside the home. One month prior to her illness, the patient had spent a week at a friend’s house in the suburban Los Angeles area. Two weeks prior to her illness, the patient and her friend were at the patient’s home and had spent a few mouse droppings out of the garage. After that, the patient went alone for a few days of hiking along the Appalachian Trail.

In their grief, the family was searching for clues as to what caused the woman’s death. In addition to questions directed at state and federal health and environment officials, the family asked the following questions of their private veterinarian.

Q: What is the official name of the disease she died of?
A: Hantavirus pulmonary syndrome (HPS).1,2

Q: Why have we never heard of this disease before?
A: Human cases of this disease appear to have occurred in the United States as early as 1959.3 However, HPS was not recognized as a distinct clinical entity until laboratory tests were developed to diagnose it after a focus of cases was found in the Southwest in 1993.4,6

Q: What is the cause of the disease?
A: The cause of HPS is infection with a virus from the genus Hantavirus, in the family Bunyaviridae. The strain of the virus found throughout most of the United States, and linked to most of the human cases, has been named Sin Nombre virus.7,8 Rodents are the principal reservoir for all hantaviruses, shedding virus from feces, urine, and saliva.9 People acquire infection most often by inhalation of the virus from aerosolized rodent excreta. The deer mouse (Peromyscus maniculatus) has been closely linked to most of the cases,10 especially in the West, with 1 case in Florida linked to the cotton rat (Sigmodon hispidus).8 1 case in New York linked to the white-footed mouse (Peromyscus leucopus),11 and cases in eastern Texas and Louisiana not yet linked to a rodent reservoir.12

Q: What did the virus do to cause the illness?
A: The main distinguishing feature of this syndrome is noncardiogenic pulmonary edema. Increased pulmonary vascular permeability appears to be the most likely explanation for the findings of pulmonary edema and pleural effusions. These pulmonary manifestations may be attributable to a direct cellular effect of viral infection, presence of viral antigen in pulmonary capillary endothelium, or a virus-induced, immune-mediated response.1,3,14

Q: How can the physicians be certain she had hantavirus?
A: A number of diagnostic tests are available from state laboratories and the federal Centers for Disease Control and Prevention.13,15,16 These include testing sera for IgM and IgG antibodies, finding hantavirus antigens in postmortem tissue samples by use of immunohistochemistry, and using reverse transcription and polymerase chain reaction to identify specific viral sequences from postmortem tissues.
Q: Were the signs and symptoms typical of the disease?
A: Yes. The most common early symptoms are fever and myalgia, with headache, cough, nausea, vomiting, chills, malaise, and diarrhea also quite common. The most common physical findings at hospital admission are increased respiratory rate (tachypnea), increased heart rate (tachycardia), and hypotension.\(^1\)\(^3\) Hantavirus patients frequently have platelet count lower than 150,000 cells/μL, oxygen saturation less than 90%, bilateral interstitial pulmonary infiltrates, development of ARDS within 1 week of hospital admission, high hematocrit, and leukocytosis with a high proportion of band neutrophils and atypical lymphocytes. Prolonged prothrombin and partial thromboplastin times, high serum lactate dehydrogenase activity, decreased serum protein concentration, and proteinuria also usually are present.

Q: Does the fact that she died mean that the physicians failed to treat her properly?
A: No. Because this is a viral infection, there are no specific drugs, such as antibiotics, that are effective for treatment. Certain antiviral agents, such as ribavirin, are under investigational use, but preliminary evidence from cases in the United States does not clearly indicate that it is effective.\(^1\)\(^3\) In east Asia, ribavirin appeared to have more effect in infections with different hantavirus strains where there was more renal involvement and duration of symptoms was more prolonged.\(^1\)\(^7\) Good supportive intensive care measures appear to be the most important treatment, with oxygen administered for hypoxemia, mechanical ventilation as necessary, and inotropic and vasopressor agents administered as needed and in conjunction with judicious use of fluids to maintain tissue perfusion.\(^1\)\(^3\) Even with use of such measures, the percentage of infected patients who die is greater than 50% on the basis of data obtained through November 1994.\(^3\)

Q: Could she have acquired the infection when she hurt herself with the fishhook?
A: No. The incubation period, the time between exposure to the virus and developing symptoms, appears to average 2 weeks or more.\(^1\)\(^3\) Thus, there was insufficient time between the cut with the fishhook and development of the symptoms for the fishing trip to have had a role in the infection. Also, there is no evidence that the virus enters the body through an open wound; rather, it appears to enter through the respiratory system, via inhalation.

Q: Could she have been infected by her pets, and should we get rid of them?
A: Results of studies in the United States to date do not appear to indicate that pets are a risk factor for acquiring infection.\(^1\)\(^8\) Studies of hantavirus in Great Britain indicated that cats occasionally develop antibodies to hantavirus and a higher percent age are chronically ill than is the general cat population.\(^1\)\(^9\) These illnesses could not be confirmed as being related to hantaviral infection. In a Korean study\(^2\)\(^0\) of the Hantaan virus, a related strain, cat ownership was statistically associated with human infection; however, households with heavy rodent infestations also were more likely to have cats to control the rodents. There is a report of Hantaan virus being isolated from 1 cat in China.\(^2\)\(^1\) In the United States, pets could have a role in human infection if they bring infected rodents into the household and human beings come in contact with them. However, pets may also have a role in disease control if they are killing rodents and thus, reducing the number of rodents having contact with people. There are no recommendations that people should get rid of their pets to avoid hantaviral infection, but steps should be taken to keep pets from bringing rodents indoors.

Q: Where do you think she most likely acquired the infection?
A: Given the time frame of her illness, the most likely exposure would be either aerosolization of rodent excreta when she swept out the garage or contact with rodent excreta during the hiking trip in the Appalachians. One case has recently been reported where exposure most likely occurred during hiking and camping.\(^1\) Exposure in California a month previous also is a possibility if her incubation period was slightly longer than the reported average, although cases there have occurred principally from exposures in more rural settings.\(^2\)\(^1\)\(^2\)\(^1\)\(^4\)

Q: Are her husband or neighbors at risk of coming down with this disease, from being around her when she was sick?
A: No. There is no evidence that the virus is transmissible from person to person, even in very close contact situations, such as ventilatory care or resuscitation in a hospital.\(^1\)\(^3\) However, if her exposure was from rodents in the home or neighborhood, relatives or neighbors could also become exposed through contact with rodent excrement.

Q: Should the family members or neighbors be tested for this disease?
A: No, not unless they develop similar symptoms. Testing so far appears to indicate that, unlike most diseases, asymptomatic or mild infections with Sin Nombre virus rarely, if ever, occur.\(^1\)\(^5\)\(^2\)\(^2\) Although such mild infections have not been documented for this strain, several people in the Southwest have tested seropositive. Further testing has not been done to ascribe positively to the Sin Nombre strain or to other strains known to have existed for years in the area. These other strains do not appear to cause disease in human beings. Without illness, the family members or neighbors can be reasonably assured they are not infected, and laboratory tests would find no evidence of infec-
tion. Thus, tests provide no useful information to asymptomatic members of the general public.

Q: Was there anything special about her that caused her to get this disease?
A: So far, no particular host factors or characteristics of patients appear to be associated with infection. Patients do not appear to necessarily have any previous medical problems; in fact, many of them are extremely healthy and physically fit prior to infection with and death from hantavirus. There has been a lack of very old and very young patients. The reason for this is not known; however, possible theories include a lower ventilatory rate in the old and young, and thus, less virus inhaled, or lower immune response, which leads to less immunologic reaction to the virus and less lung damage, or less exposure through activities such as cleaning up rodent debris, which would lead to infection.1,2,3,13,18

Q: We’ve seen a few dead rodents around her neighborhood. Shouldn’t someone be testing them and getting rid of them so they don’t spread this disease?
A: No. Hantavirus does not make rodents ill, and thus, could not be the cause of the rodent deaths. Testing throughout the United States is revealing evidence of hantaviral infection in a certain percentage of multiple rodent species,10,13 and so, testing of individual rodents in neighborhoods is not a useful way of ruling in or out infection in a neighborhood. Rather, the safest course of action is to assume that a certain percentage of rodents are hantavirus-positive and take appropriate precautions.

Q: How can people prevent this disease?
A: More details on prevention are available from local and state health departments.23 The most important prevention activity is to avoid contact with rodents and their excrement. Rodents should be prevented from coming into homes, barns, cottages, and garages. Rodent excrement and trapped dead rodents should first be sprayed with a disinfectant, allowed a certain amount of contact time for the disinfectant to kill the virus, then wiped or cleaned up and disposed of in double garbage bags. Depending on the situation, ventilation of the area before cleanup, along with protective equipment, such as clothing, eye protection, gloves, and possibly face masks, including high-efficiency particulate (HEPA) filters may be necessary.

References